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Highly cited German research contributions to the fields of radiation oncology, biology, and physics: focus on collaboration and diversity

Background and purpose

Significant progress in the clinical practice of radiotherapy has been made during the last two decades. Both radiotherapy alone and multimodal treatment approaches have been gradually refined [1, 2, 3, 5]. Landmark phase III randomized trials provided the framework for these advances. In parallel, research into physical, technical, imaging, and biological aspects revealed new strategies that will impact on the next generation of potentially practice-changing studies. Research is performed in a large number of single institutions and/or by cooperative groups that compete for funding. Eventually, researchers attempt to publish their results in a way that ensures high visibility and allows for broad adaptation of the progress achieved. Successful publication is desirable for several reasons related to the investigators' career advancement or likelihood of future funding, and may be defined by various measures. The impact factor of journals is a two-edged sword, for example, regarding its correlation with the true scientific or practical impact of trials and the publication bias against negative or inconclusive studies [6, 7, 8, 9, 10]. Article download rates can provide some indication of visibility and impact, but they will depend on the presence and the amount of fees charged by the publisher. Another potential measure of quality and impact of research is the citation rate. Landmark or practice-changing research is likely to be cited by successor trials, editorials, review articles, meta-analyses, and guidelines. The number of highly cited research articles published by an individual or research group might better reflect their true contribution to the advancement of their field than the absolute number of published articles. This review of the most significant contributions of German authors to recent advances in radiotherapy, including related areas of biology and physics, therefore relied on citation rates of articles published between 1990 and 2010. Information about highly cited article types can be useful for preparation of future research projects. Moreover, identification of underrepresented areas might facilitate efforts to increase their visibility.

Methods

A systematic search of the abstract and citation database Scopus (Elsevier B.V., www.scopus.com) using the keywords "radiotherapy," "radiation," "brachytherapy," or"radiobiology" and"Germany" was performed on 11 and 12 November 2011. A second, confirmatory search was made by author name, using the author names in articles identified during the first keyword-based search and the membership directory of the German Society for Radiation Oncology, DEGRO. An arbitrary average citation rate of 15 citations per year was chosen (13 citations for January—October 2011). For example, articles published in 2010 were included if they were cited at least 28 times (43 times for those published in 2009 etc.). To account for a decreasing likelihood of citation over a very long time, the average citation rate was reduced to 10 per year 10 years after publication and 5 per year 15 years after publication. Therefore, the cut-off was 243 citations for articles published in 1990. This simplified approach was used because the aim of this study is to provide a general overview rather than an exact quantification, which might be used for ranking or other formal evaluation purposes. Thus, no statistical tests were performed. It has previously been shown that the actual time course of citation is hard to predict and varies, for example, according to the field of research and journal [11, 12]. Both accumulation of citations of recently published articles and reduced interest in older articles over time pose challenges if reliable quantitative analysis is attempted. With average citation rates of less than 15 per year as an arbitrary cut-off, the number of articles (and thus references to be cited) would increase very rapidly and make this overview both cumbersome for the readers and difficult to publish in a journal with significant competition for space.

Results

Overall, 106 publications were identified [13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37,

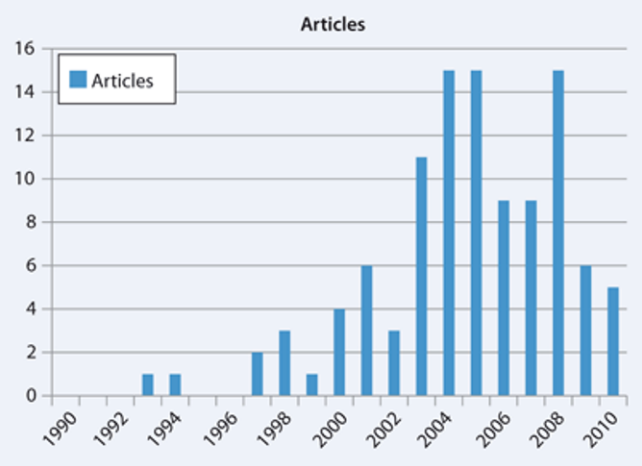

Fig. 1 ◀ Numbers of highly cited publications per year

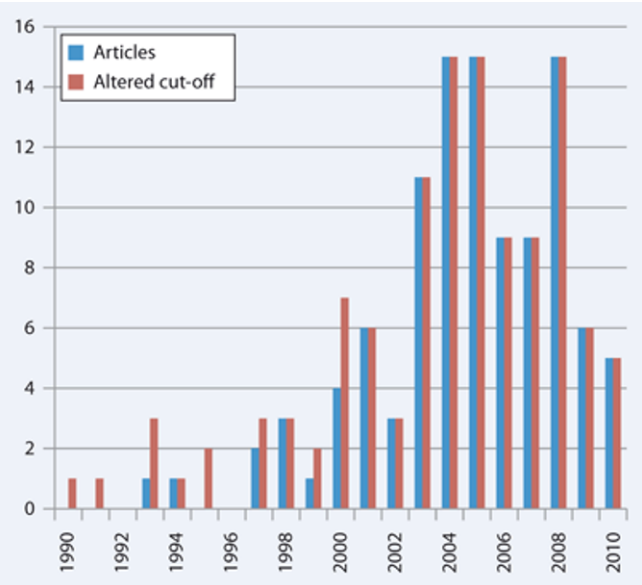

Fig. 2 ◀ Numbers of highly cited publications per year when a different cut-off for inclusion was chosen

38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118]. **Fig. 1** shows the numbers of publications per year, which are clearly higher after the year 2002. In order to explore whether this trend is artificial and caused by unrealistic high estimates of continued citation of older articles, the cut-off value was lowered. All articles published before the year 2003 that were cited at least 150 times were identified. However, only 11 additional articles were found [119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129]. As shown in **Fig. 1**, a lower cut-off did not change the impression of increasing numbers of citations during the last decade. Further results relate to the 106 originally selected publications. For these, the minimum number of citations per year was 15, the maximum 167, and the median 21 (average annual numbers). Further details are provided in **Tab. 1** and **Tab. 2**. Fifteen percent of all articles had ≥40 citations per year and 42% had between 20 and 39. All articles with ≥40 citations per year were published between 2003 and 2009, consistent with the assumption that the citation rate gradually increases for up to 2 years after publication. After several years with a large number of citations, annual rates for older articles clearly decline. The fact that none of the articles published between 2007 and 2010 was among the ten most cited publications (absolute number of citations) is also compatible with this kinetics of citation.

Stratified by article type, 17 publications (16%) reported on randomized phase III trials, three on meta-analyses of randomized trials (3%), 22 on non-phase III prospective clinical trials (21%), 15 on retrospective clinical studies (14%), four on treatment guidelines (4%), six on consensus meeting or expert panel reports (6%), 24 on biology studies (23%), five on physics (5%), and ten were review articles (9%). **Tab. 3** provides further information on research areas. Most citations per year were recorded for meta-analyses (median 47) and randomized phase III trials (median 30). The lowest figures were recorded for review articles (median 17), non-phase III prospective clinical trials (median 17), and retrospective clinical studies (median 18). Intermediate figures were recorded for consensus meeting or expert panel reports (median 26.5), treatment guidelines (median 25), biology studies (median 24), and physics (median 22) studies.

The articles were published in 44 scientific journals. Twenty-three articles (22%) were published in the *Journal of Clinical Oncology*, 11 (10%) in the *International Journal of Radiation Oncology, Biology, Physics*, 5 each (5%) in *the New England Journal of Medicine* and in *Cancer Research*, and four each (4%) in the *Lancet*, *Blood*, and *Radiotherapy and Oncology* (**Tab. 4**). The median number of citations per year was 46 for articles published in the *Lancet*, 32 for those published in the *New England Journal of Medicine*, 26 for those published in *Blood*, 23 each for those published in the *Journal of Clinical Oncology* and in *Radiotherapy and Oncology*, 19 for those published in *Cancer Research*, and 18 for those published in the *International Journal of Radiation Oncology, Biology, Physics*.

All 17 randomized phase III trials were performed in a multicenter setting (four international and 13 German multicenter studies). Only a minority of other clinical studies were performed in a collaborative group setting (four international and five German multicenter studies). All three meta-analyses were derived from research collaborations (two international and one German). Clinical studies (regardless of

clinical phase) dealt with head and neck cancer (n=8), rectal cancer (n=7), non-Hodgkin's lymphoma (n=5), lung cancer (n=4), esophageal cancer (n=4), Hodgkin's lymphoma (n=4), prostate cancer (n=2), primary brain tumors (n=2), and brain metastases, Ewing sarcoma, liver tumors, bladder cancer, breast cancer, and chordoma (one each).

Discussion

This overview is based on a systematic literature search where a broad definition of radiotherapy-, biology-, or physics-related publications and also author affiliation was applied. Some of the selected articles might be subject to debate. It should be kept in mind that not all completed research projects will be published [130]. It is also known that searches in different databases yield varying results. Because of controversy and concerns about the number of publications and the impact factor as valid measures of scientific impact [6, 8], and because the productivity of a researcher or institution was not relevant for this overview, citation rate was chosen. Articles with high numbers of citations are likely those that impressed other scientists and had profound influence on clinical practice or future developments in the field. In a study covering the *Lancet*, *JAMA*, and the *New England Journal of Medicine*, from October 1999 to March 2000, the authors found that the presence of industry funding and an industry-favoring result was associated with an increase in annual citation rates of 25.7 (95% confidence interval, 8.5–42.8) compared to the absence of both industry funding and industry-favoring results [131]. Higher annual rates of citation were also associated with articles dealing with cardiovascular medicine (13.3 more; 95% confidence interval, 3.9–22.3) and oncology (12.6 more; 95% confidence interval, 1.2–24.0), articles with group authorship (11.1 more; 95% confidence interval, 2.7–19.5), larger sample size, and the selected publication journal.

As stated in the"Methods" section, some arbitrary decisions had to be made regarding renunciation of statistical tests and number of required citations. Moreover, average annual citation rate was cho-

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Highly cited German research contributions to the fields of radiation oncology, biology, and physics: focus on collaboration and diversity

Abstract

Background and purpose. Tight budgets and increasing competition for research funding pose challenges for highly specialized medical disciplines such as radiation oncology. Therefore, a systematic review was performed of successfully completed research that had a high impact on clinical practice. These data might be helpful when preparing new projects.

Methods. Different measures of impact, visibility, and quality of published research are available, each with its own pros and cons. For this study, the article citation rate was chosen (minimum 15 citations per year on average). Highly cited German contributions to the fields of radiation oncology, biology, and physics (published between 1990 and 2010) were identified from the Scopus database.

Results. Between 1990 and 2010, 106 articles published in 44 scientific journals met the citation requirement. The median average of yearly citations was 21 (maximum 167, minimum 15). All articles with ≥40 citations per year were published between 2003 and 2009, consistent with the assumption that the citation rate gradually increases for up to 2 years after publication. Most citations per year were recorded for meta-analyses and randomized phase III trials, which typically were performed by collaborative groups.

Conclusion. A large variety of clinical radiotherapy, biology, and physics topics achieved high numbers of citations. However, areas such as quality of life and side effects, palliative radiotherapy, and radiotherapy for nonmalignant disorders were underrepresented. Efforts to increase their visibility might be warranted.

Keywords

Radiotherapy · Scientific publishing · Citation · Research evaluation · German research

Vielzitierte deutsche Forschungsbeiträge auf den Gebieten der Radioonkologie, -biologie und -physik: Fokus auf Zusammenarbeit und Vielfalt

Zusammenfassung

Hintergrund und Ziel. Begrenzte Budgets und zunehmender Wettbewerb um Forschungsmittel stellen eine Herausforderung für hochspezialisierte medizinische Disziplinen wie die Radioonkologie dar. Deshalb wurde eine systematische Analyse erfolgreich durchgeführter Projekte mit hohem Einfluss auf die klinische Praxis durchgeführt. Diese Daten können bei der Vorbereitung neuer Vorhaben hilfreich sein.

Methoden. Es existieren unterschiedliche Möglichkeiten zur Bewertung publizierter Forschung, die alle ihre Vor- und Nachteile haben. Für diese Studie wurde ausgewertet, wie oft Artikel von anderen Publikationen zitiert wurden (ein minimaler Durchschnitt von 15 Zitaten pro Jahr wurde gefordert). Oft zitierte deutsche Beiträge auf den Gebieten der Radioonkologie, -biologie und -physik, welche zwischen 1990 und 2010 publiziert wurden, wurden in der Datenbank Scopus identifiziert.

Ergebnisse. In diesem Zeitraum erreichten 106 Artikel, die in 44 verschiedenen wissenschaftlichen Zeitschriften erschienen, die geforderte Anzahl an Zitaten. Im Median betrug der Durchschnitt jährlicher Zitate 21 (15–167). Alle Artikel mit mindestens 40 Zitaten pro Jahr wurden zwischen 2003 und 2009 publiziert. Dies deutet darauf hin, dass die Rate an Zitaten innerhalb von 2 Jahren nach Publikation allmählich ansteigt. Die meistzitierten Artikel waren Metaanalysen und randomisierte Phase-III-Studien, die meist in multizentrischer Kooperation durchgeführt wurden.

Schlussfolgerung. Eine Vielzahl unterschiedlicher Themen auf den Gebieten der Radioonkologie, -biologie und -physik wurden in häufig zitierten Artikeln veröffentlicht. Allerdings waren die Themen Lebensqualität, Nebenwirkungen, palliative Strahlentherapie und Strahlentherapie nichtmaligner Erkrankungen unterrepräsentiert. Es sollten Anstrengungen unternommen werden, um diese Themen besser hervorzuheben.

Schlüsselwörter

Strahlentherapie · Wissenschaftliche Publikationen · Zitat · Forschungsevaluierung · Deutsche Forschungsbeiträge

Tab. 1 Articles with most citations (absolute count)

Authors and year of publication	Short title	Absolute citation count	Citations per year
Sauer et al., German Rectal Cancer Study Group [72]	Preoperative versus postoperative chemoradiotherapy for rectal cancer	1,319	167
Henke et al. [87]	Randomized erythropoietin study in head and neck cancer	748	84
Rothkamm and Löbrich [88]	Evidence for a lack of DNA double-strand break repair in human cells exposed to very low x-ray doses	552	62
Wendt et al. [112]	Randomized radiochemotherapy study in head and neck cancer	416	30
Haas et al. [117]	Mobilizing and autografting of peripheral blood progenitor cells in malignant lymphoma	411	23
Brizel et al. [107]	Randomized amifostine study in head and neck cancer	409	34
Rothkamm et al. [89]	Pathways of DNA double-strand break repair during the mammalian cell cycle	408	46
Stiff et al. [73]	ATM and DNA-PK function redundantly to phosphorylate H2AX after exposure to ionizing radiation	392	49
Diehl et al., German Hodgkin's Lymphoma Study Group. [90]	Standard and increased-dose BEACOPP compared with COPP-ABVD	361	40
American Society of Clinical Oncology et al. [48]	American Society of Clinical Oncology guideline for antiemetics in oncology: update 2006	360	61

Tab. 2 Articles with most citations per year

Authors and year of publication	Short title	Citations per year	Absolute citation count
Sauer et al., German Rectal Cancer Study Group [72]	Preoperative versus postoperative chemoradiotherapy for rectal cancer	167	1,319
Henke et al. [87]	Randomized erythropoietin study in head and neck cancer	84	748
Bennett et al. [24]	Venous thromboembolism and mortality associated with erythropoietin for cancer-associated anemia	65	254
Rothkamm and Löbrich [88]	Evidence for a lack of DNA double-strand break repair in human cells exposed to very low x-ray doses	62	552
American Society of Clinical Oncology, Kris et al. [48]	American Society of Clinical Oncology guideline for antiemetics in oncology: update 2006	61	360
Stiff et al. [73]	ATM and DNA-PK function redundantly to phosphorylate H2AX after exposure to ionizing radiation	49	392
Stahl et al. [57]	Chemoradiation with and without surgery in squamous cell carcinoma of the esophagus	49	339
Bohlius et al. [18]	Erythropoiesis-stimulating agents and mortality in patients with cancer (meta-analysis of randomized trials)	47	137
Rothkamm et al. [89]	Pathways of DNA double-strand break repair during the mammalian cell cycle	46	408
Goodarzi et al. [25]	ATM signaling facilitates repair of DNA double-strand breaks associated with heterochromatin	46	181
Pfreundschuh et al., German High-Grade Non-Hodgkin Lymphoma Study Group [26]	RICOVER-60 randomized trial	46	180

sen because the exact kinetics of citation varies according to the topic and journal [11, 12]. The analysis did not account for date of publication, i.e., whether an article was published earlier or later during a given year. For the purpose of this overview, the chosen methods are sufficient. Of course, more detailed and quantitative analyses can be performed with the Internet-based tools available. Self-citation could influence the final citation count of rather sparsely cited articles, whereas its impact on highly cited research might be less pronounced. It was recently estimated that 6.4% of all citations per article (interquartile range 2.8–11.3, mean 8.4) were self-citations [132]. Studies most vulnerable to this effect were those with more authors and small sample size.

The results are consistent with the assumption that the citation rate gradually increases for up to 2 years after publication. After several years with large numbers of citations, annual rates for older articles clearly decline. However, the purpose of this overview was not to explore the dynamics of citation count. A trend toward increasing numbers of highly cited publications after the year 2002 was seen. Given the fact that major scientific journals in the field had steady increases in the number of published issues and articles over the last few years and that each article contains a certain number of references, the increase in total number of publications over time is expected to lead

Tab. 3 Selected cancer types/research areas versus research type (number of publications)

Research area	Randomized trial	Nonrandomized prospective study	Retrospective study	Meta-analysis	Guideline, expert panel or consensus meeting report	Biology	Physics
Brain		3	2			1	
Head and neck	6	1	1	1	1		
Breast	1				2		
Lung		4	3		1		1
Esophagus	2		2				
Colorectal	1	5	2		1	1	
Prostate	1	1	2				
Germ cell					3		
Hodgkin's lym.	3	1					
Non-Hodgkin's lym.	3						
Particle RT		1	1				1
DNA repair						13	

RT radiotherapy; lym lymphoma

Tab. 4 List of scientific journals chosen for publication (minimum two articles)

Number of published articles	Percent	Journal name
23	22	*Journal of Clinical Oncology*
11	10	*International Journal of Radiation Oncology, Biology, Physics*
5	5	*New England Journal of Medicine; Cancer Research*
4	4	*Lancet; Blood; Radiotherapy and Oncology*
3	3	*Strahlentherapie und Onkologie; Molecular Cell*
2	2	*Annals of Oncology; Clinical Cancer Research; Journal of Clinical Investigation; Lancet Oncology; European Urology; Nature Reviews Cancer; Journal of Nuclear Medicine; Medical Physics; Oncogene*

to a parallel increase in citation rates. It is also interesting to note that highly cited research was published in a large number of different scientific journals with or without high impact factor (exclusively in the English language). As already noted in a study that was not limited to radiation oncology or oncology in general, meta-analyses received more citations than other study designs [133]. Comparable to the present results, randomized controlled trials were the second most cited study design. Another group of authors described that the number of times an article was cited correlated significantly with the number of authors and the number of institutions [134].

The large diversity of topics covering basically all clinical, preclinical, biological, and technical aspects of the field is noteworthy. However, clinical studies in two common diseases, i.e., breast and prostate cancer, were underrepresented. Research in areas such as quality of life and side effects, palliative radiotherapy, and radiotherapy for nonmalignant disorders was also less likely to result in highly cited articles. In other words, even within the field of radiotherapy, heterogeneous citation properties were seen. While this does not mean that such research remains unrecognized or has a generally low likelihood of publication, efforts to increase the number of highly prestigious and cited articles might be warranted. Symptom palliation, organ preservation, noninvasiveness, and the resulting consequences for quality of life are important advantages of radiotherapy, especially in aging populations [135].

Conclusion

Meta-analyses and randomized phase III trials, which typically were performed by collaborative groups, received more citations than other study designs. A large variety of clinical radiotherapy, biology, and physics topics achieved high numbers of citations, but studies on quality of life and side effects, palliative radiotherapy, and radiotherapy for nonmalignant disorders were underrepresented.

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Conflict of interest. On behalf of all authors, the corresponding author states that there are no conflicts of interest.

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