



# Radiotherapy for osteoarthritis—an analysis of 295 joints treated with a linear accelerator

Matthias G. Hautmann<sup>1</sup> · Philipp Rechner<sup>2</sup> · Ulrich Neumaier<sup>3</sup> · Christoph Süß<sup>1</sup> · Barbara Dietl<sup>1</sup> · Franz Josef Putz<sup>4</sup> · Michael Behr<sup>5</sup> · Oliver Kölbl<sup>1</sup> · Felix Steger<sup>1</sup>

Received: 12 August 2019 / Accepted: 28 November 2019 / Published online: 23 December 2019  
© Springer-Verlag GmbH Germany, part of Springer Nature 2019

## Abstract

**Purpose** Osteoarthritis is a common disease, with a prevalence of symptomatic disease of 8.9%. One treatment option is radiotherapy. Most published samples were treated with an orthovoltage technique or with a telecobalt device. A lot of radiotherapy institutions are nowadays using linear accelerators for treatment of osteoarthritis. There is a discussion on whether the treatment results achieved with a linear accelerator are comparable to those with the orthovoltage technique. The aim of this study is to analyze the results of radiotherapy for osteoarthritis with a linear accelerator and compare the results with reference to different joints.

**Materials and Methods** The analysis was performed in patients of two German radiotherapy institutions and included 295 irradiated joints. Pain was documented with the numeric rating scale (NRS). Evaluation of the NRS was done before and directly after each radiation therapy course as well as for the follow-up of 24 months.

The median age of the patients was 65 years, with 39.0% male and 61.0% female patients. Most frequently, osteoarthritis of the knee (34.6%) or the finger (15.9%) was treated.

**Results** We could find a significant response to radiotherapy. Median pain for the whole sample was 7 on the NRS before radiotherapy, 4 after 6 weeks, and 3 after 12 and 24 months. The percentage of patients with 0 or 1 on the NRS was 33.8% 12 months after radiotherapy. All investigated subgroups had a significant reduction of pain.

**Conclusion** Radiotherapy of osteoarthritis with a linear accelerator is an effective treatment which is very well tolerated. All analyzed subgroups show a good response to radiotherapy for at least 24 months. Orthovoltage therapy seems to be superior to treatment with a linear accelerator in a case-related analysis of the published samples. Further investigations should be performed for a definitive answer to this question.

**Keywords** Osteoarthritis · Osteoarthrosis · Arthrosis · Radiotherapy · Linear accelerator

## Introduction

Osteoarthritis is a common disease, especially in elderly people. The prevalence of symptomatic osteoarthritis is

about 8.9% among the adult population [1]. Most frequently the knee is affected, with about 6% symptomatic knee arthritis among the adult population [1, 2]. For example, for the population older than 70 years, the prevalence of knee arthritis is about 40% [2, 3]. As life expectancy is rising and the prevalence of risk factors for osteoarthritis like overweight or inactivity is growing, an increasing prevalence of osteoarthritis can be expected in the future [3].

Several therapeutic options for treatment of osteoarthritis are in use [2]. There is good evidence for arthroplasty for advanced osteoarthritis [4, 5]. For joint-conserving therapies there is not a high level of evidence [3]. Beside ice, heat, ultrasound treatment, splinting, and physiotherapy, many patients get a drug therapy. The drug therapy can be systemic, for example with NSAIDs (non-steroidal anti-inflammatory drugs), or can consist of local injections of anesthetics or steroids [6–9].

✉ Matthias G. Hautmann, PD, MD  
matthias.hautmann@ukr.de

<sup>1</sup> Department of Radiotherapy, University of Regensburg, 94042 Regensburg, Germany

<sup>2</sup> Privat Clinic for Dentistry, Dr. Kreps, Ergoldsbach, Germany

<sup>3</sup> MVZ Dr. Neumaier & Kollegen, Regensburg, Germany

<sup>4</sup> Department of Nephrology, University of Regensburg, Regensburg, Germany

<sup>5</sup> Department of Prosthetic Dentistry, University of Regensburg, Regensburg, Germany

One effective non-invasive treatment for osteoarthritis is radiotherapy [10–31]. Like for several other bone and joint disorders, low-dose radiation has shown an anti-inflammatory effect [10, 13, 32–40].

Most of the published samples were treated with orthovoltage therapy [35, 41–43]. Some others were irradiated with telecobalt devices or cesium devices [18, 28, 30, 44]. Only a few relatively small samples exist where patients were treated with a linear accelerator [21, 40, 45, 46]. Detailed information is missing in some of these manuscripts and the objective was different than that of our survey.

There is one retrospective trial comparing the results of orthovoltage therapy versus radiotherapy with a linear accelerator just for osteoarthritis of the knee [47]. This trial is only available in German language and has not been published in a magazine so far.

Many radiotherapy institutions do not use orthovoltage therapy anymore [48–50]. The therapy with telecobalt devices is obsolete in developed countries.

The objective of this survey is to document and analyze the results of radiotherapy for osteoarthritis with a linear accelerator and to compare these results with those of orthovoltage therapy.

A second ongoing discussion is whether small or large joints respond better to radiotherapy. The risk factors and etiology seem to be somewhat different [1, 51]. For this reason, the other objective of this analysis was to compare the results upon treating different joints or joint regions with radiotherapy, with the main focus on the comparison of small and large joints.

## Patients and methods

The study was approved by the Ethics Committee of the University of Regensburg.

The retrospective analysis was performed on patients of two German radiotherapy institutions. We identified all patients receiving one or more courses of radiotherapy for osteoarthritis.

Radiotherapy to different joints was separated in the analysis. Some joints were cumulated to certain regions, like Heberden or Bouchard arthrosis, upper and lower ankle joint, or omarthrosis and acromioclavicular arthritis.

The patients' data from the regular follow-up were analyzed. Additionally, the patients were questioned about their current status and constantly clinically examined. We identified the etiology of the pain and registered possible risk factors for a lack of response to radiation.

Pain was documented with the numeric rating scale (NRS). Evaluation of the NRS was done before and directly after each radiation treatment as well as for the follow-up. Follow-up was done 6 weeks, 12 weeks, 6, 12,

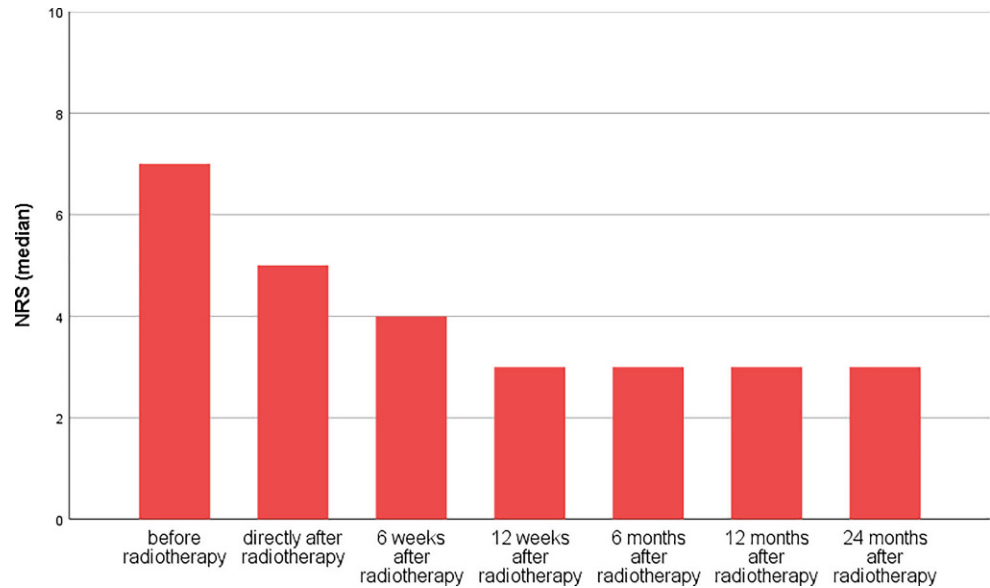
**Table 1** Demographic data

Criteria		
<i>Patients [n]</i>	159	
<i>Joints or joint regions [n]</i>	295	
<i>Gender [n]</i>		
Male	62	
Female	97	
<i>Age [years]</i>		
Median	65	
First quartile	56	
Third quartile	73	
<i>Joints or joint regions [n]</i>		
Hip	13	4.4%
Knee	102	34.6%
Ankle	29	9.8%
Shoulder	36	12.2%
Wrist	8	2.7%
Thumb (rhizarthritis)	35	11.8%
Finger (Heberden/Bouchard arthritis)	47	15.9%
Other	25	8.5%
<i>Single dose [n]</i>		
0.5 Gy	62	21.0%
1.0 Gy	233	79.0%
<i>Total dose</i>		
3.0 Gy	56	19.0%
6.0 Gy	229	77.6%
<i>Time of pain onset [n]</i>		
Median	48	
First quartile	20	
Third quartile	96	
<i>Pretreatment beside radiation [n]</i>	–	94.2%
<i>Number of modalities [n]</i>		
Median	2	
Mode	2	
<i>Number of radiation courses [n]</i>		
One course	229	77.6%
Two or more courses	66	22.4%

and 24 months after treatment. An arthroplasty was defined as end of follow-up.

We performed descriptive statistics, calculating median, range, and interquartile range (IQR) of NRS for all time periods. To analyze significant differences in the chronological sequence of NRS, the paired Wilcoxon test for dependent variables was used. The Mann–Whitney U test for independent variables was used for subgroup analyses and the Fisher–Yates test or chi<sup>2</sup> test for testing of binomial variables. We postulated that  $p < 0.05$  was significant. Statistical analyses were performed with IBM SPSS Statistics 23.0 (IBM, Armonk, NY, USA).

**Fig. 1** Median pain on the numeric rating scale (NRS) during the follow-up



We defined several subgroups by gender, age (separated by the median age of 65 years), etiology, and the other parameters listed in Table 1.

Hip, knee, ankle, and shoulder were classified as large joints, whereas the finger, thumb, and big toe were categorized as small joints.

## Results

In total, 159 patients could be identified, questioned, and clinically examined. 295 joints or joint regions were treated due to the fact that some patients were irradiated on more than one joint or region.

The median age of the patients was 65 years with a range from 21 to 91 years and an IQR from 56 to 73 years. 97 of the patients were female and 62 male. Most frequently patients suffered from arthritis of the knee (102 courses, 34.6%), followed by Bouchard and Heberden arthritis (47 courses, 15.9%) and arthritis of the shoulder (36 courses, 12.2%; Table 1).

94.2% of the joints were pretreated before radiotherapy. Most of the time patients had taken non-steroidal drugs for a long time, had had intraarticular injections with hyaluronidase, or had used orthoses.

The median follow-up was 19 months.

Radiotherapy was performed with a linear accelerator (Siemens Primus and Elekta Synergy) using 6- or 15-MV photons. Dose calculation was done to the isocenter or middle of the joint. Joints or regions were either treated with a fractionated dose of 0.5 Gy (62 joints, 21.0%) to a total dose of 3.0 Gy (56 joints, 19.0%) or 5.0 Gy (4 joints, 1.4%) or 1.5 Gy (2 joints, 0.7%) or with a fractionated dose of 1.0 Gy (233 joints, 79.0%) to a total dose of 6.0 Gy

(229 joints, 77.6%) or 5.0 Gy (3 joints, 1.0%) or 1.0 Gy (1 joint, 0.3%). In the majority of cases the treatment time was 2 weeks (median 13 days, IQR 12 to 15 days). 66 (22.4%) of the joints received a second or even third course of radiotherapy, most of the time within a 6–12-week interval after the initial radiation course.

Acute or long-term side effects did not occur in our sample.

The median pain before irradiation was 7 on the NRS (IQR 5 to 8). On the last day of radiation, the median was 5 (IQR 3 to 7) and 6 weeks after radiotherapy it was 4 (IQR 2 to 5). After 12 weeks it was 3 (IQR 1 to 5), after 6 months 3 (IQR 1 to 5.75), and after 12 and 24 months 3 (IQR 1 to 6). At the time of the last follow-up (median 19 months), NRS was 4 (IQR 2 to 7; Fig. 1).

Pain reduction compared to the pain level before irradiation was significant, with  $p < 0.0001$  during the entire follow-up.

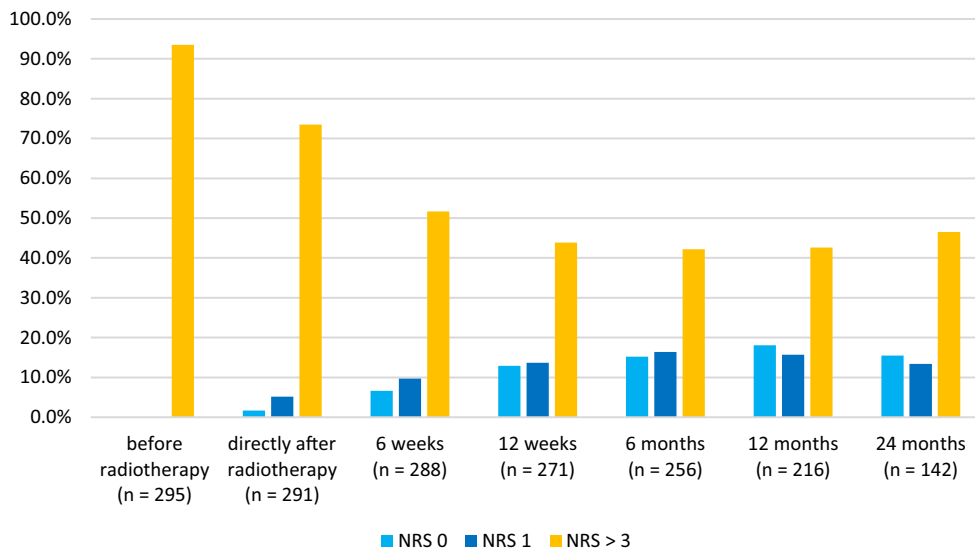
The pain improved continuously up to 6 months after radiotherapy ( $p < 0.0001$ ).

The percentage of patients being free of pain (NRS 0) or scoring pain 1 on the NRS increases with time (Fig. 2).

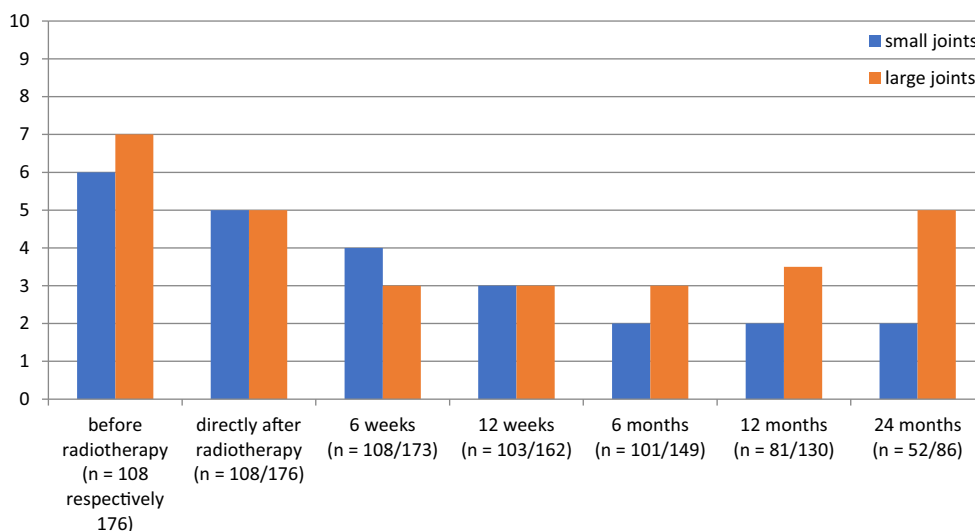
6 weeks after radiotherapy, 47 joints out of 288 (16.3%) scored 0 or 1 on the NRS. After 12 weeks it was 72 out of 271 joints (26.6%), after 6 months 81 out of 256 joints (31.6%), after 12 months 73 out of 216 (33.8%), and after 24 months it was 41 out of 142 joints (28.9%). Compared with the level before radiotherapy, there was a significant increase ( $p < 0.001$  during the entire follow-up period) in the percentage of joints with no pain (NRS 0) or very little pain (NRS 1).

The general response rate was 45.7% directly after radiotherapy, 63.2% after 6 weeks, and 65.7% after 12 weeks. 6 months after radiotherapy it was 64.8%, 12 months af-

**Fig. 2** Percentage of joints being free of pain (numeric rating scale, NRS, 0), scoring pain 1, or more than 3



**Fig. 3** Comparison of small and large joints (median pain on the numeric rating scale)



ter radiotherapy 63.4%, and 24 months after radiotherapy 64.8%, respectively.

In 32.5% of the patients no improvement of joint mobility could be detected. A distinct improvement could be achieved in 32.9% and a slight improvement of joint mobility could be achieved in 31.3% of the patients.

There was no significant difference in the remaining pain level and absence of pain for gender and age (patients older or younger than 65 years) during the entire follow-up. Male as well as female patients older and younger than 65 years (median age of our sample) had a significant reduction in pain ( $p < 0.0001$  for all categories and the entire follow-up).

Patients were analyzed separately for different joints affected by osteoarthritis. Patients with osteoarthritis of the knee as well as patients with osteoarthritis of the shoulder or acromioclavicular joint showed positive responses to radiotherapy during the entire follow-up ( $p < 0.001$ ). Patients with osteoarthritis of the hip had significant reduction of pain for the entire follow-up except at 24 months ( $p < 0.05$ ).

Patients with osteoarthritis of the finger (Bouchard arthritis or Heberden arthritis) as well as patients with osteoarthritis of the base of the thumb (rhizarthritis) showed significant reduction of pain during the entire follow-up ( $p < 0.001$ ). There was no significant difference for absence of pain and remaining NRS level.

Both idiopathic and secondary osteoarthritis had a significant reduction of pain ( $p < 0.0001$  for the entire follow-up). Twelve weeks and 6 months after radiotherapy there was a significantly better pain reduction in favor of idiopathic osteoarthritis ( $p < 0.05$ ).

Both large Joints and small joints had a significant reduction in pain for the entire follow-up ( $p < 0.0001$ ). There was no significant difference in pain reduction for the entire follow-up. The remaining NRS level was significantly lower for small joints 12 and 24 months after radiotherapy ( $p < 0.05$ ). There was no significant difference for the other times (Fig. 3).

Patients irradiated with 0.5 Gy fractionated dose to a total dose of 3 Gy had a significant response from treatment with  $p < 0.005$  for the entire follow-up. Patients irradiated with 1.0 Gy fractionated dose to a total dose of 6 Gy also had a significant response with  $p < 0.0001$  during the entire follow-up.

There is no significant difference in pain reduction between 3.0 Gy in 6 fractions compared to 6.0 Gy in 6 fractions. The remaining NRS level 12 weeks and 6 and 12 months after radiotherapy was worse for 6 times 1.0 Gy compared to 6 times 0.5 Gy ( $p < 0.05$ ).

There was no significant difference in the long-term response (6, 12, and 24 months after completion of radiotherapy) between patients treated with one course of radiotherapy or those patients with the need for two courses of radiotherapy.

## Discussion

The role of radiotherapy for osteoarthritis is under discussion [52]. Recently, two randomized trials for osteoarthritis of the knee and hand were published, both showing no significant benefit from radiotherapy [53, 54]. Despite this, there are data about measurable shrinkage of Baker's cyst after RT for osteoarthritis of the knee, which represents a surrogate marker for the effect of RT in this indication [55].

With less than 60 patients in each study, the statistical power is somewhat limited. Furthermore, details about radiation technique, especially the machine used for treatment, are lacking and could not be inquired about.

There are many retrospective studies and some prospective studies strongly assuming radiotherapy to be an effective treatment for osteoarthritis. Beside this, there are prospective trials showing the effectiveness of low-dose radiotherapy by means of objective response criteria [55, 56]. There are many presently unanswered questions. It might be that there is a difference in response due to the use of orthovoltage therapy or a linear accelerator. Maybe just some subgroups, like for example those with activated arthrosis, have a benefit from radiotherapy. All in all, there is need for further investigation.

To our knowledge, this sample is one of the first and largest in which radiotherapy of osteoarthritis with a linear accelerator has been systematically examined. We could identify only the verifiable data of 149 patients treated with a linear accelerator, published by Kaltenborn et al., Keilholz et al., and Bartmann [40, 45, 47]. Only Bartmann investigated the problem of orthovoltage therapy versus radiotherapy with a linear accelerator. But he included only patients with knee arthritis in his survey. Besides that, the study has not yet been fully published and is available only in Ger-

man language. Kaltenborn focused on rhizarthritis, and in the survey of Keilholz, only seven patients with hip arthritis had been treated with a linear accelerator.

Summarizing the patients of all published samples of radiotherapy of osteoarthritis with linear accelerators we could identify, our sample seems to be larger than the sum of all other samples.

Among other parameters, the dose rate, depth dose, and energy are different between orthovoltage devices and linear accelerator. There is a discussion on whether the published results can be transferred for treatment of osteoarthritis with a linear accelerator [57].

Nevertheless, many German radiotherapy institutions use linear accelerators for treatment of osteoarthritis. In the patterns of care analysis of 2016, only 27 institutions in Germany (23%) stated that they have the opportunity to use orthovoltage therapy. Beside this, most of the orthovoltage devices were quite old, with a median age of 17 years [58].

A retrospective comparison between orthovoltage therapy and treatment with a linear accelerator has already been done for heel spur syndrome and humeral epicondylitis. For heel spur syndrome, it was published only in German language and showed no significant difference between the groups [59]. For humeral epicondylitis, it was mainly a review of the literature, the results seeming to be superior for orthovoltage therapy [60]. Nevertheless, these results can't easily be transferred to radiotherapy of osteoarthritis, because it is a different disease with different target volumes and target structures.

Our sample seems to be comparable to other published samples with respect to patients' parameters. For example, the median age of 65 years is nearly equal to that of the samples of Micke et al., a clinical quality assessment (average age 63.3 years) [46]. In addition, the samples of Keilholz et al. (median age 64 years), Mahler et al. (median age 62 years), and Minten et al. (mean age 65 years) show a similar age distribution [40, 53, 54]. Also, the proportion of male to female patients with a ratio of approximately 1:2 is representative [46, 53].

The radiation technique and dose concept are equivalent to the recommended concept of the German Cooperative Group on Radiotherapy for Benign Diseases. Most of the published samples, especially the published samples of recent decades, were treated that way [61].

Radiotherapy of osteoarthritis with linear accelerators has proven beneficial to our sample. The median pain level on the NRS decreases with time and seems to reach a stable low level 6 months after the end of radiotherapy. The median follow-up of 19 months allows a statement of long-term results.

Most of the patients have a response to radiation and about one quarter of the patients are free of pain or score

**Table 2** Summary of the published manuscripts concerning low-dose radiotherapy for osteoarthritis and case-related analysis

Author and year	Joint region	Device	Joints	Response rate (%)	Complete or very good response (%)	Partial response (%)
Heidenhein (1923) [66]	Mixed	Orthovoltage	18	83.3	16.7	66.7
Kreuzwald (1926) [67]	Mixed	Orthovoltage	100	80.0	–	–
Kahlmeter (1930) [68]	Mixed	Orthovoltage	323	88.0	–	–
Fried (1934) [69]	Mixed	Orthovoltage	226	92.5	34.5	58.0
Balike (1939) [70]	Mixed	Orthovoltage	555	88.3	38.4	49.9
Toschke (1941) [71]	Mixed	Orthovoltage	232	71.0	4.7	66.3
Cocchi (1943) [72]	Mixed	Orthovoltage	582	70.5	25.3	45.2
Reichel (1949) [73]	Mixed	Orthovoltage	133	73.0	51.9	21.1
Glauner (1951) [74]	Mixed	Orthovoltage	800	85.0	15.0	70.0
Fuchs (1951) [27]	Mixed	Orthovoltage	40	90.0	40.0	50.0
Pape et al. (1954) [75]	Mixed	Orthovoltage	533	76.0	25.0	51.0
Hess et al. (1955) [76]	Mixed	Orthovoltage	664	56.5	12.7	43.8
Geyer (1955) [77]	Knee	Orthovoltage	800	78.0	52.0	26.0
Pizon (1957) [78]	Knee	Orthovoltage	201	87.4	43.7	43.7
Murley (1957) [79]	Hip	Orthovoltage	59	22.0	5.0	16.9
Barth et al. (1961) [80]	Mixed	Orthovoltage	473	86.0	9.0	77.0
Keim (1965) [28]	Mixed	Cobalt device	25	48.0	–	–
Thurmayr et al. (1966) [81]	Mixed	Orthovoltage	50	44.0	22.0	22.0
Wieland (1966) [65]	Knee	Orthovoltage, cesium device, cobalt device	500	96.0	60.6	35.4
Mitrov et al. (1967) [82]	Mixed	Orthovoltage	1120	87.8	50.3	37.5
Schertel et al. (1968) [83]	Hip, knee	Orthovoltage	77	59.8	22.1	37.7
Goldie et al. (1969) [84]	Mixed	Orthovoltage	83	67.5	–	–
Von Pannewitz (1970) [39]	Knee	Orthovoltage	Not known	85.0	46.0	39.0
Grasshoff (1971) [85]	Hip, knee	Orthovoltage	106	65.1	10.4	54.7
Gibson et al. (1972) [26]	Knee	Orthovoltage	29	Not known	–	–
Zschache (1972) [86]	Hip, knee	Orthovoltage	534	81.6	17.0	64.6
Hartweg et al. (1973) [87]	Knee	Orthovoltage	124	87.0	29.0	58.0
Hassenstein (1974) [88]	Hip	Orthovoltage	120	69.2	35.9	33.3
Valtonen et al. (1975) [11]	Hip, knee	Orthovoltage	18	77.8	27.8	50.0
Hassenstein et al. (1976) [89]	Knee	Orthovoltage	124	85.5	29.0	56.5
Keiner et al. (1982) [43]	Knee	Orthovoltage	290	81.0	38.0	43.0
Lindner et al. (1982) [90]	Mixed	Cesium device	207	57.5	9.7	47.8
Yaneva et al. (1986) [42]	Hip, knee	Orthovoltage	363	91.8	4.7	87.1
Gaertner et al. (1988) [91]	Mixed	Orthovoltage	9	22.2	–	–
Gaertner et al. (1988) [91]	Mixed	Cobalt device	27	12.5	–	–
Sautter-Bihl et al. (1993) [44]	Knee	Cobalt device	21	81.0	14.0	57.0
Merte et al. (1995) [92]	Hip, knee	Orthovoltage	134	59.7	35.1	24.6
Keilholz et al. (1998) [40]	Mixed	Orthovoltage	96	60.4	21.9	38.6
Keilholz et al. (1998) [40]	Hip	Linear accelerator	7	85.7	28.6	57.2
Schultze (2000) [41]	Mixed	Orthovoltage	462	57.0	–	–
Glatzel et al. (2004) [93]	Knee	Orthovoltage	214	68.2	9.3	58.9
Ruppert et al. (2004) [35]	Knee	Orthovoltage	73	63.0	41.0	22.0



**Table 2** (Continued)

Author and year	Joint region	Device	Joints	Response rate (%)	Complete or very good response (%)	Partial response (%)
Keller et al. (2013) [21]	Knee	Orthovoltage, cesium device, Linear accelerator	1039	79.3	10.5	68.8
Bartmann (2016) [47]	Knee	Orthovoltage	37	40.5	21.6	18.9
Bartmann (2016) [47]	Knee	Linear accelerator	77	55.9	33.8	22.1
Kaltenborn et al. (2016) [45]	Thumb	Linear accelerator	65	63.0	13.8	49.2
Micke et al. (2018) [46]	Knee	Orthovoltage, linear accelerator	139	–	29.3	–
Minten et al. (2018) [53]	Finger	Data missing	28	25.0	–	–
Mahler et al. (2019) [54]	Knee	Data missing	27	44.0	–	–
Case-related average	–	All	11,909	78.0	27.9	51.3
Case-related average	–	Orthovoltage	9802	77.7	28.5	50.1
Case-related average	–	Cobalt and cesium device, linear accelerator	429	56.2	15.9	44.0
Present study 2019	Mixed	Linear accelerator	295	64.8	26.6	38.2
Case-related average (including present study)	–	All	12,204	77.7	27.9	51.0
Case-related average (including present study)	–	Cobalt and cesium device, linear accelerator	724	60.0	20.5	42.0

very low pain with NRS 1 during the long-term follow-up period. This effect lasts for at least 2 years.

The overall response rate of our sample (approximately 65%) is within the range or slightly lower than that of most other published studies (case-related average 77.7%) and seems to be comparable with the results of orthovoltage therapy.

Because of the different anatomical regions, it is difficult to give a universal recommendation for target volumes and radiation dose or technique. We used 6- or 15-MV photons in opposing fields or with a single field. Initially, patients were treated with 6 times 1.0Gy in both institutions. In analogy to the data presented by Ott et al. for the radiotherapy of other non-malignant disorders, the dose concept was changed to  $6 \times 0.5$  Gy [62–64]. There was a higher remaining NRS level for patients treated with 6.0Gy in 6 fractions. Anyhow, a general recommendation cannot be given. Regarding the results of Ott et al. for other non-malignant diseases, we would rather recommend applying a fractionated dose of 0.5Gy to a total dose of 3.0Gy for reasons of radiation protection [62–64].

Whether orthovoltage therapy is superior to treatment with a linear accelerator is an interesting question. We could identify just one direct comparison of both modalities for osteoarthritis of the knee [47]. This study found no significantly different results for treatment with a linear accelerator compared to orthovoltage therapy. A slight tendency toward radiotherapy with a linear accelerator is speculated by the author. He states that it was a small sample and therefore does not have enough power to detect a difference.

For that reason, we did a case-related analysis of the published samples irradiated because of osteoarthritis. Altogether, 11,909 published patients could be identified. 9802 patients were verifiably treated with orthovoltage therapy, 429 patients (excluding our sample) were treated with photons or gamma rays (Table 2).

Most of the 429 patients were irradiated with a telecobalt or cesium device. We could identify only 149 cases, published in three samples, for which it is clearly stated that they were treated with a linear accelerator [40, 45, 47]. Detailed information is missing in some other samples [21, 46, 53, 54, 65]. We found data of complete response and partial response for 89% of all published patients. We performed statistical comparison with the  $\chi^2$  test.

For all published samples in the literature the average response rate was 78%, for the joints treated with orthovoltage therapy it was 77.7%, for all other (photons and gamma ray), including our sample, it was 60%. There was a significant difference between these groups in favor of treatment with orthovoltage therapy ( $\chi^2 = 144.9$ ). We could find a significant benefit for orthovoltage for complete response ( $\chi^2 = 56.4$ ) and for partial response ( $\chi^2 = 30.5$ ).

Just comparing the response rate of patients treated with orthovoltage therapy and a linear accelerator, a significant difference in favor of treatment with orthovoltage therapy can be identified for the entire time period ( $\chi^2 = 57.9$ ).

If one just compares the newer studies since 1995 and just include patients with quite a similar dose concept to that recommended in the German guideline (fractionated dose 0.5 to 1.0Gy and total dose 3.0 to 6.0Gy), a significant difference (59.6% versus 64%;  $\chi^2 = 3.2$ ) could no longer

be found in the response rate between patients treated with orthovoltage ( $n = 1016$ ) and photons/gamma rays ( $n = 444$ ).

There are limitations to comparing all the published samples receiving radiotherapy for osteoarthritis. Beside different dose concepts, inclusion criteria, and radiation techniques, the response criteria were also different, as are the follow-up periods and the timepoints at which the response was evaluated.

Over all published samples, excluding our sample, a significant difference between the samples treated with orthovoltage therapy compared to those treated with photons or gamma rays in favor of orthovoltage therapy could be found. But less than 10% of the joints had been treated with photons or gamma rays, and it was a heterogeneous group by itself. The lack of a significant difference upon comparing the newer studies since 1995 might be due to the relatively small number of cases with sufficient information in this period.

It might be interesting to conduct a prospective trial comparing orthovoltage therapy and radiotherapy with photons by a linear accelerator.

Differences between orthovoltage therapy and photon therapy are the different peak energies, dose distributions (mostly due to different absorption), and dose rates, among others. One reason for the possible superiority of orthovoltage therapy might for example be the higher absorption of X-rays within the tissue—in particular the bone tissue—compared to photons.

Another reason might be the higher absorption in the soft tissues, with a better anti-inflammatory effect of the surrounding organs. Also, the dose rate might be one possible explanation.

Further investigations of the finding that orthovoltage therapy might be superior to photons in the radiotherapy of osteoarthritis seem to be reasonable. A prospective study to clarify a possible different effect of these modalities should be performed.

A significant difference in the response between small and large joints could not be detected. The remaining lower NRS level for small joints 12 and 24 months after radiotherapy might be random. A certain joint or joint region with clear better or worse response to radiotherapy could not be detected in our survey. It appears, that radiotherapy of osteoarthritis can be offered to patients independently of the localization of the degenerative affected joint or joint region.

## Conclusion

Radiotherapy of osteoarthritis with a linear accelerator is widely used and is an effective treatment which is very well tolerated. A clear difference in the response rate between

small and large joints could not be detected. All analyzed subgroups show a good response to radiation for at least 24 months. A fractionated dose of 0.5 Gy and a total dose of 3.0 Gy seem to be recommendable. Comparing treatment with a linear accelerator and orthovoltage therapy in a case-related analysis, orthovoltage therapy seems to be beneficial. Upon just comparing recent literature (since 1995), no significant difference can be detected.

**Conflict of interest** M.G. Hautmann, P. Rechner, U. Neumaier, C. Stieß, B. Dietl, F.J. Putz, M. Behr, O. Kölbl, and F. Steger declare that they have no competing interests.

## References

1. Andrianakos AA, Kontelis LK, Karamitsos DG et al (2006) Prevalence of symptomatic knee, hand, and hip osteoarthritis in Greece. The ESORDIG study. *J Rheumatol* 33(12):2507–2513
2. Michael JW-P, Schlüter-Brust KU, Eysel P (2010) The epidemiology, etiology, diagnosis, and treatment of osteoarthritis of the knee. *Dtsch Arztebl Int* 107(9):152–162
3. Rabenberg M (2013) Arthrose. Gesundheitsberichterstattung des Bundes vol 54. Robert Koch-Inst, Berlin
4. Grayson CW, Decker RC (2012) Total joint arthroplasty for persons with osteoarthritis. *PM R* 4(5 Suppl):97–103
5. Gutowski CJ, Parvizi J, Purtill JJ (2015) Protocol-based arthroplasty. Less is more. *Orthopedics* 38(10):631–638
6. Taruc-Uy RL, Lynch SA (2013) Diagnosis and treatment of osteoarthritis. *Prim Care* 40(4):821–836, vii
7. Smelter E, Hochberg MC (2013) New treatments for osteoarthritis. *Curr Opin Rheumatol* 25(3):310–316
8. Schuh A, Jezussek D, Fabijani R et al (2007) Bleiben Sie kritisch bei der Wahl Ihrer Therapie! *MMW Fortschr Med* 149(25–26):31–32
9. Rehart S, Arnold I, Fürst M (2007) Die konservative Lokalthherapie des entzündeten Gelenks. Lokal-invasive Therapieformen. *Z Rheumatol* 66(5):382–387
10. Trott KR, Parker R, Seed MP (1995) Die Wirkung von Röntgenstrahlen auf die experimentelle Arthritis der Ratte. *Strahlenther Onkol* 171(9):534–538
11. Valtonen EJ, Lilius HG, Malmio K (1975) The value of roentgen irradiation in the treatment of painful degenerative and inflammatory musculoskeletal conditions. A double-blind study. *Scand J Rheumatol* 4(4):247–249
12. Stech H (1954) Zur Frage der Röntgen-Ganzkörper-Abschnittsbestrahlung (RöGKAB.) bei gutartigen Erkrankungen (chronische Ekzeme, Heuschnupfen, Akne vulgaris, Psoriasis, endogen bedingte Arthrosen und Depressionen). *Wien Klin Wochenschr* 66(43):829–832
13. Seegenschmiedt MH, Micke O (2012) Strahlentherapie nichtmaligner Erkrankungen. Vergangenheit, Gegenwart und Zukunft. *Strahlenther Onkol* 188(Suppl 3):272–290
14. Mücke R, Seegenschmiedt MH, Heyd R et al (2010) Strahlentherapie bei schmerzhafter Kniegelenkarthrose (Gonarthrose). Ergebnisse einer deutschen Patterns-of-Care-Studie. *Strahlenther Onkol* 186(1):7–17
15. Minten MJM, Mahler E, den Broeder AA et al (2016) The efficacy and safety of low-dose radiotherapy on pain and functioning in patients with osteoarthritis. A systematic review. *Rheumatol Int* 36(1):133–142
16. Merte H, Pfab R (1995) Strahlentherapie degenerativ-entzündlicher Gelenkerkrankungen im Alter. Eine lohnende Therapiemaßnahme. *Fortschr Med* 113(22–23):323–324



17. Fischer U, Kamprad F, Koch F et al (1998) Effekte einer niedrig dosierten Co-60-Bestrahlung auf den Verlauf einer aseptischen Arthritis am Kniegelenk des Kaninchens. *Strahlenther Onkol* 174(12):633–639
18. Lindner H, Freisleeder R (1982) Langzeitergebnisse der Bestrahlung von degenerativen Gelenkerkrankungen. *Strahlentherapie* 158(4):217–223
19. Krautzun K, Elingshausen HP (1955) Beitrag zur Röntgentherapie der Kniegelenkarthrosen. *Strahlentherapie* 96(1):82–85
20. Kern PM (2013) Wie Strahlen gegen Entzündung wirken. *MMW Fortschr Med* 155(1):47–48
21. Keller S, Müller K, Kortmann R-D et al (2013) Efficacy of low-dose radiotherapy in painful gonarthrosis. Experiences from a retrospective East German bicenter study. *Radiat Oncol* 8:29
22. Keller HL (1974) Röntgenbestrahlung bei Arthrosis deformans. *Med Klin* 69(20):930
23. Kapatkin AS, Nordquist B, Garcia TC et al (2016) Effect of single dose radiation therapy on weight-bearing lameness in dogs with elbow osteoarthritis. *Vet Comp Orthop Traumatol* 29(4):338–343
24. Hess P, Bonmann KH (1955) Die Röntgentherapie der Arthrosen, Spondylosen, der Periarthritis humeroscapularis und der Epikondylitis. *Strahlentherapie* 96(1):75–81
25. Grosu AL (2001) Radiotherapie ausserhalb der Onkologie. Wann ist sie sinnvoll? (interview by Waltraud Paukstadt). *MMW Fortschr Med* 143(48):16
26. Gibson TJ, Winter PJ, Grahame R (1972) Radiotherapy in the treatment of osteoarthritis of the knee. *Ann Rheum Dis* 31(5):423–424
27. Fuchs G (1951) Zur Strahlenbehandlung der Arthrosis deformans. *Wien Klin Wochenschr* 63(16):295–296
28. Keim H (1965) Mitteilung ueber die Durchfuehrung der Entzündungsbestrahlung mit dem Telekobaltgeraet. *Strahlentherapie* 127:49–52
29. Weitmann HD, Niewald M (2013) Nicht nur bei Arthrosen erfolgversprechend. *MMW Fortschr Med* 155(1):43–46
30. Wieland C, Kuttig H (1965) Hochvolttherapie bei Arthrosen und Entzündungen. *Strahlentherapie* 127:44–48
31. Thurmayer R, Bohmert H (1966) Zur konservativen Behandlung der Arthrosis deformans. Vergleichende Untersuchungen über die therapeutische Wirksamkeit von Eleparon und Röntgenbestrahlungen. *Munchener Medizinische Wochenschrift* 108(4):213–216
32. Schertel L, Roos A (1968) Strahlenbehandlung bei degenerativen Skeletterkrankungen? *Med Klin* 63(28):1112–1115
33. Schäfer U, Micke O, Seegenschmiedt HM et al (2010) Low-dose radiotherapy. *Dtsch Arztebl Int* 107(34–35):603–604
34. Schäfer U, Micke O, Willich N (1996) Schmerzbestrahlung bei degenerativ bedingten Skeletterkrankungen. *Rontgenpraxis* 49(10):251–254
35. Ruppert R, Seegenschmiedt MH, Sauer R (2004) Radiotherapie von Arthrosen. Indikation, Technik, klinische Ergebnisse. *Orthopäde* 33(1):56–62
36. Rossi F, Cancedda S, Leone VF et al (2018) Megavoltage radiotherapy for the treatment of degenerative joint disease in dogs. Results of a preliminary experience in an Italian radiotherapy centre. *Front Vet Sci* 5:74
37. Robson PN, van Miert PJ (1962) Treatment of osteo-arthritis of the hip by interstitial cobalt 60 irradiation. *Br J Surg* 49:624–636
38. Prokein B, Holtmann H, Hautmann MG et al (2017) Strahlentherapie des Fersensporns mit 2 Fraktionierungsschemata. Ergebnisse einer randomisierten Multizenterstudie nach 48 Wochen Follow-up. *Strahlenther Onkol* 193(6):483–490
39. von Pannowitz G (1970) Strahlentherapie der Arthrosis deformans. Technik und Ergebnisse. *Radiologe* 10(2):51–54
40. Keilholz L, Seegenschmiedt H, Sauer R (1998) Radiotherapie bei schmerzhaften degenerativ-entzündlichen Gelenkerkrankungen. Indikation, Technik und klinische Ergebnisse. *Strahlenther Onkol* 174(5):243–250
41. Schultze J (2000) Ergebnisse der Strahlentherapie degenerativer Skeletterkrankungen. *Strahlenther Onkol* 176(Sondernummer 1):192
42. Yaneva M, Vlaikova M, Dimitrova M et al (1986) X-ray therapy in degenerative-dystrophic diseases of the bones and joints. *Folia Med* 28(2):26–28
43. Keiner K, Schalldach U, Schumann E (1982) Ergebnisse der Strahlentherapie der Arthrosis deformans des Kniegelenkes. *Dtsch Gesundheitsw Z Klin Med* (10):445–447
44. Sautter-Bihl ML, Liebermeister E, Scheurig H et al (1993) Analgetische Bestrahlung degenerativentzündlicher Skeletterkrankungen. Nutzen und Risiko. *Dtsch Med Wochenschr* 118(14):493–498
45. Kaltenborn A, Bulling E, Nitsche M et al (2016) The field size matters: low dose external beam radiotherapy for thumb carpometacarpal osteoarthritis. *Strahlenther Onkol* 192(8):582–588
46. Micke O, Ugrak E, Bartmann S et al (2018) Radiotherapy for calcaneodinia, achillodynia, painful gonarthrosis, bursitis trochanterica, and painful shoulder syndrome—early and late results of a prospective clinical quality assessment. *Radiat Oncol* 13(1):71
47. Bartmann S (2016) Langzeiteffekte der niedrigdosierten Schmerzbestrahlung bei Gonarthrose und Bursitis trochanterica – Vergleich der Resultate nach bestrahlung am Linearbeschleuniger versus Orthovoltgerät. Dissertation, Ruhr-Universität Bochum, Medizinische Fakultät. <https://hss-opus.ub.ruhr-uni-bochum.de/opus4/frontdoor/index/index/docId/5496>
48. Seegenschmiedt MH, Micke O, Willich N (2004) Radiation therapy for nonmalignant diseases in Germany. Current concepts and future perspectives. *Strahlenther Onkol* 180(11):718–730
49. Seegenschmiedt MH, Katalinic A, Makoski HB et al (1999) Strahlentherapie von gutartigen Erkrankungen: eine Bestandsaufnahme für Deutschland. *Strahlenther Onkol* 175(11):541–547
50. Seegenschmiedt MH, Katalinic A, Makoski H et al (2000) Radiation therapy for benign diseases: patterns of care study in Germany. *Int J Radiat Oncol Biol Phys* 47(1):195–202
51. Arnold I (2016) Arthrose. Was gibt es Neues? *Dtsch Arztebl* 113(44):A-1976/B-1658/C-1645
52. Ott OJ, Micke O, Mücke R et al (2019) Low-dose radiotherapy. Mayday, mayday. We've been hit! *Strahlenther Onkol* 195(4):285–288
53. Minten MJM, Leseman-Hoogenboom MM, Kloppenburg M et al (2018) Lack of beneficial effects of low-dose radiation therapy on hand osteoarthritis symptoms and inflammation. A randomised, blinded, sham-controlled trial. *Osteoarthr Cartil* 26(10):1283–1290
54. Mahler EAM, Minten MJ, Leseman-Hoogenboom MM et al (2019) Effectiveness of low-dose radiation therapy on symptoms in patients with knee osteoarthritis. A randomised, double-blinded, sham-controlled trial. *Ann Rheum Dis* 78(1):83–90
55. Hautmann MG, Jung E-M, Beyer LP et al (2019) Ist die Strahlentherapie eine effektive Behandlungsoption der Bakerzyste? *Strahlenther Onkol* 195(1):69–76
56. Riesterer O, Eberle B, Rogers S, Vogt DR (2019) Schmerz- und Funktionsverbesserung durch analgetische, entzündungshemmende Radiotherapie bei Patienten mit Fingerarthrosen, Epicondylitis radialis/ulnaris oder mit Fasziiitis plantaris – Ergebnisse einer prospektiven single center Studie. *Strahlenther Onkol* 195(Suppl 1):49
57. Reichl B, Block A, Schäfer U et al (2015) DEGRO practical guidelines for radiotherapy of non-malignant disorders. Part I: physical principles, radiobiological mechanisms, and radiogenic risk. *Strahlenther Onkol* 191(9):701–709
58. Kriz J, Seegenschmiedt HM, Bartels A et al (2018) Updated strategies in the treatment of benign diseases—a patterns of care study of the german cooperative group on benign diseases. *Advances in Radiation Oncology* 3(3):240–244
59. Schlöcker I (2008) Vergleich der Wirksamkeit von Orthovoltbestrahlung und Hochvoltbestrahlung bei schmerzhaftem Fersen-

- sporn (FS) anhand des Parameters Schmerzbefreiung. doctoral thesis, Universität Halle. [https://sundoc.bibliothek.uni-halle.de/diss-online/08/08H107/of\\_index.htm](https://sundoc.bibliothek.uni-halle.de/diss-online/08/08H107/of_index.htm)
60. Hautmann MG, Beyer LP, Stöß C et al (2019) Strahlentherapie der Epicondylitis humeri. Analyse von 138 mit Linearbeschleuniger bestrahlten Ellenbogen. *Strahlenther Onkol* 195(4):343–351
  61. Ott OJ, Niewald M, Weitmann H-D et al (2015) DEGRO guidelines for the radiotherapy of non-malignant disorders. Part II. Painful degenerative skeletal disorders. *Strahlenther Onkol* 191(1):1–6
  62. Ott OJ, Jeremias C, Gaipl US et al (2015) Radiotherapy for benign achillodynia. Long-term results of the Erlangen Dose Optimization Trial. *Strahlenther Onkol* 191(12):979–984
  63. Ott OJ, Hertel S, Gaipl US et al (2014) The Erlangen Dose Optimization Trial for radiotherapy of benign painful shoulder syndrome. Long-term results. *Strahlenther Onkol* 190(4):394–398
  64. Ott OJ, Hertel S, Gaipl US et al (2014) The Erlangen Dose Optimization Trial for low-dose radiotherapy of benign painful elbow syndrome. Long-term results. *Strahlenther Onkol* 190(3):293–297
  65. Wieland C (1966) Indikationsstellung und Ergebnisse der Strahlentherapie bei Arthrosen. *Z Rheumaforsch* 25(9):324–329
  66. Heidenhein L (1923) Über die Arthritis senilis bilateralis symetrica. *Langenbecks Arch Klin Chir* 127:514–528
  67. Kreuzwald T (1926) Röntgenbestrahlung der Arthristis deformans. *Fortschr Röntgenstr* 35:102
  68. Kahlmeter G, Åkerlund Å (1930) The roentgen treatment of arthritis. *Acta Medica Scandinavica* <https://doi.org/10.1111/j.0954-6820.1930.tb14931.x>
  69. Fried G (1934) Die Röntgentherapie der Arthritis. *Strahlenther* 49:634–675
  70. (1939) Über die Röntgenbehandlung chronischer unspezifischer Gelenkleiden. *Acta radiologica* 20:357–364
  71. Toschke G (1941) Zur Röntgenbehandlung von Gelenkerkrankungen. *Strahlenther* 70:443–456
  72. Cocchi U (1943) Erfolge und Mißerfolge bei der Röntgenbestrahlung nicht krebssiger Leiden. I. gutartige nicht tuberkulöse nicht aktinomykotische Prozesse. *Strahlenther* 73:255–305
  73. Reichel WS (1949) Radiotherapy for pain. *Strahlentherapie*. 80(4):483–534
  74. Glauner R (1951) Die Entzündungs-Bestrahlung. Stuttgart: Thieme
  75. Pape R, Gölles D (1954) Direkte und indirekte Röntgentherapie bei Gelenkerkrankungen. *Radiol Aust* 6:245–254
  76. Hess P, Bonmann KH (1955) Roentgen therapy of arthroses, spondyloses, peri-arthritis humeroscapularis and epicondylitis. *Strahlentherapie* 96(1):75–81
  77. Geyer E, Landgraf K (1955) Results of radiotherapy and ultrasonic therapy in 1000 cases of arthrosis deformans of the knee. *Z Arztl Fortbild (Jena)* 49(8):273–6
  78. Pizon P (1957) La roentgentherapie des affections rhumatismales. Mason & Cie, Paris, p 142–143
  79. Murley AH (1957) Results of radiotherapy in osteo-arthritis of the hip. *Lancet* 272(6973):818–819
  80. Barth G, Kern W, Schnoeckel F (1961) Results of roentgen irradiation in arthrosis deformans. *Med Welt* 11:506–509
  81. Thurmayer R, Bohmert H (1966) On the conservative treatment of arthrosis deformans. Comparative studies on the therapeutic effectiveness of Eleparon and radiotherapy. *Munch Med Wochenschr* 108(4):213–216
  82. Mitrov G, Harbov I (1967) Our experiences with radiation treatment of non-tumorous diseases. *Radiobiol Radiother (Berl)* 8(4):419–422
  83. Schertel L, Roos A (1968) Radiotherapy in degenerative skeletal diseases. *Med Klin* 63(28):1112–1115
  84. Goldie I, Rosengren B, Moberg E, et al (1970) Evaluation of the radiation treatment of painful conditions of the locomotor system. *Acta Radiol Ther Phys Biol* 9:311–322
  85. Grasshoff H (1971) Results of x-ray treatment in cox- and gonarthroses. *Beitr Orthop Traumatol* 18(2):72
  86. Zschache H (1972) Results of low-intensity roentgen irradiation. *Radiol Diagn (Berl)* 13(2):181–186
  87. Hartweg H, Faust H, Renner K, Renner H (1973) Radiotherapy of gonarthrosis. *Strahlentherapie* 145(4):373–7
  88. Hassenstein E, Nüsslin F, Renner K. (1974) Radiation treatment of coxarthrosis (author's transl). *Strahlentherapie* 147(3):213–218
  89. (1976) Radiotherapy of inflammatory diseases – indicated still today? *Med Klin* 71(26):1117–1119
  90. Lindner H, Freislederer R. (1982) Long term results of radiotherapy of degenerative joint diseases (author's transl). *Strahlentherapie* 158(4):217–223
  91. Gärtner C, Schüttauf M, Below M, Motorina LI, Michina ZP (1988) The radiotherapeutic treatment of chronically relapsing, degenerative skeletal changes at the Oncology Clinic (Charité) [Article in German]. *Radiobiol Radiother (Berl)* 29(6):689–698
  92. Merte H, Pfab R (1995) Radiotherapy of degenerative inflammatory joint diseases in the elderly. A worthwhile therapeutic measure. *Fortschr Med* 113(22–23):323–324
  93. Glatzel M, Fröhlich D, Bäsecke S, et al. (2004) Ergebnisse der Strahlentherapie der Gonarthrose. *Strahlenther Onkol* 177(Sonderdr. 1):27