Citation analysis of the most influential ependymoma research articles illustrates improved knowledge of the molecular biology of ependymoma

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Abstract
The history of academic research on ependymoma is expansive. This review summarizes its history with a bibliometric analysis of the 100 most cited articles on ependymoma. In March 2020, we queried the Web of Science database to identify the most cited articles on ependymoma using the terms “ependymoma” or “ependymal tumors,” yielding 3145 publications. Results were arranged by the number of times each article was cited in descending order. The top 100 articles spanned across nearly a century; the oldest article was published in 1924, while the most recent was in 2017. These articles were published in 35 unique journals, including a mix of basic science and clinical journals. The three institutions with the most papers in the top 100 were St. Jude Children’s Research Hospital (16%), the University of Texas MD Anderson Cancer Center (6%), and the German Cancer Research Center (5%). We analyzed the publications that may be considered the most influential in the understanding and treatment management of ependymoma. Studies focused on the molecular classification of ependymomas were well-represented among the most cited articles, reflecting the field’s current area of focus and its future directions. Additionally, this article also offers a reference for further studies in the ependymoma field.

Keywords  Ependymoma · Ependymal tumors · Citation analysis · Bibliometric analysis

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Introduction

Ependymomas are rare primary tumors of the central nervous system (CNS) that affect both children and adults [40, 42]. The 2016 World Health Organization (WHO) Classification of Tumors of the CNS categorizes them into four subtypes: subependymoma and myxopapillary ependymoma (grade I), ependymoma (grade II), ependymoma RELA (v-rel avian reticuloendotheliosis viral oncogene homolog A) fusion-positive (grade II or III), and anaplastic ependymoma (grade III) [12, 58]. Ependymomas are more commonly found in children and at this age more likely to be located intracranially and harbor more aggressive molecular variants, leading to worse overall survival (OS) when compared to adult variants [6, 14, 28, 30, 55].

Ependymomas have been extensively studied with respect to molecular subtyping, prognostication, and clinical outcomes [4, 8, 14, 30, 56, 58]. Therapy focuses on strategic surgical approaches to achieve gross total resection (GTR), and conformal radiation therapy (CRT) is the most common adjunctive treatment [6, 20, 21, 24, 38, 49]. Chemotherapy has been studied primarily in children under 3 years of age due to their susceptibility to radiotherapy-induced neurotoxicity. However, chemotherapy has failed to demonstrate improved outcomes compared to CRT [53]. At present, several clinical trials are underway scrutinizing promising neoadjuvant chemotherapeutic strategies [13, 32, 53]. Presently, effective treatment of ependymoma requires a multi-modal approach, involving an interdisciplinary team of neurosurgeons, neurologists, oncologists, radiologists, and primary care physicians, among others [14, 29]. Prognosis varies by type and location; pediatric ependymomas are more commonly intracranial with a 10-year estimated survival rate of 13–50%, while adult ependymomas have a predilection for the spine and have a 5-year survival rate of 67 to 85% and a 10-year survival rate of 72% [14, 30, 37]. In both populations, complete resection is the most consistent factor correlated with improved outcomes [6, 14, 37].

Given the diversity, volume, and interdisciplinary nature of ependymoma research, a bibliometric analysis focused on the history, recent developments, and trajectory of research can help frame our current understanding of the disease [3, 17]. The objective of this study is to analyze the most influential articles on ependymoma and identify the most relevant clinical problems in the field to guide further investigation. While bibliometric analyses have been published for neoplastic lesions of the brain [2, 3, 7, 17, 25] and for the spinal cord [1, 9, 10], no such investigation currently exists for ependymoma.

Methods

On March 22, 2020, we performed a title-specific search of the Thomson Reuters Web of Science (WoS) database (Thomson Reuters, NY, USA) to identify the most cited articles on ependymoma. We used “ependymoma” or “ependymal tumors” as our query term for the years 1900 to 2020 selecting the “all databases” option. The results were arranged according to the number of times each article was cited in descending order. To avoid the subjective exclusion of studies from our analysis, all papers from our query were included if they were ranked 1 to 100 in terms of number of total citations. The following variables were extracted: rank of article by total citations, rank of article by average citations per year, first and last author, title of article, publication, year, total citations for each article, average citations per year for each article, article country of origin, and institution of the first author. In cases of co-first authorship, country and institution of the author listed first were used [3, 7, 17, 31]. The average citations per year for each article was calculated as previously described [10].

We categorized the articles as either clinical, basic science, or literature review. Articles were independently classified by LRK and DH and reexamined by BVL and AP. Any inconsistencies were resolved by discussion with the senior author (IY) after careful review of full-text articles. Studies that were primarily focused on basic tumor biology or molecular classification of ependymoma were classified as basic science (e.g., involving genome sequencing) as described previously [25]. Studies that were patient-focused and reported outcomes were classified as clinical, which included histopathological studies [25].

Results

Our query yielded 3145 publications on ependymoma. The top 100 most cited articles were selected for review based on overall citation count and are shown in Tables 1 and 2, organized by total citations and average citations per year, respectively. These articles were published between 1924 and 2017. They have been cited a collective 11,640 times, averaging 116.4 citations per article (Table 1). The top 10 articles on the list were published between 1977 and 2015 and averaged 304 total citations (standard deviation [SD], 106.5; range, 206–551) (Table 1).

The most cited article overall was a basic science article entitled “Radial glia cells are candidate stem cells of ependymoma,” published in Cancer Cell in 2005 (Table 3) [51]. The second most cited article overall was a clinical article entitled “Intramedullary ependymoma of the spinal cord,” published in the Journal of Neurosurgery in 1990 (Table 4) [34]. Basic science and clinical articles comprised the majority of the top 50. The first review article ranked forty-second overall was titled “Pediatric
| Rank by total citations | Rank by average citations per year | Title                                                                 | Authors (first/last)             | Journal title | Publication year | Total citations | Average citations per year | Country | Type of study |
|-------------------------|-----------------------------------|----------------------------------------------------------------------|---------------------------------|---------------|-----------------|----------------|----------------------------|---------|--------------|
| 1                       | 3                                 | Radial glia cells are candidate stem cells of ependymoma             | Taylor MD, Gilbertson RJ        | Cancer Cell   | 2005            | 551            | 34.44                      | USA     | Basic science |
| 2                       | 8                                 | Intramedullary ependymoma of the spinal cord                         | McCormick PC, Stein BM          | Journal of Neurosurgery | 1990            | 453            | 14.61                      | USA     | Clinical     |
| 3                       | 1                                 | Molecular classification of ependymal tumors across all CNS compart-ments, histopathological grades, and age groups | Pajtler KW, Pfister SM           | Cancer Cell   | 2015            | 321            | 53.5                       | Germany | Basic science |
| 4                       | 33                                | Ependymoma: follow-up study of 101 cases                             | Mork SJ, Loken AC               | Cancer        | 1977            | 290            | 6.59                       | Norway  | Clinical     |
| 5                       | 2                                 | C11orf95-RELA fusions drive oncogenic Nf-kappa B signalling in ependymoma | Parker M, Gilbertson RJ          | Nature        | 2014            | 272            | 38.86                      | USA     | Basic science |
| 6                       | 6                                 | Conformal radiotherapy after surgery for paediatric ependymoma: a prospective study | Merchant TE, Sanford RA          | Lancet Oncology | 2009            | 258            | 21.5                       | USA     | Clinical     |
| 7                       | 4                                 | Delineation of two clinically and molecularly distinct subgroups of posterior fossa ependymoma | Witt H, Pfister SM               | Cancer Cell   | 2011            | 244            | 24.4                       | Germany | Basic science |
| 8                       | 38                                | Myxopapillary ependymoma: a clinicopathologic and immunocytochemical study of 77 cases | Sonneland PR, Onofrio BM         | Cancer        | 1985            | 226            | 6.28                       | USA     | Clinical     |
| 9                       | 7                                 | Cross-species genomics matches driver mutations and cell compartments to model ependymoma | Johnson RA, Gilbertson RJ        | Nature        | 2010            | 219            | 19.91                      | USA     | Basic science |

Table 1: Top 100 cited articles on ependymoma by citation number.
| Rank | Rank by average citations per year | Title                                                                 | Authors (first/last)                      | Journal title                      | Publication year | Total citations | Average citations per year | Country | Type of study |
|------|-----------------------------------|----------------------------------------------------------------------|------------------------------------------|-----------------------------------|------------------|-----------------|---------------------------|---------|---------------|
| 10   | 25                                | Natural simian-virus-40 strains are present in human choroid-plexus and ependymoma tumors | Lednicky JA, Butel JS                     | Virology                          | 1995             | 206             | 7.92                      | USA     | Basic science |
| 11   | 12                                | Preliminary results from a phase II trial of conformal radiation therapy and evaluation of radiation-induced CAS efficacy for patients with localized ependymoma | Merchant TE, Sanford RA                   | Journal of Clinical Oncology       | 2004             | 201             | 11.82                     | USA     | Clinical      |
| 12   | 40                                | The prognostic significance of postoperative residual tumor in ependymoma | Haley EA, Tanabe NJ                      | Neurosurgery                      | 1991             | 184             | 6.13                      | USA     | Clinical      |
| 13   | 21                                | Postoperative demography of ependymomas: implications for postoperative residual tumor in ependymoma | Grill J, Kallio C                         | Journal of Clinical Oncology       | 2001             | 173             | 8.65                      | France  | Clinical      |
| 14   | 14                                | Identification of tumor-specific molecular signatures in intracranial ependymoma and association with clinical characteristics | Modena P, Sozzi G                         | Journal of Clinical Oncology       | 2006             | 160             | 10.67                     | Italy   | Basic science |
| 15   | 15                                | Identification of gains on 1q and epidermal growth factor receptor expression in ependymoma as independent prognostic markers in intracranial ependymoma | Mendrzyk F, Lichter P                    | Clinical Cancer Research           | 2006             | 156             | 10.4                      | Germany | Basic science |
| Rank by total citations | Rank by average citations per year | Title                                                                 | Authors (first/last)                                                                 | Journal title                                      | Publication year | Total citations | Average citations per year | Country | Type of study |
|------------------------|-------------------------------------|-----------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------|-----------------|-----------------|---------------------------|---------|---------------|
| 16                     | 29                                  | Molecular genetic analysis of ependymal tumors: Nf2 mutations and chromosome 22q loss occur preferentially in intramedullary spinal ependymomas | Ebert C, Von Deimling A                                                              | American Journal of Pathology                      | 1999            | 154             | 7                         | USA     | Basic science |
| 17                     | 44                                  | Treatment of intracranial ependymomas of children: review of a 15-year experience | Rousseau P, Rey A                                                                   | International Journal of Radiation Oncology Biology Physics | 1994            | 154             | 5.7                       | France  | Clinical       |
| 18                     | 34                                  | Expression of vascular endothelial growth factor and its receptors in the anaplastic progression of astrocytoma, oligodendroglioma, and ependymoma | Chan AS, Chung LP                                                                   | American Journal of Surgical Pathology             | 1998            | 151             | 6.57                      | Hong Kong | Basic science |
| 19                     | 63                                  | Improved survival in cases of intracranial ependymoma after radiation-therapy: late report and recommendations | Salazar OM, Aygun C                                                                 | Journal of Neurosurgery                          | 1983            | 150             | 3.95                      | USA     | Clinical       |
| 20                     | 94                                  | A metastasizing ependymoma of the cauda equina                         | Weiss, L                                                                            | Cancer                                            | 1955            | 148             | 2.24                      | USA     | Clinical       |
| 21                     | 41                                  | Analyses of prognostic factors in a retrospective review of 92 children with ependymoma: Italian pediatric neuro-oncology group | Perilongo G, Madon E                                                                | Medical and Pediatric Oncology                     | 1997            | 144             | 6                         | Italy   | Clinical       |
| 22                     | 75                                  | Symptomatic subependymoma: report of 21 cases with review of literature | Scheithauer BW                                                                       | Journal of Neurosurgery                          | 1978            | 141             | 3.28                      | USA     | Clinical       |
| Rank by total citations | Rank by average citations per year | Title | Authors (first/last) | Journal title | Publication year | Total citations | Average citations per year | Country | Type of study |
|-------------------------|-----------------------------------|-------|----------------------|---------------|------------------|----------------|---------------------------|---------|--------------|
| 23                      | 16                                | Primary postoperative chemotherapy without radiotherapy for intracranial ependymoma in children: the UKCCSG/SIOP prospective study | Grundy RG, Machin D | Lancet Oncology | 2007 | 139 | 9.93 | UK | Clinical |
| 24                      | 74                                | Differential-diagnosis of chordoma, chondroid, and ependymal tumors as aided by anti-intermediate filament antibodies | Miettinen M, Virtanen I | American Journal of Pathology | 1983 | 129 | 3.39 | Finland | Clinical |
| 25                      | 57                                | Intracranial ependymoma: long-term results of a policy of surgery and radiotherapy | Vanuytsel LJ, Brada M | International Journal of Radiation Oncology Biology Physics | 1992 | 128 | 4.41 | UK | Clinical |
| 26                      | 32                                | Spinal cord ependymoma: radical surgical resection and outcome | Hanbali F, Gokaslan ZL | Neurosurgery | 2002 | 127 | 6.68 | USA | Clinical |
| 27                      | 17                                | Proton radiotherapy for childhood ependymoma: initial clinical outcomes and dose comparisons | Macdonald SM, Yock T | International Journal of Radiation Oncology Biology Physics | 2008 | 126 | 9.69 | USA | Clinical |
| 28                      | 47                                | Ependymoma: results, prognostic factors and treatment recommendations | Mclaughlin MP, Million RR | International Journal of Radiation Oncology Biology Physics | 1998 | 126 | 5.48 | USA | Clinical |
| 29                      | 69                                | Postoperative radiotherapy of intracranial ependymoma in pediatric and adult patients | Shaw EG, Earle JD | International Journal of Radiation Oncology Biology Physics | 1987 | 126 | 3.71 | USA | Clinical |
| 30                      | 11                                | Histopathological grading of pediatric ependymoma: reproducibility and clinical relevance in European trial cohorts | Ellison DW, Grundy RG | Journal of Negative Results in Biomedicine | 2011 | 123 | 12.3 | USA | Clinical |
| Rank by total citations | Rank by average citations per year | Title                                                                 | Authors (first/last)                                      | Journal title                                      | Publication year | Total citations | Average citations per year | Country | Type of study |
|------------------------|-----------------------------------|----------------------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------|------------------|------------------|---------------------------|---------|---------------|
| 31                     | 35                                | Erbb receptor signaling promotes ependymoma cell proliferation and represents a potential novel therapeutic target for this disease | Gilbertson RJ, Ellison DW                                   | Clinical Cancer Research                             | 2002             | 123              | 6.47                      | USA     | Basic science |
| 32                     | 26                                | Monomorphic angiocentric glioma: a distinctive epileptogenic neoplasm with features of infiltrating astrocytoma and ependymoma | Wang M, Burger PC                                           | Journal of Neuropathology and Experimental Neurology | 2005             | 121              | 7.56                      | USA     | Clinical      |
| 33                     | 46                                | A multi-institutional retrospective study of intracranial ependymoma in children: identification of risk factors | Horn B, Russo C                                             | Journal of Pediatric Hematology Oncology               | 1999             | 121              | 5.5                       | USA     | Clinical      |
| 34                     | 61                                | Identification of a germline mutation in the p53 gene in a patient with an intracranial ependymoma | Metzger AK, Cogen PH                                        | Proceedings of The National Academy of Sciences of the United States of America | 1991             | 120              | 4                         | USA     | Clinical      |
| 35                     | 13                                | Molecular staging of intracranial ependymoma in children and adults | Korshunov A, Pfister SM                                     | Journal of Clinical Oncology                          | 2010             | 119              | 10.82                     | Germany | Basic science |
| 36                     | 45                                | Combined postoperative irradiation and chemotherapy for anaplastic ependymomas in childhood: results of the German prospective trials hit 88/89 and hit 91 | Timmermann B, Bamberg M                                     | International Journal of Radiation Oncology Biology Physics | 2000             | 118              | 5.62                      | Germany | Clinical      |
| 37                     | 65                                | Histologic prognostic factors in ependymoma                         | Schiffer D, Tribolo A                                       | Childs Nervous System                                | 1991             | 116              | 3.87                      | Italy   | Clinical      |
| 38                     | 19                                | Incidence patterns for ependymoma: a surveillance, epidemiology, and end results study clinical article | Mcguire CS, Fisher PG                                        | Journal of Neurosurgery                                | 2009             | 112              | 9.33                      | USA     | Clinical      |
| Rank | Rank by total citations | Title | Authors (first/last) | Journal title | Publication year | Total citations | Average citations per year | Country | Type of study |
|------|-------------------------|-------|----------------------|---------------|-----------------|-----------------|---------------------------|---------|--------------|
| 39   | 59                      | Adjuvant chemotherapy of childhood posterior fossa ependymoma: cranio-spinal irradiation with or without adjuvant CCNU, vincristine, and prednisone: a children’s cancer group study | Evans AE, Finlay JL | Medical and Pediatric Oncology | 1996 | 106 | 4.24 | USA | Clinical |
| 40   | 73                      | Postoperative radiotherapy in the management of spinal cord ependymoma | Whitaker SJ, Brada M | Journal of Neurosurgery | 1991 | 105 | 3.5 | UK | Clinical |
| 41   | 82                      | Subcutaneous sacrococcygeal myxopapillary ependymoma: a clinicopathologic study of 32 cases | Helwig EB, Stern JB | American Journal of Clinical Pathology | 1984 | 102 | 2.76 | USA | Clinical |
| 42   | 22                      | Pediatric ependymoma: biological perspectives | Kilday JP, Grundy R | Molecular Cancer Research | 2009 | 101 | 8.42 | UK | Review |
| 43   | 93                      | Extra-spinal ependymomas: report of 3 cases | Morantz RA, Masterson BJ | Journal of Neurosurgery | 1979 | 99 | 2.36 | USA | Clinical |
| 44   | 51                      | Chromosomal abnormalities subdivide ependymal tumors into clinically relevant groups | Hirose Y, Feuerstein BG | American Journal of Pathology | 2001 | 98 | 4.9 | USA | Basic science |
| 45   | 60                      | Adjuvant chemotherapy for the treatment of intracranial ependymoma of childhood | Needle MN, Phillips PC | Cancer | 1997 | 97 | 4.04 | USA | Clinical |
| 46   | 27                      | A retrospective study of surgery and reirradiation for recurrent ependymoma | Merchant TE, Sanford RA | International Journal of Radiation Oncology Biology Physics | 2008 | 96 | 7.38 | USA | Clinical |
| 47   | 96                      | Secretory ependymoma of filum terminale | Miller CA, Tonack RA | Acta Neuropathologica | 1970 | 95 | 1.86 | USA | Clinical |
| Rank by total citations | Rank by average citations per year | Title | Authors (first/last) | Journal title | Publication year | Total citations | Average citations per year | Country | Type of study |
|------------------------|-----------------------------------|-------|----------------------|---------------|------------------|-----------------|--------------------------|---------|--------------|
| 48                     | 95                                | Delayed distant metastasis from a subcutaneous sacrococcygeal ependymoma: case report, with tissue-culture, ultrastructural observations and review of literature | Wolff M, Duby MM | Cancer | 1972 | 93 | 1.9 | USA | Review |
| 49                     | 36                                | Ependymoma | Reni M, Vecht C | Critical Reviews in Oncology Hematology | 2007 | 90 | 6.43 | Italy | Review |
| 50                     | 5                                 | The current consensus on the clinical management of intracranial ependymoma and its distinct molecular variants | Pajtler KW, Taylor MD | Acta Neuropathologica | 2017 | 89 | 22.25 | Germany | Review |
| 51                     | 97                                | Is subependymoma (subependymal glomerate astrocytoma) an astrocytoma or ependymoma: comparative ultrastructural and tissue-culture study | Fu YS, Young HF | Cancer | 1974 | 86 | 1.83 | USA | Clinical |
| 52                     | 71                                | Anaplastic ependymoma: treatment of pediatric patients with or without craniospinal radiation therapy | Merchant TE, Leibel SA | Journal of Neurosurgery | 1997 | 85 | 3.54 | USA | Clinical |
| 53                     | 87                                | Ependymal and choroid-plexus tumors: cytokeratin and GFAP expression | Mannoji H, Becker LE | Cancer | 1988 | 84 | 2.55 | Canada | Clinical |
| 54                     | 37                                | Predicting change in academic abilities after conformal radiation therapy for localized ependymoma | Conklin HM, Merchant TE | Journal of Clinical Oncology | 2008 | 83 | 6.38 | USA | Clinical |
| 55                     | 31                                | Both location and age predict survival in ependymoma: a seer study | Mcguire CS, Fisher PG | Pediatric Blood & Cancer | 2009 | 81 | 6.75 | USA | Clinical |
| Rank by total citations | Rank by average citations per year | Title                                                                 | Authors (first/last)                                                                 | Journal title                             | Publication year | Total citations | Average citations per year | Country   | Type of study |
|-------------------------|----------------------------------|----------------------------------------------------------------------|-------------------------------------------------------------------------------------|------------------------------------------|------------------|-----------------|---------------------------|-----------|---------------|
| 56                      | 72                               | Treatment of intracranial ependymoma by surgery alone                | Hukin J, Allen J                                                                    | Pediatric Neurosurgery                   | 1998             | 81              | 3.52                      | USA       | Clinical       |
| 57                      | 24                               | Identification of micro-RNAs as potential prognostic markers in ependymoma | Costa FF Soares MB                                                                 | Plos One                                 | 2011             | 80              | 8                         | USA       | Basic science  |
| 58                      | 39                               | Biological background of pediatric medullo-blastoma and ependymoma: a review from a translational research perspective | De Bont JM, Pieters R                                                               | Neuro-Oncology                           | 2008             | 80              | 6.15                      | Netherlands | Review         |
| 59                      | 48                               | Spinal myxopapillary ependymoma outcomes in patients treated with surgery and radiotherapy at MD Anderson Cancer Center | Akyurek S, Woo SY                                                                   | Journal of Neuro-Oncology                | 2006             | 80              | 5.33                      | USA       | Clinical       |
| 60                      | 84                               | Ependymoma: internal correlations among pathological signs: the anaplastic variant | Schiffer D, Vigliani MC                                                             | Neurosurgery                             | 1991             | 80              | 2.67                      | Italy      | Clinical       |
| 61                      | 99                               | Ependymoma of the brain: pathologic aspects                           | Svien HJ, Craig WM                                                                  | Neurology                                | 1953             | 80              | 1.18                      | USA       | Review         |
| 62                      | 85                               | The role of prophylactic spinal irradiation in localized intracranial ependymoma | Vanuytsel L, Brada M                                                                | International Journal of Radiation Oncology Biology Physics | 1991             | 79              | 2.63                      | UK        | Clinical       |
| 63                      | 20                               | A prognostic gene expression signature in infratentorial ependymoma  | Wani K, Aldape K                                                                     | Acta Neuropathologica                    | 2012             | 78              | 8.67                      | USA       | Basic science  |
| 64                      | 42                               | Multifactorial analysis of predictors of outcome in pediatric intracranial ependymoma | Ridley L, Grundy RG                                                                  | Neuro-Oncology                           | 2008             | 78              | 6                         | UK        | Clinical       |
| Rank by total citations | Rank by average citations per year | Title | Authors (first/last) | Journal title | Publication year | Total citations | Average citations per year | Country | Type of study |
|--------------------------|-----------------------------------|-------|---------------------|---------------|-----------------|----------------|---------------------------|---------|---------------|
| 65                       | 52                                | Radiation dosimetry predicts IQ after conformal radiation therapy in pediatric patients with localized ependymoma | Merchant TE, Mulhern RK | International Journal of Radiation Oncology Biology Physics | 2005 | 78 | 4.88 | USA | Clinical |
| 66                       | 53                                | Ependymoma: new therapeutic approaches including radiation and chemotherapy | Merchant TE, Fouladi M | Journal of Neuro-Oncology | 2005 | 78 | 4.88 | USA | Clinical |
| 67                       | 81                                | Intracranial ependymoma long-term outcome, patterns of failure | Kovalic JJ, Roth KA | Journal of Neuro-Oncology | 1993 | 78 | 2.79 | USA | Clinical |
| 68                       | 88                                | Intracranial ependymoma and subependymoma: MR manifestations | Spoto GP, Solomon M | American Journal of Neuroradiology | 1990 | 78 | 2.52 | USA | Clinical |
| 69                       | 18                                | Proton radiotherapy for pediatric central nervous system ependymoma: clinical outcomes for 70 patients | Macdonald SM, Yock TI | Neuro-Oncology | 2013 | 76 | 9.5 | USA | Clinical |
| 70                       | 50                                | Human telomere reverse transcriptase expression predicts progression and survival in pediatric intracranial ependymoma | Tabori U, Hawkins C | Journal of Clinical Oncology | 2006 | 76 | 5.07 | Canada | Clinical |
| 71                       | 100                               | A study of tumors arising from ependymal cells | Bailey P | Archives of Neurology And Psychiatry | 1924 | 75 | 0.77 | USA | Clinical |
| 72                       | 89                                | Intracranial ependymoma in children: analysis of prognostic factors | Chiu JK, Shallenberger R | Journal of Neuro-Oncology | 1992 | 73 | 2.52 | USA | Clinical |
| 73                       | 66                                | Ependymoma in childhood: prognostic factors, extent of surgery, and adjuvant therapy | van Veelen-Vincent, ML, Renier D | Journal of Neurosurgery | 2002 | 72 | 3.79 | Netherlands | Clinical |
| 74                       | 28                                | An integrated in vitro and in vivo high-throughput screen identifies treatment leads for ependymoma | Atkinson JM, Gilbertson RJ | Cancer Cell | 2011 | 71 | 7.1 | USA | Basic science |
| Rank by total citations | Rank by average citations per year | Title                                                                 | Authors (first/last)                           | Journal title                                                                 | Publication year | Total citations | Average citations per year | Country | Type of study |
|-------------------------|-----------------------------------|-----------------------------------------------------------------------|-----------------------------------------------|--------------------------------------------------------------------------------|------------------|------------------|---------------------------|---------|---------------|
| 75                      | 67                                | Influence of tumor grade on time to progression after irradiation for localized ependymoma in children | Merchant TE, Kun LE                           | International Journal of Radiation Oncology Biology Physics                    | 2002             | 71               | 3.74                      | USA     | Clinical       |
| 76                      | 68                                | Preliminary results from a phase II trial of conformal radiation therapy for pediatric patients with localized low-grade astrocytoma and ependymoma | Merchant TE, Kun LE                           | International Journal of Radiation Oncology Biology Physics                    | 2002             | 71               | 3.74                      | USA     | Clinical       |
| 77                      | 58                                | The high incidence of tumor dissemination in myxopapillary ependymoma in pediatric patients: report of five cases and review of the literature | Fassett DR, Kestle JRW                         | Journal of Neurosurgery                                                        | 2005             | 70               | 4.38                      | USA     | Clinical       |
| 78                      | 49                                | Differential expression and prognostic significance of sox genes in pediatric medulloblastoma and ependymoma identified by microarray analysis | De Bont JM, Pieters R                         | Neuro-Oncology                                                                  | 2008             | 69               | 5.31                      | Netherlands | Basic science |
| 79                      | 62                                | A multicenter study of the prognosis and treatment of adult brain ependymal tumors | Reni M, Villa E                               | Cancer                                                                         | 2004             | 68               | 4                         | Italy    | Clinical       |
| 80                      | 54                                | Ependymoma gene expression profiles associated with histological subtype, proliferation, and patient survival | Lukashova-Von Zangen I, Roggendorf W         | Acta Neuropathologica                                                           | 2007             | 66               | 4.71                      | Germany  | Basic science |
| 81                      | 64                                | Ki-67 immunolabeling index is an accurate predictor of outcome in patients with intracranial ependymoma | Wolfsberger S, Hainfellner J                   | American Journal of Surgical Pathology                                         | 2004             | 66               | 3.88                      | Austria  | Clinical       |
| Rank by total citations | Rank by average citations per year | Title                                                                                     | Authors (first/last)          | Journal title                       | Publication year | Total citations | Average citations per year | Country | Type of study |
|-------------------------|-----------------------------------|-------------------------------------------------------------------------------------------|-------------------------------|-------------------------------------|-----------------|-----------------|--------------------------|---------|---------------|
| 82                      | 9                                 | Clinical evidence of variable proton biological effectiveness in pediatric patients treated for ependymoma | Peeler CR, Grosshans DR       | Radiotherapy and Oncology          | 2016            | 65              | 13                       | USA     | Clinical       |
| 83                      | 10                                | Therapeutic impact of cytoreductive surgery and irradiation of posterior fossa ependymoma in the molecular era: a retrospective multi-cohort analysis | Ramaswamy V, Taylor MD        | Journal of Clinical Oncology       | 2016            | 65              | 13                       | Canada  | Clinical       |
| 84                      | 43                                | Primary postoperative chemotherapy without radiotherapy for treatment of brain tumours other than ependymoma in children under 3 years: results of the first UKCCSG/SIOP CNS 9204 trial | Grundy RG, Machin D           | European Journal of Cancer         | 2010            | 65              | 5.91                     | UK      | Clinical       |
| 85                      | 78                                | Chromosome arm 6q loss is the most common recurrent autosomal alteration detected in primary pediatric ependymoma | Reardon DA, Look AT           | Genes Chromosomes & Cancer         | 1999            | 65              | 2.95                     | USA     | Basic science  |
| 86                      | 90                                | MR characteristics of histopathologic subtypes of spinal ependymoma                        | Kahan H, Bruce JH             | American Journal of Neuroradiology | 1996            | 63              | 2.52                     | USA     | Clinical       |
| 87                      | 98                                | Melanin as a component of cerebral gliomas: melanotic cerebral ependymoma                  | Mccloskey JJ, Blacker HM      | Cancer                             | 1976            | 63              | 1.4                      | USA     | Clinical       |
| 88                      | 30                                | Survival benefit for pediatric patients with recurrent ependymoma treated with reirradiation | Bouffet E, Tabori U           | International Journal of Radiation Oncology Biology Physics | 2012            | 62              | 6.89                     | Canada  | Clinical       |
| Rank by total citations | Rank by average citations per year | Title | Authors (first/last) | Journal title | Publication year | Total citations | Average citations per year | Country | Type of study |
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| 89                      | 56                                | Outcome for young children newly diagnosed with ependymoma, treated with intensive induction chemotherapy followed by myeloablative chemotherapy and autologous stem cell rescue | Zacharoulis S, Finlay J | Pediatric Blood & Cancer | 2007 | 62 | 4.43 | USA | Clinical |
| 90                      | 70                                | Hyperfractionated radiotherapy and chemotherapy for childhood ependymoma: final results of the first prospective AIEOP (Associazione Italiana di Ematologia-Oncologia Pediatrica) study | Massimino M, Madon E | International Journal of Radiation Oncology Biology Physics | 2004 | 62 | 3.65 | Italy | Clinical |
| 91                      | 76                                | Postoperative radiotherapy for intracranial ependymoma: analysis of prognostic factors and patterns of failure | Oya N, Hiraoka M | Journal of Neuro-Oncology | 2002 | 62 | 3.26 | Japan | Clinical |
| 92                      | 92                                | A high-dose busulfan-thiotepa combination followed by autologous bone marrow transplantation in childhood recurrent ependymoma: a phase-II study | Grill J, Hartmann O | Pediatric Neurosurgery | 1996 | 61 | 2.44 | France | Clinical |
| 93                      | 83                                | Clinicopathologic study of 61 patients with ependymoma including MIB-1 immunohistochemistry | Prayson RA | Annals of Diagnostic Pathology | 1999 | 60 | 2.73 | USA | Clinical |
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| 94                     | 86                                | Survival following intensive chemotherapy with bone marrow reconstruction for children with recurrent intracranial ependymoma: a report of the children's cancer group | Mason WP, Finlay JL                  | Journal of Neuro-Oncology                                                     | 1998             | 60             | 2.61                     | USA     | Clinical       |
| 95                     | 55                                | Central nervous system tumors with ependymal features: a broadened spectrum of primarily ependymal differentiation? | Lehman NL                           | Journal of Neuropathology And Experimental Neurology                         | 2008             | 59             | 4.54                     | USA     | Review         |
| 96                     | 77                                | Astroblastoma: radiologic-pathologic correlation and distinction from ependymoma | Port JD, Pomper MG                   | American Journal of Neuroradiology                                          | 2002             | 59             | 3.11                     | USA     | Clinical       |
| 97                     | 79                                | Stereotactic radiosurgery for recurrent ependymoma                   | Stafford SL, Schomberg PJ            | Cancer                                                                        | 2000             | 59             | 2.81                     | USA     | Clinical       |
| 98                     | 80                                | Pediatric low-grade and ependymal spinal cord tumors                 | Merchant TE, Kun LE                  | Pediatric Neurosurgery                                                       | 2000             | 59             | 2.81                     | USA     | Clinical       |
| 99                     | 91                                | Tanyctic ependymoma                                                  | Langford LA, Barre GM, Ellison DW    | Ultrastructural Pathology and Applied Neurobiology                          | 1997             | 59             | 2.46                     | USA     | Clinical       |
| 100                    | 23                                | Clinical, radiological, histological and molecular characteristics of paediatric epithelioid glioblastoma | Langford LA, Barre GM, Ellison DW    | Neuropathology and Applied Neurobiology                                       | 2014             | 58             | 8.29                     | USA     | Clinical       |
| Rank by total citations | Rank by average citations per year | Title                                                                 | Authors (first and last)                      | Journal title       | Publication year | Total citations | Average citations per year | Country  | Type of study |
|-------------------------|------------------------------------|----------------------------------------------------------------------|----------------------------------------------|---------------------|-----------------|-----------------|--------------------------|----------|---------------|
| 3                       | 1                                  | Molecular classification of ependymal tumors across all CNS compart-ments, histopathological grades, and age groups | Pajtler KW, Pfister SM                          | Cancer Cell         | 2015            | 321             | 53.5                     | Germany  | Basic science |
| 5                       | 2                                  | C11orf95-RELA fusions drive oncogenic Nfkappa B signalling in ependymoma | Parker M, Gilbertson RJ                        | Nature              | 2014            | 272             | 38.86                    | USA      | Basic science |
| 1                       | 3                                  | Radial glia cells are candidate stem cells of ependymoma             | Taylor MD, Gilbertson RJ                       | Cancer Cell         | 2005            | 551             | 34.44                    | USA      | Basic science |
| 7                       | 4                                  | Delineation of two clinically and molecularly distinct subgroups of posterior fossa ependymoma | Witt H, Pfister SM                             | Cancer Cell         | 2011            | 244             | 24.4                     | Germany  | Basic science |
| 50                      | 5                                  | The current consensus on the clinical management of intracranial ependymoma and its distinct molecular variants | Pajtler KW, Taylor MD                           | Acta Neuropathologica | 2017            | 89              | 22.25                    | Germany  | Review        |
| 6                       | 6                                  | Conformal radiotherapy after surgery for paediatric ependymoma: a prospective study | Merchant TE, Sanford RA                         | Lancet Oncology     | 2009            | 258             | 21.5                     | USA      | Clinical       |
| 9                       | 7                                  | Cross-species genomics matches driver mutations and cell compartments to model ependymoma | Johnson RA, Gilbertson RJ                       | Nature              | 2010            | 219             | 19.91                    | USA      | Basic science |
| 2                       | 8                                  | Intramedullary ependymoma of the spinal cord                          | McCormick PC, Stein BM                         | Journal of Neurosurgery | 1990            | 453             | 14.61                    | USA      | Clinical       |
| 82                      | 9                                  | Clinical evidence of variable proton biological effectiveness in pediatric patients treated for ependymoma | Peeler CR, Grosshans DR                         | Radiotherapy and Oncology | 2016            | 65              | 13                       | USA      | Clinical       |
| Rank by total citations | Rank by average citations per year | Title                                                                 | Authors (first and last)                     | Journal title                          | Publication year | Total citations | Average citations per year | Country   | Type of study |
|-------------------------|-----------------------------------|----------------------------------------------------------------------|---------------------------------------------|----------------------------------------|------------------|------------------|-----------------------------|------------|---------------|
| 83                      | 10                                | Therapeutic impact of cytoreductive surgery and irradiation of posterior fossa ependymoma in the molecular era: a retrospective multicohort analysis | Ramaswamy V, Taylor MD                        | Journal of Clinical Oncology             | 2016             | 65               | 13                          | Canada     | Clinical       |
| 30                      | 11                                | Histopathological grading of pediatric ependymoma: reproducibility and clinical relevance in European trial cohorts | Ellison DW, Grundy RG                          | Journal of Negative Results in Biomedicine | 2011             | 123              | 12.3                        | USA        | Clinical       |
| 11                      | 12                                | Preliminary results from a phase II trial of conformal radiation therapy and evaluation of radiation-related CNS effects for pediatric patients with localized ependymoma | Merchant TE, Sanford RA                         | Journal of Clinical Oncology             | 2004             | 201              | 11.82                       | USA        | Clinical       |
| 35                      | 13                                | Molecular staging of intracranial ependymoma in children and adults | Korshunov A, Pfister SM                        | Journal of Clinical Oncology             | 2010             | 119              | 10.82                       | Germany    | Basic science   |
| 14                      | 14                                | Identification of tumor-specific molecular signatures in intracranial ependymoma and association with clinical characteristics | Modena P, Sozzi G                               | Journal of Clinical Oncology             | 2006             | 160              | 10.67                       | Italy      | Basic science   |
| 15                      | 15                                | Identification of gains on 1q and epidermal growth factor receptor overexpression as independent prognostic markers in intracranial ependymoma | Mendrzyk F, Lichter P                           | Clinical Cancer Research                  | 2006             | 156              | 10.4                        | Germany    | Basic science   |
| Rank by | Rank by average citations per year | Title                                                                 | Authors (first and last) | Journal title                                      | Publication year | Total citations | Average citations per year | Country | Type of study |
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| 23      | 16                                 | Primary postoperative chemotherapy without radiotherapy for intracranial ependymoma in children: the UKCCSG/SIOP prospective study | Grundy RG, Machin D      | Lancet Oncology                                   | 2007             | 139              | 9.93                        | UK      | Clinical      |
| 27      | 17                                 | Proton radiotherapy for childhood ependymoma: initial clinical outcomes and dose comparisons | Macdonald SM, Yock T     | International Journal of Radiation Oncology Biology Physics | 2008             | 126              | 9.69                        | USA     | Clinical      |
| 69      | 18                                 | Proton radiotherapy for pediatric central nervous system ependymoma: clinical outcomes for 70 patients | Macdonald SM, Yock TI    | Neuro-Oncology                                    | 2013             | 76               | 9.5                         | USA     | Clinical      |
| 38      | 19                                 | Incidence patterns for ependymoma: a surveillance, epidemiology, and end results study clinical article | McGuire CS, Fisher PG    | Journal of Neurosurgery                           | 2009             | 112              | 9.33                        | USA     | Clinical      |
| 63      | 20                                 | A prognostic gene expression signature in infratentorial ependymoma | Wani K, Aldape K         | Acta Neuropathologica                             | 2012             | 78               | 8.67                        | USA     | Basic science |
| 13      | 21                                 | Postoperative chemotherapy without irradiation for ependymoma in children under 5 years of age: a multicenter trial of the French society of pediatric oncology | Grill J, Kalifa C        | Journal of Clinical Oncology                      | 2001             | 173              | 8.65                        | France  | Clinical      |
| 42      | 22                                 | Pediatric ependymoma: biological perspectives                        | Kilday JP, Grundy R      | Molecular Cancer Research                        | 2009             | 101              | 8.42                        | UK      | Review        |
| 100     | 23                                 | Clinical, radiological, histological and molecular characteristics of paediatric epithelioid glioblastoma | Broniscer A, Ellison DW  | Neuropathology and Applied Neurobiology           | 2014             | 58               | 8.29                        | USA     | Clinical      |
| Rank by total citations | Rank by average citations per year | Title                                                                 | Authors (first and last)                                | Journal title                          | Publication year | Total citations | Average citations per year | Country | Type of study   |
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| 57                      | 24                                 | Identification of micro-RNAs as potential prognostic markers in ependymoma | Costa FF Soares MB                                     | Plos One                               | 2011             | 80              | 8                           | USA     | Basic science   |
| 10                      | 25                                 | Natural simian-virus-40 strains are present in human choroid-plexus and ependymoma tumors | Lednicky JA, Butel JS                                    | Virology                               | 1995             | 206             | 7.92                        | USA     | Basic science   |
| 32                      | 26                                 | Monomorphous angiocentric glioma: a distinctive epileptogenic neoplasm with features of infiltrating astrocytoma and ependymoma | Wang M, Burger PC                                       | Journal of Neuropathology and Experimental Neurology | 2005             | 121             | 7.56                        | USA     | Clinical        |
| 46                      | 27                                 | A retrospective study of surgery and reirradiation for recurrent ependymoma | Merchant TE, Sanford RA                                  | International Journal of Radiation Oncology Biology Physics | 2008             | 96              | 7.38                        | USA     | Clinical        |
| 74                      | 28                                 | An integrated in vitro and in vivo high-throughput screen identifies treatment leads for ependymoma | Atkinson JM, Gilbertson RJ                               | Cancer Cell                            | 2011             | 71              | 7.1                         | USA     | Basic science   |
| 16                      | 29                                 | Molecular genetic analysis of ependymal tumors: NF2 mutations and chromosome 22q loss occur preferentially in intramedullary spinal ependymomas | Ebert C, Von Deimling A                                  | American Journal of Pathology          | 1999             | 154             | 7                           | USA     | Basic science   |
| 88                      | 30                                 | Survival benefit for pediatric patients with recurrent ependymoma treated with reirradiation | Bouffet E, Tabori U                                     | International Journal of Radiation Oncology Biology Physics | 2012             | 62              | 6.89                        | Canada  | Clinical        |
| 55                      | 31                                 | Both location and age predict survival in ependymoma: a seer study | Mcguire CS, Fisher PG                                    | Pediatric Blood & Cancer                | 2009             | 81              | 6.75                        | USA     | Clinical        |
| Rank by total citations | Rank by average citations per year | Title                                                                 | Authors (first and last) | Journal title                        | Publication year | Total citations | Average citations per year | Country   | Type of study |
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| 26                      | 32                                 | Spinal cord ependymoma: radical surgical resection and outcome       | Hanbali F, Gokaslan ZL   | Neurosurgery                         | 2002             | 127            | 6.68          | USA                   | Clinical |
| 4                       | 33                                 | Ependymoma: follow-up-study of 101 cases                            | Mork SJ, Loken AC        | Cancer                               | 1977             | 290            | 6.59          | Norway                | Clinical |
| 18                      | 34                                 | Expression of vascular endothelial growth factor and its receptors in the anaplastic progression of astrocytoma, oligodendroglioma, and ependymoma | Chan AS, Chung LP        | American Journal of Surgical Pathology | 1998             | 151            | 6.57          | Hong Kong             | Basic science |
| 31                      | 35                                 | ErbB receptor signaling promotes ependymoma cell proliferation and represents a potential novel therapeutic target for this disease | Gilbertson RJ Ellison DW | Clinical Cancer Research             | 2002             | 123            | 6.47          | USA                   | Basic science |
| 49                      | 36                                 | Ependymoma                                                           | Reni M, Vecht C          | Critical Reviews in Oncology Hematology | 2007             | 90             | 6.43          | Italy                 | Review    |
| 54                      | 37                                 | Predicting change in academic abilities after conformal radiation therapy for localized ependymoma | Conklin HM, Merchant TE  | Journal of Clinical Oncology         | 2008             | 83             | 6.38          | USA                   | Clinical |
| 8                       | 38                                 | Myxopapillary ependymoma: a clinicopathologic and immunocytochemical study of 77 cases | Sonneland PR, Onofrio BM | Cancer                               | 1985             | 226            | 6.28          | USA                   | Clinical |
| 58                      | 39                                 | Biological background of pediatric medulloblastoma and ependymoma: a review from a translational research perspective | De Bont JM, Pieters R    | Neuro-Oncology                       | 2008             | 80             | 6.15          | Netherlands           | Review    |
| 12                      | 40                                 | The prognostic-significance of postoperative residual tumor in ependymoma | Healey EA, Tarbell NJ    | Neurosurgery                         | 1991             | 184            | 6.13          | USA                   | Clinical |
| Rank by total citations | Rank by average citations per year | Title                                                                 | Authors (first and last)                                                                 | Journal title                                      | Publication year | Total citations | Average citations per year | Country | Type of study |
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| 21                      | 41                                | Analyses of prognostic factors in a retrospective review of 92 children with ependymoma: Italian Pediatric Neuro-oncology Group | Perilongo G, Madon E                                                                   | Medical and Pediatric Oncology                      | 1997             | 144             | 6                       | Italy   | Clinical       |
| 64                      | 42                                | Multifactorial analysis of predictors of outcome in pediatric intracranial ependymoma | Ridley L, Grundy RG                                                                     | Neuro-Oncology                                     | 2008             | 78              | 6                       | UK      | Clinical       |
| 84                      | 43                                | Primary postoperative chemotherapy without radiotherapy for treatment of brain tumours other than ependymoma in children under 3 years: results of the first UKCCSG/SIOP CNS 9204 trial | Grundy RG, Machin D                                                                     | European Journal of Cancer                         | 2010             | 65              | 5.91                    | UK      | Clinical       |
| 17                      | 44                                | Treatment of intracranial ependymomas of children: review of a 15-year experience | Rousseau P, Rey A                                                                       | International Journal of Radiation Oncology Biology Physics | 1994             | 154             | 5.7                     | France  | Clinical       |
| 36                      | 45                                | Combined postoperative irradiation and chemotherapy for anaplastic ependymomas in childhood: results of the German prospective trials hit 88/89 and hit 91 | Timmermann B Bamberg M                                                                  | International Journal of Radiation Oncology Biology Physics | 2000             | 118             | 5.62                    | Germany | Clinical       |
| 33                      | 46                                | A multi-institutional retrospective study of intracranial ependymoma in children: identification of risk factors | Horn B, Russo C                                                                        | Journal of Pediatric Hematology Oncology           | 1999             | 121             | 5.5                     | USA     | Clinical       |
| 28                      | 47                                | Ependymoma: results, prognostic factors and treatment recommendations | Mclaughlin MP, Million RR                                                               | International Journal of Radiation Oncology Biology Physics | 1998             | 126             | 5.48                    | USA     | Clinical       |
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| 59                      | 48                                  | Spinal myxopapillary ependymoma outcomes in patients treated with surgery and radiotherapy at MD Anderson Cancer Center | Akyurek S, Woo SY | Journal of Neuro-Oncology | 2006 | 80 | 5.33 | USA | Clinical |
| 78                      | 49                                  | Differential expression and prognostic significance of sox genes in pediatric medulloblastoma and ependymoma identified by microarray analysis | De Bont JM, Pieters R | Neuro-Oncology | 2008 | 69 | 5.31 | Netherlands | Basic science |
| 70                      | 50                                  | Human telomere reverse transcriptase expression predicts progression and survival in pediatric intracranial ependymoma | Tabori U, Hawkins C | Journal of Clinical Oncology | 2006 | 76 | 5.07 | Canada | Clinical |
| 44                      | 51                                  | Chromosomal abnormalities subdivide ependymal tumors into clinically relevant groups | Hirose Y, Feuerstein BG | American Journal of Pathology | 2001 | 98 | 4.9 | USA | Basic science |
| 65                      | 52                                  | Radiation dosimetry predicts IQ after conformal radiation therapy in pediatric patients with localized ependymoma | Merchant TE, Mulhern RK | International Journal of Radiation Oncology Biology Physics | 2005 | 78 | 4.88 | USA | Clinical |
| 66                      | 53                                  | Ependymoma: new therapeutic approaches including radiation and chemotherapy | Merchant TE, Fouladi M | Journal of Neuro-Oncology | 2005 | 78 | 4.88 | USA | Clinical |
| 80                      | 54                                  | Ependymoma gene expression profiles associated with histological subtype, proliferation, and patient survival | Lukashova-Von Zangen I, Roggendorf W | Acta Neuropathologica | 2007 | 66 | 4.71 | Germany | Basic science |
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| 89                      | 56                                | Outcome for young children newly diagnosed with ependymoma, treated with intensive induction chemotherapy followed by myeloablative chemotherapy and autologous stem cell rescue | Zacharoulis S, Finlay J                                       | Pediatric Blood & Cancer                                   | 2007            | 62             | 4.43                      | USA     | Clinical       |
| 25                      | 57                                | Intracranial ependymoma: long-term results of a policy of surgery and radiotherapy | Vanuytsel LJ, Brada M                                         | International Journal of Radiation Oncology Biology Physics | 1992            | 128            | 4.41                      | UK      | Clinical       |
| 77                      | 58                                | The high incidence of tumor dissemination in myxopapillary ependymoma in pediatric patients: report of five cases and review of the literature | Fassett DR, Kestle JRW                                        | Journal of Neurosurgery                                    | 2005            | 70             | 4.38                      | USA     | Clinical       |
| 39                      | 59                                | Adjuvant chemotherapy of childhood posterior fossa ependymoma: cranio-spinal irradiation with or without adjuvant CCNU, vincristine, and prednisone: a children’s cancer group study | Evans AE, Finlay JL                                             | Medical and Pediatric Oncology                              | 1996            | 106            | 4.24                      | USA     | Clinical       |
| 45                      | 60                                | Adjuvant chemotherapy for the treatment of intracranial ependymoma of childhood | Needle MN, Phillips PC                                         | Cancer                                                   | 1997            | 97             | 4.04                      | USA     | Clinical       |
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| 34                      | 61                                | Identification of a germ-line mutation in the p53 gene in a patient with an intracranial ependymoma | Metzger AK, Cogen PH | Proceedings of The National Academy of Sciences of the United States of America | 1991            | 120             | 4                        | USA      | Clinical       |
| 79                      | 62                                | A multicenter study of the prognosis and treatment of adult brain ependymal tumors | Reni M, Villa E | Cancer | 2004            | 68              | 4                        | Italy    | Clinical       |
| 19                      | 63                                | Improved survival in cases of intracranial ependymoma after radiation-therapy: late report and recommendations | Salazar OM, Aygun C | Journal of Neurosurgery | 1983            | 150             | 3.95                    | USA      | Clinical       |
| 81                      | 64                                | Ki-67 immunolabeling index is an accurate predictor of outcome in patients with intracranial ependymoma | Wolfsberger S, Hainfellner J | American Journal of Surgical Pathology | 2004            | 66              | 3.88                    | Austria  | Clinical       |
| 37                      | 65                                | Histologic prognostic factors in ependymoma                           | Schiffer D, Tribolo A | Childs Nervous System | 1991            | 116             | 3.87                    | Italy    | Clinical       |
| 73                      | 66                                | Ependymoma in childhood: prognostic factors, extent of surgery, and adjuvant therapy | van Veelen-Vincent, ML, Renier D | Journal of Neurosurgery | 2002            | 72              | 3.79                    | Netherlands | Clinical       |
| 75                      | 67                                | Influence of tumor grade on time to progression after irradiation for localized ependymoma in children | Merchant TE, Kun LE | International Journal of Radiation Oncology Biology Physics | 2002            | 71              | 3.74                    | USA      | Clinical       |
| 76                      | 68                                | Preliminary results from a phase II trial of conformal radiation therapy for pediatric patients with localized low-grade astrocytoma and ependymoma | Merchant TE, Kun LE | International Journal of Radiation Oncology Biology Physics | 2002            | 71              | 3.74                    | USA      | Clinical       |
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| 29                      | 69                                | Postoperative radiotherapy of intracranial ependymoma in pediatric and adult patients | Shaw EG, Earle JD                                   | International Journal of Radiation Oncology Biology Physics                  | 1987            | 126             | 3.71                      | USA      | Clinical         |
| 90                      | 70                                | Hyperfractionated radiotherapy and chemotherapy for childhood ependymoma: final results of the first prospective AIEOP (Associazione Italiana di Ematologia-Onco-gia Pediatrica) study | Massimino M, Madon E                                   | International Journal of Radiation Oncology Biology Physics                  | 2004            | 62              | 3.65                      | Italy    | Clinical         |
| 52                      | 71                                | Anaplastic ependymoma: treatment of pediatric patients with or without craniospinal radiation therapy | Merchant TE, Leibel SA                                 | Journal of Neurosurgery                                                      | 1997            | 85              | 3.54                      | USA      | Clinical         |
| 56                      | 72                                | Treatment of intracranial ependymoma by surgery alone                | Hakin J, Allen J                                      | Pediatric Neurosurgery                                                       | 1998            | 81              | 3.52                      | USA      | Clinical         |
| 40                      | 73                                | Postoperative radiotherapy in the management of spinal-cord ependymoma | Whitaker SJ, Brada M                                   | Journal of Neurosurgery                                                      | 1991            | 105             | 3.5                       | UK       | Clinical         |
| 24                      | 74                                | Differential-diagnosis of chordoma, chondroid, and ependymal tumors as aided by anti-intermediate filament antibodies | Miettinen M, Virtanen I                                | American Journal of Pathology                                                | 1983            | 129             | 3.39                      | Finland  | Clinical         |
| 22                      | 75                                | Symptomatic subependymoma: report of 21 cases with review of literature | Scheithauer BW                                         | Journal of Neurosurgery                                                      | 1978            | 141             | 3.28                      | USA      | Clinical         |
| 91                      | 76                                | Postoperative radiotherapy for intracranial ependymoma: analysis of prognostic factors and patterns of failure | Oya N, Hiraoka M                                       | Journal of Neuro-Oncology                                                    | 2002            | 62              | 3.26                      | Japan    | Clinical         |
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| 85                      | 78                                 | Chromosome arm 6q loss is the most common recurrent autosomal alteration detected in primary pediatric ependymoma | Reardon DA, Look AT                                           | Genes Chromosomes & Cancer                              | 1999             | 65               | 2.95                      | USA     | Basic science   |
| 97                      | 79                                 | Stereotactic radiosurgery for recurrent ependymoma                   | Stafford SL, Schomberg PJ                                     | Cancer                                                 | 2000             | 59               | 2.81                      | USA     | Clinical       |
| 98                      | 80                                 | Pediatric low-grade and ependymal spinal cord tumors                 | Merchant TE, Kun LE                                           | Pediatric Neurosurgery                                 | 2000             | 59               | 2.81                      | USA     | Clinical       |
| 67                      | 81                                 | Intracranial ependymoma long-term outcome, patterns of failure       | Kovalic JJ, Roth KA                                           | Journal of Neuro-Oncology                              | 1993             | 78               | 2.79                      | USA     | Clinical       |
| 41                      | 82                                 | Subcutaneous sacrococcygeal myxopapillary ependymoma: a clinicopathologic study of 32 cases | Helwig EB, Stern JB                                           | American Journal of Clinical Pathology                  | 1984             | 102              | 2.76                      | USA     | Clinical       |
| 93                      | 83                                 | Clinicopathologic study of 61 patients with ependymoma including mib-1 immunohistochemistry | Prayson RA                                                   | Annals of Diagnostic Pathology                          | 1999             | 60               | 2.73                      | USA     | Clinical       |
| 60                      | 84                                 | Ependymoma: internal correlations among pathological signs: the anaplastic variant | Schiffer D, Vigliani MC                                       | Neurosurgery                                            | 1991             | 80               | 2.67                      | Italy   | Clinical       |
| 62                      | 85                                 | The role of prophylactic spinal irradiation in localized intracranial ependymoma | Vanuytsel L, Brada M                                         | International Journal of Radiation Oncology Biology Physics | 1991             | 79               | 2.63                      | UK      | Clinical       |
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| 94                      | 86                                 | Survival following intensive chemotherapy with bone marrow reconstitution for children with recurrent intracranial ependymoma: a report of the children's cancer group | Mason WP, Finlay JL | Journal of Neuro-Oncology | 1998 | 60 | 2.61 | USA | Clinical |
| 53                      | 87                                 | Ependymal and choroid-plexus tumors: cytokeratin and GFAP expression | Mannoji H, Becker LE | Cancer | 1988 | 84 | 2.55 | Canada | Clinical |
| 68                      | 88                                 | Intracranial ependymoma and subependymoma: MR manifestations | Spoto GP, Solomon M | American Journal of Neuroradiology | 1990 | 78 | 2.52 | USA | Clinical |
| 72                      | 89                                 | Intracranial ependymoma in children: analysis of prognostic factors | Chiu JK, Shallenberger R | Journal of Neuro-Oncology | 1992 | 73 | 2.52 | USA | Clinical |
| 86                      | 90                                 | MR characteristics of histopathologic subtypes of spinal ependymoma | Kahan H, Bruce JH | American Journal of Neuroradiology | 1996 | 63 | 2.52 | USA | Clinical |
| 99                      | 91                                 | Tanycytic ependymoma | Langford LA, Barre GM | Ultrastructural Pathology | 1997 | 59 | 2.46 | USA | Clinical |
| 92                      | 92                                 | A high-dose busulfan-thiotepa combination followed by autologous bone marrow transplantation in childhood recurrent ependymoma: a phase-II study | Grill J, Hartmann O | Pediatric Neurosurgery | 1996 | 61 | 2.44 | France | Clinical |
| 43                      | 93                                 | Extra-spinal ependymomas: report of 3 cases | Morantz RA, Masterson BJ | Journal of Neurosurgery | 1979 | 99 | 2.36 | USA | Clinical |
| 20                      | 94                                 | A metastasizing ependymoma of the cauda equina | Weiss, L | Cancer | 1955 | 148 | 2.24 | USA | Clinical |
| Rank by total citations | Rank by average citations per year | Title                                                                 | Authors (first and last)                                      | Journal title          | Publication year | Total citations | Average citations per year | Country | Type of study |
|------------------------|-----------------------------------|----------------------------------------------------------------------------|--------------------------------------------------------------|------------------------|------------------|------------------|---------------------------|---------|---------------|
| 48                     | 95                                | Delayed distant metastasis from a subcutaneous sacrococcygeal ependymoma: case report, with tissue-culture, ultrastructural observations and review of literature | Wolff M, Duby MM                                            | Cancer                 | 1972             | 93               | 1.9                        | USA     | Review        |
| 47                     | 96                                | Secretory ependymoma of filum terminale                                     | Miller CA Torack RA                                         | Acta Neuropathologica  | 1970             | 95               | 1.86                       | USA     | Clinical      |
| 51                     | 97                                | Is subependymoma (subependymal glomerate astrocytoma) an astrocytoma or ependymoma: comparative ultrastructural and tissue-culture study | Fu YS, Young HF                                              | Cancer                 | 1974             | 86               | 1.83                       | USA     | Clinical      |
| 87                     | 98                                | Melanin as a component of cerebral gliomas: melanotic cerebral ependymoma   | McCloskey JJ, Blacker HM                                     | Cancer                 | 1976             | 63               | 1.4                        | USA     | Clinical      |
| 61                     | 99                                | Ependymoma of the brain: pathologic aspects                                 | Svien HJ, Craig WM                                           | Neurology              | 1953             | 80               | 1.18                       | USA     | Review        |
| 71                     | 100                               | A study of tumors arising from ependymal cells                             | Bailey P                                                     | Archives of Neurology And Psychiatry | 1924             | 75               | 0.77                       | USA     | Clinical      |
Table 3 Most cited basic science articles on ependymoma

| Basic science rank (TC) | Overall rank (TC) | Overall rank (CY) | Title | Authors (first/last) | Journal title | Publication year | Total citations | Average citations per year | Country |
|------------------------|------------------|------------------|-------|----------------------|---------------|-----------------|-----------------|---------------------------|---------|
| 1                      | 1                | 3                | Radial glia cells are candidate stem cells of ependymoma | Taylor MD, Gilbertson RJ | Cancer Cell | 2005 | 551 | 34.44 | USA |
| 2                      | 3                | 1                | Molecular classification of ependymal tumors across all CNS compartments, histopathological grades, and age groups | Pajtler KW, Pfister SM | Cancer Cell | 2015 | 321 | 53.5 | Germany |
| 3                      | 5                | 2                | C11orf95-RELA fusions drive oncogenic NF-kappa B signalling in ependymoma | Parker M, Gilbertson RJ | Nature | 2014 | 272 | 38.86 | USA |
| 4                      | 7                | 4                | Delineation of two clinically and molecularly distinct subgroups of posterior fossa ependymoma | Witt H, Pfister SM | Cancer Cell | 2011 | 244 | 24.4 | Germany |
| 5                      | 9                | 7                | Cross-species genomics matches driver mutations and cell compartments to model ependymoma | Johnson RA, Gilbertson RJ | Nature | 2010 | 219 | 19.91 | USA |
| 6                      | 10               | 25               | Natural simian-virus-40 strains are present in human choroid-plexus and ependymoma tumors | Lednicky JA, Butel JS | Virology | 1995 | 206 | 7.92 | USA |
| 7                      | 14               | 14               | Identification of tumor-specific molecular signatures in intracranial ependymoma and association with clinical characteristics | Modena P, Sozzi G | Journal of Clinical Oncology | 2006 | 160 | 10.67 | Italy |
| 8                      | 15               | 15               | Identification of gains on 1q and epidermal growth factor receptor overexpression as independent prognostic markers in intracranial ependymoma | Mendrzyk F, Lichter P | Clinical Cancer Research | 2006 | 156 | 10.4 | Germany |
| 9                      | 16               | 29               | Molecular genetic analysis of ependymal tumors: Nf2 mutations and chromosome 22q loss occur preferentially in intramedullary spinal ependymomas | Ebert C, Von Deimling A | American Journal of Pathology | 1999 | 154 | 7 | USA |
| Basic science rank (TC) | Overall rank (TC) | Overall rank (CY) | Title                                                                 | Authors (first/last)                                                                 | Journal title                     | Publication year | Total citations | Average citations per year | Country  |
|------------------------|-------------------|-------------------|-----------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------------------|------------------|-----------------|--------------------------|----------|
| 10                     | 18                | 34                | Expression of vascular endothelial growth factor and its receptors in the anaplastic progression of astrocytoma, oligodendroglioma, and ependymoma | Chan AS, Chung LP                                                                    | American Journal of Surgical Pathology | 1998             | 151             | 6.57                     | Hong Kong |
| 11                     | 31                | 35                | Erbb receptor signaling promotes ependymoma cell proliferation and represents a potential novel therapeutic target for this disease | Gilbertson RJ Ellison DW                                                              | Clinical Cancer Research          | 2002             | 123             | 6.47                     | USA      |
| 12                     | 35                | 13                | Molecular staging of intracranial ependymoma in children and adults   | Korshunov A, Pfister SM                                                               | Journal of Clinical Oncology      | 2010             | 119             | 10.82                    | Germany  |
| 13                     | 44                | 51                | Chromosomal abnormalities subdivide ependymal tumors into clinically relevant groups | Hirose Y, Feuerstein BG                                                               | American Journal of Pathology     | 2001             | 98              | 4.9                      | USA      |
| 14                     | 57                | 24                | Identification of microRNAs as potential prognostic markers in ependymoma | Costa FF Soares MB                                                                    | Plos One                         | 2011             | 80              | 8                        | USA      |
| 15                     | 63                | 20                | A prognostic gene expression signature in infratentorial ependymoma    | Wani K, Aldape K                                                                      | Acta Neuropathologica            | 2012             | 78              | 8.67                     | USA      |
| 16                     | 74                | 28                | An integrated in vitro and in vivo high-throughput screen identifies treatment leads for ependymoma | Atkinson JM, Gilbertson RJ                                                             | Cancer Cell                      | 2011             | 71              | 7.1                      | USA      |
| 17                     | 78                | 49                | Differential expression and prognostic significance of sox genes in pediatric medulloblastoma and ependymoma identified by microarray analysis | De Bont JM, Pieters R                                                                 | Neuro-Oncology                    | 2008             | 69              | 5.31                     | Netherlands |
| 18                     | 80                | 54                | Ependymoma gene expression profiles associated with histological subtype, proliferation, and patient survival | Lukashova-Von Zangen I, Roggendorf W                                                 | Acta Neuropathologica            | 2007             | 66              | 4.71                     | Germany  |
ependymoma: biological perspectives” and was published in *Molecular Cancer Research* in 2009 (Table 1) [22].

As shown in Fig. 1, the time period from 2005 to 2009 oversaw the publication of the greatest number of articles on the list (24 papers). This was followed by 2000–2004 and 1995–1999 (16 papers each) (Fig. 1). Total citations (2870) and average citations per year (204) were also highest for papers published in 2005–2009 (Fig. 2).

**Journal of publication**

The top 100 cited articles on ependymoma were published in 35 unique journals. The most frequent journals featuring the top cited articles included *International Journal of Radiation Oncology Biology Physics* (13%), *Cancer* (10%), and *Journal of Neurosurgery* (9%) (Table 5). Of the top 10 most cited, 3 articles were published in *Cancer Cell*, followed by 2 articles each in *Nature* and *Cancer*.

**Countries and institutions**

A total of 13 countries represented the top 100 articles published (Fig. 3). The USA (n = 63), Germany (n = 8), and the UK (n = 7) were the highest contributors of the top 100 articles. The top institutions contributing the greatest number of articles among the top 100 most cited articles were St. Jude Children's Research Hospital (n = 16), the University of Texas MD Anderson Cancer Center (n = 6), and the German Cancer Research Center (n = 5) (Table 6). The USA contributed 5 of the top 10 most cited articles.

**Article category**

Each article was categorized as either basic science (19%), clinical (74%), or literature review (7%) (Table 1; Fig. 1). Studies are separated into basic science and clinical studies and ranked by times cited in Tables 3 and 4, respectively. Of the top 10 articles, 6 were basic science articles and 4 were clinical articles. Of the top 20, 10 were basic science articles, and 10 were clinical articles.

**Citations per year**

Since articles published more remotely are advantaged in terms of collecting citations over time, we examined the citation frequency per year. Using this metric, the article with the greatest number of citations per year (53.5) was a basic science article entitled “Molecular classification of ependymal tumors across all CNS compartments, histopathological grades, and age groups,” published in *Cancer Cell* in 2015 (Table 2) [42]. Comparatively, the clinical article with the most citations per year — “Conformal radiotherapy after surgery for pediatric ependymoma: a
| Clinical rank (TC) | Overall rank (TC) | Overall rank (CY) | Title | Authors (first/last) | Journal title | Publication year | Total citations | Average citations per year | Country |
|-------------------|-------------------|-------------------|-------|----------------------|---------------|------------------|-----------------|---------------------------|---------|
| 1                 | 2                 | 8                 | Intramedullary ependymoma of the spinal cord | McCormick PC, Stein BM | Journal of Neurosurgery | 1990 | 453 | 14.61 | USA |
| 2                 | 4                 | 33                | Ependymoma: follow-up-study of 101 cases | Mork SJ, Loken AC | Cancer | 1977 | 290 | 6.59 | Norway |
| 3                 | 6                 | 6                 | Conformal radiotherapy after surgery for paediatric ependymoma: a prospective study | Merchant TE, Sanford RA | Lancet Oncology | 2009 | 258 | 21.5 | USA |
| 4                 | 8                 | 38                | Myxopapillary ependymoma: a clinicopathologic and immunocytochemical study of 77 cases | Sonneland PR, Onofrio BM | Cancer | 1985 | 226 | 6.28 | USA |
| 5                 | 11                | 12                | Preliminary results from a phase II trial of conformal radiation therapy and evaluation of radiation-related CNS effects for pediatric patients with localized ependymoma | Merchant TE, Sanford RA | Journal of Clinical Oncology | 2004 | 201 | 11.82 | USA |
| 6                 | 12                | 40                | The prognostic significance of postoperative residual tumor in ependymoma | Healey EA, Tarbell NJ | Neurosurgery | 1991 | 184 | 6.13 | USA |
| 7                 | 13                | 21                | Postoperative chemotherapy without irradiation for ependymoma in children under 5 years of age: a multicenter trial of the French society of pediatric oncology | Grill J, Kalifa C | Journal of Clinical Oncology | 2001 | 173 | 8.65 | France |
| 8                 | 17                | 44                | Treatment of intracranial ependymomas of children: review of a 15-year experience | Rousseau P, Rey A | International Journal of Radiation Oncology Biology Physics | 1994 | 154 | 5.7 | France |
| 9                 | 19                | 63                | Improved survival in cases of intracranial ependymoma after radiation-therapy: late report and recommendations | Salazar OM, Aygun C | Journal of Neurosurgery | 1983 | 150 | 3.95 | USA |
| 10                | 20                | 94                | A metastasizing ependymoma of the cauda equina | Weiss, L | Cancer | 1955 | 148 | 2.24 | USA |
| Clinical rank (TC) | Overall rank (TC) | Overall rank (CY) | Title | Authors (first/last) | Journal title | Publication year | Total citations | Average citations per year | Country |
|-------------------|------------------|------------------|-------|---------------------|--------------|------------------|-----------------|--------------------------|---------|
| 11                | 21               | 41               | Analyses of prognostic factors in a retrospective review of 92 children with ependymoma: Italian Pediatric Neuro-oncology Group | Perilongo G, Madon E | Medical and Pediatric Oncology | 1997 | 144 | 6 | Italy |
| 12                | 22               | 75               | Symptomatic subependymoma: report of 21 cases with review of literature | Scheithauer BW | Journal of Neurosurgery | 1978 | 141 | 3.28 | USA |
| 13                | 23               | 16               | Primary postoperative chemotherapy without radiotherapy for intracranial ependymoma in children: the UKCCSG/ SIOP prospective study | Grundy RG, Machin D | Lancet Oncology | 2007 | 139 | 9.93 | UK |
| 14                | 24               | 74               | Differential-diagnosis of chordoma, chondroid, and ependymal tumors as aided by anti-intermediate filament antibodies | Miettinen M, Virtanen I | American Journal of Pathology | 1983 | 129 | 3.39 | Finland |
| 15                | 25               | 57               | Intracranial ependymoma: long-term results of a policy of surgery and radiotherapy | Vanuytsel LJ, Brada M | International Journal of Radiation Oncology Biology Physics | 1992 | 128 | 4.41 | UK |
| 16                | 26               | 32               | Spinal cord ependymoma: radical surgical resection and outcome | Hanbali F, Gokaslan ZL | Neurosurgery | 2002 | 127 | 6.68 | USA |
| 17                | 27               | 17               | Proton radiotherapy for childhood ependymoma: initial clinical outcomes and dose comparisons | Macdonald SM, Yock T | International Journal of Radiation Oncology Biology Physics | 2008 | 126 | 9.69 | USA |
| 18                | 28               | 47               | Ependymoma: results, prognostic factors and treatment recommendations | Mclaughlin MP, Million RR | International Journal of Radiation Oncology Biology Physics | 1998 | 126 | 5.48 | USA |
| 19                | 29               | 69               | Postoperative radiotherapy of intracranial ependymoma in pediatric and adult patients | Shaw EG, Earle JD | International Journal of Radiation Oncology Biology Physics | 1987 | 126 | 3.71 | USA |
| 20                | 30               | 11               | Histopathological grading of pediatric ependymoma: reproducibility and clinical relevance in European trial cohorts | Ellison DW, Grundy RG | Journal of Negative Results in Biomedicine | 2011 | 123 | 12.3 | USA |
| Clinical rank (TC) | Overall rank (TC) | Overall rank (CY) | Title | Authors (first/last) | Journal title | Publication year | Total citations | Average citations per year | Country |
|-------------------|------------------|------------------|-------|----------------------|---------------|-----------------|-----------------|--------------------------|---------|
| 21                | 32               | 26               | Monomorphous angiocentric glioma: a distinctive epileptogenic neoplasm with features of infiltrating astrocytoma and ependymoma | Wang M, Burger PC | Journal of Neuropathology and Experimental Neurology | 2005 | 121 | 7.56 | USA |
| 22                | 33               | 46               | A multi-institutional retrospective study of intracranial ependymoma in children: identification of risk factors | Horn B, Russo C | Journal of Pediatric Hematology Oncology | 1999 | 121 | 5.5 | USA |
| 23                | 34               | 61               | Identification of a germ-line mutation in the p53 gene in a patient with an intracranial ependymoma | Metzger AK, Cogen PH | Proceedings of The National Academy of Sciences of the United States of America | 1991 | 120 | 4 | USA |
| 24                | 36               | 45               | Combined postoperative irradiation and chemotherapy for anaplastic ependymomas in childhood: results of the German prospective trials hit 88/89 and hit 91 | Timmermann B Bamberg M | International Journal of Radiation Oncology Biology Physics | 2000 | 118 | 5.62 | Germany |
| 25                | 37               | 65               | Histologic prognostic factors in ependymoma | Schiffer D, Tribolo A | Childs Nervous System | 1991 | 116 | 3.87 | Italy |
| 26                | 38               | 19               | Incidence patterns for ependymoma: a surveillance, epidemiology, and end results study clinical article | Mcguire CS, Fisher PG | Journal of Neurosurgery | 2009 | 112 | 9.33 | USA |
| 27                | 39               | 59               | Adjuvant chemotherapy of childhood posterior fossa ependymoma: cranio-spinal irradiation with or without adjuvant CCNU, vincristine, and prednisone: a children’s cancer group study | Evans AE, Finlay JL | Medical and Pediatric Oncology | 1996 | 106 | 4.24 | USA |
| 28                | 40               | 73               | Postoperative radiotherapy in the management of spinal-cord ependymoma | Whitaker SJ, Brada M | Journal of Neurosurgery | 1991 | 105 | 3.5 | UK |
| 29                | 41               | 82               | Subcutaneous sacrococcygeal myxopapillary ependymoma: a clinicopathologic study of 32 cases | Helwig EB, Stern JB | American Journal of Clinical Pathology | 1984 | 102 | 2.76 | USA |
| Clinical rank (TC) | Overall rank (TC) | Overall rank (CY) | Title | Authors (first/last) | Journal title | Publication year | Total citations | Average citations per year | Country |
|-------------------|------------------|------------------|-------|----------------------|---------------|-----------------|-----------------|--------------------------|---------|
| 30                | 43               | 93               | Extra-spinal ependymomas: report of 3 cases | Morantz RA, Masterson BJ | Journal of Neurosurgery | 1979 | 99 | 2.36 | USA |
| 31                | 45               | 60               | Adjuvant chemotherapy for the treatment of intracranial ependymoma of childhood | Needle MN, Phillips PC | Cancer | 1997 | 97 | 4.04 | USA |
| 32                | 46               | 27               | A retrospective study of surgery and reirradiation for recurrent ependymoma | Merchant TE, Sanford RA | International Journal of Radiation Oncology Biology Physics | 2008 | 96 | 7.38 | USA |
| 33                | 47               | 96               | Secretory ependymoma of filum terminale | Miller CA Torack RA | Acta Neuropathologica | 1970 | 95 | 1.86 | USA |
| 34                | 51               | 97               | Is subependymoma (sub-ependymal glomerate astrocytoma) an astrocytoma or ependymoma: comparative ultrastructural and tissue-culture study | Fu YS, Young HF | Cancer | 1974 | 86 | 1.83 | USA |
| 35                | 52               | 71               | Anaplastic ependymoma: treatment of pediatric patients with or without craniospinal radiation therapy | Merchant TE, Leibel SA | Journal of Neurosurgery | 1997 | 85 | 3.54 | USA |
| 36                | 53               | 87               | Ependymal and choroid-plexus tumors: cytokeratin and GFAP expression | Mannoji H, Becker LE | Cancer | 1988 | 84 | 2.55 | Canada |
| 37                | 54               | 37               | Predicting change in academic abilities after conformal radiation therapy for localized ependymoma | Conklin HM, Merchant TE | Journal of Clinical Oncology | 2008 | 83 | 6.38 | USA |
| 38                | 55               | 31               | Both location and age predict survival in ependymoma: a seer study | Mcguire CS, Fisher PG | Pediatric Blood & Cancer | 2009 | 81 | 6.75 | USA |
| 39                | 56               | 72               | Treatment of intracranial ependymoma by surgery alone | Hukin J, Allen J | Pediatric Neurosurgery | 1998 | 81 | 3.52 | USA |
| 40                | 59               | 48               | Spinal myxopapillary ependymoma outcomes in patients treated with surgery and radiotherapy at MD Anderson Cancer Center | Akyurek S, Woo SY | Journal of Neuro-Oncology | 2006 | 80 | 5.33 | USA |
| Clinical rank (TC) | Overall rank (TC) | Title                                                                 | Authors (first/last) | Journal title                                      | Publication year | Total citations | Average citations per year | Country |
|-------------------|-------------------|----------------------------------------------------------------------|----------------------|---------------------------------------------------|------------------|------------------|---------------------------|---------|
| 41                | 60                | Ependymoma: internal correlations among pathological signs: the anaplastic variant | Schiffer D, Vigliani MC | Neurosurgery                                      | 1991             | 80               | 2.67                      | Italy   |
| 42                | 62                | The role of prophylactic spinal irradiation in localized intracranial ependymoma | Vanuytsel L, Brada M | International Journal of Radiation Oncology Biology Physics | 1991             | 79               | 2.63                      | UK      |
| 43                | 64                | Multifactorial analysis of predictors of outcome in pediatric intracranial ependymoma | Ridley L, Grundy RG | Neuro-Oncology                                    | 2008             | 78               | 6                         | UK      |
| 44                | 65                | Radiation dosimetry predicts IQ after conformal radiation therapy in pediatric patients with localized ependymoma | Merchant TE, Mulhern RK | International Journal of Radiation Oncology Biology Physics | 2005             | 78               | 4.88                      | USA     |
| 45                | 66                | Ependymoma: new therapeutic approaches including radiation and chemotherapy | Merchant TE, Fouladi M | Journal of Neuro-Oncology                          | 2005             | 78               | 4.88                      | USA     |
| 46                | 67                | Intracranial ependymoma long-term outcome, patterns of failure | Kovalic JJ, Roth KA | Journal of Neuro-Oncology                          | 1993             | 78               | 2.79                      | USA     |
| 47                | 68                | Intracranial ependymoma and subependymoma: MR manifestations | Spoto GP, Solomon M | American Journal of Neuroradiology                | 1990             | 78               | 2.52                      | USA     |
| 48                | 69                | Proton radiotherapy for pediatric central nervous system ependymoma: clinical outcomes for 70 patients | Macdonald SM, Yock TI | Neuro-Oncology                                    | 2013             | 76               | 9.5                       | USA     |
| 49                | 70                | Human telomere reverse transcriptase expression predicts progression and survival in pediatric intracranial ependymoma | Tabori U, Hawkins C | Journal of Clinical Oncology                       | 2006             | 76               | 5.07                      | Canada  |
| 50                | 71                | A study of tumors arising from ependymal cells | Bailey P | Archives of Neurology And Psychiatry               | 1924             | 75               | 0.77                      | USA     |
| 51                | 72                | Intracranial ependymoma in children: analysis of prognostic factors | Chiu JK, Shallenberger R | Journal of Neuro-Oncology                          | 1992             | 73               | 2.52                      | USA     |
| 52                | 73                | Ependymoma in childhood: prognostic factors, extent of surgery, and adjuvant therapy | van Veelen-Vincent, ML, Renier D | Journal of Neurosurgery                            | 2002             | 72               | 3.79                      | Netherlands |
| Clinical rank (TC) | Overall rank (TC) | Overall rank (CY) | Title | Authors (first/last) | Journal title | Publication year | Total citations | Average citations per year | Country |
|-------------------|------------------|------------------|-------|----------------------|---------------|-----------------|-----------------|----------------------------|---------|
| 53                | 75               | 67               | Influence of tumor grade on time to progression after irradiation for localized ependymoma in children | Merchant TE, Kun LE | International Journal of Radiation Oncology Biology Physics | 2002           | 71             | 3.74                      | USA     |
| 54                | 76               | 68               | Preliminary results from a phase II trial of conformal radiation therapy for pediatric patients with localized low-grade astrocytoma and ependymoma | Merchant TE, Kun LE | International Journal of Radiation Oncology Biology Physics | 2002           | 71             | 3.74                      | USA     |
| 55                | 77               | 58               | The high incidence of tumor dissemination in myxo-papillary ependymoma in pediatric patients: report of five cases and review of the literature | Fassett DR, Kestle JRW | Journal of Neurosurgery | 2005           | 70             | 4.38                      | USA     |
| 56                | 79               | 62               | A multicenter study of the prognosis and treatment of adult brain ependymal tumors | Reni M, Villa E | Cancer | 2004           | 68             | 4                         | Italy    |
| 57                | 81               | 64               | Ki-67 immunolabeling index is an accurate predictor of outcome in patients with intracranial ependymoma | Wolfsberger S, Hainfellner J | American Journal of Surgical Pathology | 2004           | 66             | 3.88                      | Austria |
| 58                | 82               | 9                | Clinical evidence of variable proton biological effectiveness in pediatric patients treated for ependymoma | Peeler CR, Grosshans DR | Radiotherapy and Oncology | 2016           | 65             | 13                        | USA     |
| 59                | 83               | 10               | Therapeutic impact of cytoreductive surgery and irradiation of posterior fossa ependymoma in the molecular era: a retrospective multicohort analysis | Ramaswamy V, Taylor MD | Journal of Clinical Oncology | 2016           | 65             | 13                        | Canada  |
| Clinical rank (TC) | Overall rank (TC) | Overall rank (CY) | Title | Authors (first/last) | Journal title | Publication year | Total citations | Average citations per year | Country |
|-------------------|------------------|------------------|-------|----------------------|---------------|-----------------|-----------------|--------------------------|---------|
| 60 84 43          |                  |                  | Primary postoperative chemotherapy without radiotherapy for treatment of brain tumours other than ependymoma in children under 3 years: results of the first UKCCSG/SIOP CNS 9204 trial | Grundy RG, Machin D | European Journal of Cancer | 2010 | 65 | 5.91 | UK |
| 61 86 90          |                  |                  | MR characteristics of histopathologic subtypes of spinal ependymoma | Kahan H, Bruce JH | American Journal of Neuroradiology | 1996 | 63 | 2.52 | USA |
| 62 87 98          |                  |                  | Melanin as a component of cerebral gliomas: melanotic cerebral ependymoma | Mccloskey JJ, Blacker HM | Cancer | 1976 | 63 | 1.4 | USA |
| 63 88 30          |                  |                  | Survival benefit for pediatric patients with recurrent ependymoma treated with reirradiation | Bouffet E, Tabori U | International Journal of Radiation Oncology Biology Physics | 2012 | 62 | 6.89 | Canada |
| 64 89 56          |                  |                  | Outcome for young children newly diagnosed with ependymoma, treated with intensive induction chemotherapy followed by myeloablative chemotherapy and autologous stem cell rescue | Zacharoulis S, Finlay J | Pediatric Blood & Cancer | 2007 | 62 | 4.43 | USA |
| 65 90 70          |                  |                  | Hyperfractionated radiotherapy and chemotherapy for childhood ependymoma: final results of the first prospective aieop (Associazione Italiana di Ematologia-Oncologia Pediatrica) study | Massimino M, Madon E | International Journal of Radiation Oncology Biology Physics | 2004 | 62 | 3.65 | Italy |
| 66 91 76          |                  |                  | Postoperative radiotherapy for intracranial ependymoma: analysis of prognostic factors and patterns of failure | Oya N, Hiraoka M | Journal of Neuro-Oncology | 2002 | 62 | 3.26 | Japan |
| Clinical rank (TC) | Overall rank (TC) | Overall rank (CY) | Title | Authors (first/last) | Journal title | Publication year | Total citations | Average citations per year | Country |
|--------------------|------------------|------------------|-------|---------------------|---------------|-----------------|-----------------|--------------------------|---------|
| 67                 | 92               | 92               | A high-dose busulfan-thiotepa combination followed by autologous bone marrow transplantation in childhood recurrent ependymoma: a phase-II study | Grill J, Hartmann O | Pediatric Neurosurgery | 1996 | 61 | 2.44 | France |
| 68                 | 93               | 83               | Clinicopathologic study of 61 patients with ependymoma including mib-1 immunohistochemistry | Prayson RA | Annals of Diagnostic Pathology | 1999 | 60 | 2.73 | USA |
| 69                 | 94               | 86               | Survival following intensive chemotherapy with bone marrow reconstitution for children with recurrent intracranial ependymoma: a report of the children’s cancer group | Mason WP, Finlay JL | Journal of Neuro-Oncology | 1998 | 60 | 2.61 | USA |
| 70                 | 96               | 77               | Astroblastoma: radiologic-pathologic correlation and distinction from ependymoma | Port JD, Pomper MG | American Journal of Neuroradiology | 2002 | 59 | 3.11 | USA |
| 71                 | 97               | 79               | Stereotactic radiosurgery for recurrent ependymoma | Stafford SL, Schomberg PJ | Cancer | 2000 | 59 | 2.81 | USA |
| 72                 | 98               | 80               | Pediatric low-grade and ependymal spinal cord tumors | Merchant TE, Kun LE | Pediatric Neurosurgery | 2000 | 59 | 2.81 | USA |
| 73                 | 99               | 91               | Tanycytic ependymoma | Langford LA, Barre GM | Ultrastructural Pathology | 1997 | 59 | 2.46 | USA |
| 74                 | 100              | 23               | Clinical, radiological, histological and molecular characteristics of paediatric epithelioid glioblastoma | Broniscer A, Ellison DW | Neuropathology and Applied Neurobiology | 2014 | 58 | 8.29 | USA |
prospective study,” published in *Lancet Oncology* in 2009 — averaged far fewer (21.5) (Table 2) [35].

**Authors**

The first and senior authors of each paper in the top 100 list were analyzed (Table 1). Thomas E. Merchant from St Jude Children’s Research Hospital authored the greatest number of articles (10), followed by Richard G. Grundy (5) from Children’s Brain Tumour Research Centre, University of Nottingham, and Richard J. Gilbertson (4) from St Jude Children’s Research Hospital (Fig. 4).

**Discussion**

This study identifies the most widely cited articles related to the understanding of ependymoma. Our bibliometric analysis revealed 100 articles published across 35 distinct journals, which highlighted a broad international interest
Table 5  Number of articles per journal

| Journals of publication                                      | Number of articles (n = 100) |
|-------------------------------------------------------------|------------------------------|
| International Journal of Radiation Oncology Biology Physics | 13                           |
| Cancer                                                      | 10                           |
| Journal of Neurosurgery                                     | 9                            |
| Journal of Clinical Oncology                                | 7                            |
| Journal Of Neuro-Oncology                                   | 6                            |
| Acta Neuropathologica                                       | 4                            |
| Cancer cell                                                 | 4                            |
| Neuro-Oncology                                             | 4                            |
| American Journal of Neuroradiology                         | 3                            |
| American Journal of Pathology                              | 3                            |
| Neurosurgery                                                | 3                            |
| Pediatric Neurosurgery                                      | 3                            |
| American Journal of Surgical Pathology                     | 2                            |
| Clinical Cancer Research                                    | 2                            |
| Journal of Neuropathology and Experimental Neurology        | 2                            |
| Lancet Oncology                                             | 2                            |
| Medical and Pediatric Oncology                              | 2                            |
| Nature                                                      | 2                            |
| Pediatric Blood & Cancer                                    | 2                            |
| Other *                                                     | 17                           |

*Journals with one article on the top 100 list

Fig. 3  Proportion of articles coming from each country of origin. The category “other” includes Japan, Austria, Hong Kong, Finland, and Norway, each of which had 1 article.
in ependymoma research. While a large majority of the top 100 cited articles were clinical (74%), basic science research (19%) comprised half of the top 20 most cited articles. This is likely the result of a recent focus on novel molecular classifications for the disease, as well as an effort to better understand the biochemical underpinnings of its development to guide therapeutic strategies. The large volume of literature focused on ependymoma research can pose a challenge for anyone searching for significant, impactful studies in the field [17]. Our hope is that this bibliometric analysis informs researchers in their efforts to understand the most relevant and significant literature relating to ependymoma.

It is important to note that while overall citation number is an important indicator of an article’s impact and importance, it can be misleading in older articles that have more time to be cited with each passing year. To account for this, our analysis included another important metric: citations per year (Table 2). As an example, the article ranked sixth overall on our list — “Conformal radiotherapy after surgery for pediatric ependymoma: a prospective study” published in *Lancet Oncology* in 2009 — also ranked sixth in citations per year [35]. This article reported a high rate of local tumor control and event-free survival following aggressive surgical intervention and adjuvant high-dose conformal radiotherapy in pediatric patients, including those younger than 3 years of age [35]. Its presence within the top 10 in both overall and average yearly citations indicates its continued relevance in our understanding of ependymoma, particularly for pediatric patients, despite having been published over ten years ago.

In bibliometric analyses, it is not uncommon to find several articles with drastically different positions on these two lists. Such articles tend to be highly impactful articles published very recently. Two such articles on our list worth examining in closer detail are studies by Peeler et al. and Ramaswamy et al. in 2016. Ranked 81st and 82nd overall and 9th and 10th in citations per year, respectively, these two studies provided novel insights into two well-established treatment modalities. Specifically, Peeler et al. discovered that proton therapy-induced damage to normal tissue dependent on the physical radiation dose and track-averaged linear energy transfer, one of the main determinants of proton therapy’s biological effectiveness [45]. Ramaswamy et al. reported that incomplete resection of molecular variant EPN_PFA (posterior fossa ependymoma A) ependymomas was associated with poor prognosis and that adjuvant radiation is preferred for patients with complete resections, while delayed external-beam radiation is preferred for relapsing cases of EPN_PFB (posterior fossa ependymoma B) tumors [46]. Both articles highlight critical discoveries in our understanding of current therapeutics for ependymoma, so it is unsurprising that they have each been given considerable attention since publication. Their place on the overall citation list is likely just a consequence of having less time to gather citations.

A closer examination of the top 20 articles in particular revealed a trend with respect to article type and publication year. Clinical articles within the top 20 tended to be published earlier (i.e., 1955 to 2009), while basic science

| Institution                                | Country | Number of articles |
|--------------------------------------------|---------|--------------------|
| St Jude Children’s Research Hospital       | USA     | 16                 |
| The University of Texas MD Anderson Cancer Center | USA   | 6                  |
| German Cancer Research Center               | Germany | 5                  |
| Hospital for Sick Children                  | Canada  | 4                  |
| Mayo Clinic                                | USA     | 4                  |
| Stanford University                        | USA     | 4                  |
| Royal Marsden Hospital                     | UK      | 3                  |
| University of Nottingham                   | UK      | 3                  |
| Children’s Hospital of Philadelphia         | USA     | 2                  |
| Institut Gustave Roussy                    | France  | 2                  |
| Istituto Nazionale Tumori                  | Italy   | 2                  |
| Memorial Sloan-Kettering Cancer Center      | USA     | 2                  |
| San Raffaele Scientific Institute          | Italy   | 2                  |
| Sophia Children’s Hospital                  | Netherlands | 2                |
| University of California, San Francisco     | USA     | 2                  |
| Washington University School of Medicine   | USA     | 2                  |
| University of Turin                        | Italy   | 2                  |
articles tended to be published later (i.e., 1995 to 2015). Logically, the basic science articles in the top 20 had higher average citations per year (21.4) than clinical articles (8.7). These clinical articles tended to focus on the initial clinical presentations and pathophysiologic prognosticators of the disease, much of which is considered common knowledge today. One such article, entitled “Ependymoma: follow-up study of 101 cases,” published in *Cancer* in 1977 (fourth most cited overall), managed to follow a cohort of patients who underwent ependymoma treatment over a considerable period of time (22 years) [37]. The authors reported favorable clinical outcomes in cases of spinal ependymoma, which more commonly affects adults (10-year survival of 72%), compared to intracranial ependymoma, which more commonly affects children (10-year survival of 13%) [37]. They also reported a survival benefit with postoperative radiation therapy but failed to find much prognostic value in tissue histopathology, an issue still under debate in current literature [27, 52, 57, 59]. Given the extensive follow-up reported by the authors as well as the relatively novel findings with respect to clinical course of ependymoma at the time of publication (1977), it is not surprising that this clinical article has maintained citation prevalence to date. The article entitled “Myxopapillary ependymoma: a clinicopathologic and immunocytochemical study of 77 cases,” published in *Cancer* in 1985 and eighth overall on our list, is another example of a clinical article that has maintained relevance despite its remote publication date [50]. This study focused on gross tumor characteristics as prognosticators for postoperative course, reporting that certain physical findings, such as the presence of a tumor capsule, were more indicative of prognosis than histological features [50]. Since
The top cited clinical studies on ependymoma are among the most often case series describing key clinical features, diagnostic modalities, different treatment regimens, and outcomes. One common theme among studies is that GTR is the single factor most consistently associated with improved survival and reduced recurrence compared to subtotal resection (STR) [15, 18, 35, 36, 47, 50]. There were no prospective randomized controlled trials in the top 100 most cited articles. The most cited clinical article (ranked second overall) — titled “Intramedullary ependymoma of the spinal cord,” was published in 1990 and described a retrospective series of 23 patients who underwent surgical resection of this entity [34]. All tumors were histologically benign, gross total resection was achieved in all cases, and no recurrences were reported. Other series reported outcomes in various treatment strategies combining surgical resection, radiation therapy, and chemotherapy. For instance, the 19th most cited study (by Salazar et al. published in the Journal of Neurosurgery in 1983) was one of the first studies to establish efficacy of adjunctive radiotherapy in ependymoma treatment [48]. The authors reported a 10-year overall survival of 69% in a series of patients with intracranial ependymoma treated with resection and whole-brain radiation therapy [48]. The progression from whole-brain radiation to localized radiation was demonstrated in a more recent prospective trial by Merchant et al. in 2009. These authors published a large series of 153 pediatric patients who underwent surgery and conformal radiation therapy (CRT) and reported 85% overall survival in patients who received CRT without delay [35]. In addition to their excellent outcomes, this study irradiated pediatric patients younger than 3 years old, which has been historically avoided due to concerns for delayed radiation neurotoxicity [16]. The role of adjunctive chemotherapy in ependymoma treatment was the topic of two prospective trials that were 13th [15] and 23rd [16] most cited studies overall. The 13th most cited study involved treatment of 73 children with primarily high-grade ependymoma with surgery and chemotherapy, without radiation [15]. The authors reported a low 4-year progression-free survival rate at 22% and overall survival rate of 59% [15]. The 23rd most cited study treated 89 children aged 3 years or younger with surgical resection and chemotherapy. Similarly, disease progression occurred in 62.5% of patients with non-metastatic disease, and overall survival at 5 years was 63.4% [16]. Notably, the authors did report that higher doses of chemotherapy were associated with improved 5-year overall survival compared to low doses (76% vs. 52%) [16]. Several clinical studies were lower in overall citations but higher in citations per year, suggesting that they are impactful articles published more recently. For instance, the study entitled —“Histopathological grading of pediatric ependymoma: reproducibility and clinical relevance in European trial cohorts,” published in 2011 was 30th in overall citations but 11th in citations per year [11]. This study developed a novel method for ependymoma grading that demonstrated higher concordance among pathologists than the traditional WHO grading method. However, the study found little correlation between ependymoma grade and clinical outcomes, calling into question the clinical utility of histological grading of ependymoma [11]. Two studies ranked 9th [45] and 17th [26] in average citations per year, utilized proton beam radiation for adjunctive ependymoma treatment. Peeler et al. created linear regression models correlating proton beam radiation dose and linear energy transfer with post-treatment changes on imaging. This demonstrated objective clinical changes caused by proton beam radiation, although did not report patient outcomes such as overall or progression-free survival [45]. On the other hand, MacDonald et al. reported excellent 2-year overall survival (89%) and progression-free survival (80%) in 17 pediatric patients treated with proton therapy after surgical resection. These studies together may represent a promising new adjunct to GTR in the treatment of ependymoma. Finally, as previously mentioned, one study ranked 83rd overall and 10th by citations per year addressed the effect of distinct molecular profiles of posterior fossa ependymoma on outcomes after surgery and radiation [46]. The authors report EPN_PFA was a highly significant predictor of poor progression-free survival (hazard ratio [HR], 2.14; 95% confidence interval [CI], 1.31 to 3.49, \( P < 0.002 \)) and overall survival (HR, 4.30; 95% CI, 1.88 to 9.87; \( P < 0.001 \)). Conversely, EPN_PFB was associated with excellent 10-year overall survival of 96.1% after GTR [46]. These findings in this recent article with a high citations per year count highlight the new appreciation of ependymoma molecular subtyping in treatment prognosis.

The WHO grading criteria for ependymoma based on tumor histopathology (most recently updated in 2016) have been shown to have poor predictive value for overall survival for the disease [27]. Given the limited clinical utility of these criteria, recent research has focused on understanding the molecular biology of ependymoma to improve on our current prognostic capabilities [27]. Six of the 10 most cited articles were basic science studies aimed at addressing the issue of ependymoma subtyping. The top article overall, entitled “Radial glia cells are candidate stem cells of ependymoma,” published in Cancer
Cell in 2005, found that supratentorial, infratentorial, and spinal cord ependymomas are derived from radial glial cells [51]. From this, the authors suggested that historically similar ependymomas from different regions of the central nervous system represent molecularly distinct diseases and that ependymomas have gene expression profiles that resemble regionally specific radial glial cells. More recently, the article entitled “C11orf95-RELA fusions drive oncogenic NF-kappa B signalling in ependymoma” published in Nature in 2015 elaborated upon the genetic underpinnings of a well-known oncogenic pathway (NF-κB; nuclear factor kappa-light-chain-enhancer of activated B cells), which was found to exist in two-thirds of supratentorial ependymomas [43]. Subsequently, a RELA fusion-positive (grade II or III) ependymoma subtype was included in the 2016 WHO Classification of Tumors of the CNS [12].

Another 2015 study focusing on ependymal classification — “Molecular classification of ependymal tumors across all CNS compartments, histopathological grades, and age groups” published in Cancer Cell — ranked third overall and first in citations per year [42]. This study used DNA methylation profiling to identify nine distinct molecular subgroups of ependymoma and subcategorized each according to its location within the CNS (supratentorial, posterior fossa, and spine) [42]. The novel predictive system developed by this study outperformed previously published histopathological classifications in predicting overall and progression-free survival. The DNA-methylation-specific categorization was not included in the 2016 WHO Classification of Tumors of the CNS likely because DNA methylation profiling is only available in restricted institutions [23] and is therefore not amenable to widespread implementation [41]. Collectively, the recent momentum favoring biomolecular research in ependymoma has led to a more robust classification system for the disease, which will allow for improved prognostication and narrowed molecular targeting for therapeutic development. Such advancements are imperative given the high (40%) prevalence of incurable tumors, poor postoperative prognosis, and chemotherapy-resistant properties of ependymomas [19, 43, 51]. Continued research will reveal the impact of these basic science investigations on the therapeutic and diagnostic landscape of these tumors.

Limitations

This study has several limitations. First, as previously discussed, our list of the top 100 most cited papers was generated based on the total number of citations, which is subject to bias towards papers published earlier [3, 10]. Conversely, more recently published articles are often shown more frequently in research databases, which may also contribute to bias. To address this issue, we included data on the total number of citations (Table 1) and average citations per year in our analysis (Table 2), in order to provide a comprehensive view of ependymoma research. This analysis also demonstrated that basic science articles have enjoyed more citations on average in the last 10 years than clinical articles. Taken in combination with overall citation data, these findings suggest that the current direction of ependymoma research will focus more heavily on research examining the biomolecular characteristics of ependymoma. Second, while WoS is the most commonly used and validated resource for bibliometric analyses, it is not comprehensive of all medical literature and does not include citations from textbooks or non-English journal articles [10, 17]. Our WoS search was also title-specific, which may have led to the unintentional exclusion of relevant papers in the top 100 list since abstracts and full-text articles were not included in the search. Third, bibliometric analyses carry the inherent limitation that the citation frequency does not always correlate with impact. For instance, a basic science article published in 2016 on childhood posterior fossa ependymomas published in Science Translational Medicine determined that reduced H3K27me3 and DNA hypomethylation were associated with poor clinical outcomes [5]. However, this impactful study did not make the top 100 list. Fourth, our list is subject to inaccuracy due to the phenomenon of “obliteration by incorporation,” whereby highly important articles can become less frequently cited over time as their ideas or findings become so widely accepted as to be considered common knowledge (and thus cited anonymously) [33]. As such, citation numbers may not always accurately reflect the influence or impact of studies, a limitation that is not completely addressed despite our using previously validated bibliometric analysis methodologies for CNS tumors [3, 17, 25]. Fifth, we categorized studies as basic science and clinical based on the focus of each article as previously performed [25]. However, this dichotomization did not account for studies that may be further subclassified as translational in nature. Despite these limitations, this article seeks to present publishing trends within the ependymoma literature and provides a categorized reference of articles and synthesis that will be helpful for future clinical trainees and scientists in the neuro-oncological and neurosurgical fields.

Conclusion

This study used a validated bibliometric analysis to identify the top 100 most cited articles on ependymoma. Careful examination of the list, in conjunction with another
important metric — average number of citations per year — helps paint a picture of the history and behavior of ependymoma research over the last 50 years, as its focus migrated from clinical correlates and histopathologic prognosticators to genetic and molecular underpinnings of the disease. That we observe a high proportion of recently published basic science articles in the top 20 papers of our list points to a tendency to improve upon what were once widely accepted histopathological grading criteria. Ependymomas are chemotherapy-resistant, and a large proportion of tumors are incurable even with surgery and radiotherapy. Our results suggest that the field of ependymoma research is moving towards a more robust basic biological understanding and molecular classification system to guide clinical decision-making and future research endeavors into potential therapeutic options.

**Author contribution** Nolan J. Brown composed the original draft, revised the draft, gathered data, and approved the final draft.

Bayard Wilson composed the original draft, revised the draft, gathered data, and approved the final draft.

Brian V. Lien composed the original draft, revised the draft, gathered data, and approved the final draft.

Alexander Himstead revised the draft, gathered data, and approved the final draft.

Ali R. Tafreshi revised the draft, gathered data, and approved the final draft.

Shane Shahrestani revised the draft, gathered data, and approved the final draft.

Jack Birkenbeuel revised the draft and approved the final draft.

Katelynn Tran revised the draft and is responsible for formatting and editing.

David Horton is responsible for data collection.

Anushka Paladugu is responsible for data collection.

Lydia R. Kirillova is responsible for data collection.

Chen Yi Yang revised the draft and is responsible for approval of the final draft.

Seth C. Ransom revised the draft and is responsible for approval of the final draft.

Alvin Y. Chan revised the draft and is responsible for approval of the final draft.

Ronald Sahyouni revised the draft and is responsible for approval of the final draft.

Isaac Yang is responsible for the original conception and approval of the final draft.

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