Acta Oncologica, 2007; 46: 239–246

ORIGINAL ARTICLE

Demographic, clinical and treatment related predictors for event-free probability following low-dose radiotherapy for painful heel spurs – a retrospective multicenter study of 502 patients

RALPH MUECKE[1,2], OLIVER MICKE[3,4], BERTHOLD REICHL[2], RAINER HEYDER[2], FRANZ-JOSEF PROTT[1], M. HEINRICH SEEGENSCHMIEDT[5], MICHAEL GLATZEL[6], OLIVER SCHNEIDER[7], ULRICH SCHÄFER[8] & GUENTHER KUNDT[9]

[1]*Department of Radiotherapy, St. Josefs-Hospital, Wiesbaden, Germany,* [2]*Department of Radiotherapy, Weiden Hospital, Germany,* [3]*Department of Radiotherapy, Münster University Hospital, Germany,* [4]*Department of Radiotherapy and Radiation Oncology, Franziskus Hospital Bielefeld, Germany,* [5]*Department of Radiotherapy, Alfried Krupp Hospital Essen, Germany,* [6]*Department of Radiotherapy, Suhl Central Hospital, Germany,* [7]*Department of Radiotherapy, Bochum University Hospital, Germany,* [8]*Department of Radiotherapy, Lippe Hospital Lemgo, Germany, and* [9]*Institute of Medical Informatics and Biometry, Rostock University Hospital, Germany*

Abstract

A total of 502 patients treated between 1990 and 2002 with low-dose radiotherapy (RT) for painful heel spurs were analysed for prognostic factors for long-term treatment success. The median follow-up was 26 months, ranging from 1 to 103 months. Events were defined as (1) slightly improved or unchanged pain after therapy, or (2) recurrent pain sensations during the follow-up period. Overall 8-year event-free probability was 60.9%. Event-free probabilities of patients with one/two series (414/88) were 69.7%/32.2% ($p < 0.001$); $>58/\leq 58$ years (236/266), 81.3%/47.9% ($p = 0.001$); high voltage/orthovoltage (341/161), 67.9%/60.6% ($p = 0.019$); pain anamnesis ≤ 6 months/ >6 months (308/194), 76.3%/43.9% ($p = 0.001$); single dose 0.5/1.0 Gy (100/401), 86.2%/55.1% ($p = 0.009$); without/with prior treatment (121/381), 83.1%/54.9% ($p = 0.023$); men/women (165/337), 61.2%/61.5% ($p = 0.059$). The multivariate Cox regression analysis with inclusion of the number of treatment series, age, photon energy, pain history, single dose and prior treatments revealed patients with only one treatment series ($p < 0.001$), an age >58 years ($p = 0.011$) and therapy with high voltage photons ($p = 0.050$) to be significant prognostic factors for pain relief. Overall low-dose RT is a very effective treatment in painful heel spurs.

The term "heel spur" was coined in 1900 by the German surgeon Plettner, who first used the anatomical term "Kalkaneussporn" (English: calcaneal spur). In his radio-morphological study, he described an exostotic plantar bone formation at the insertion of the plantar fascia and muscles of the calf (37) which is today termed "Plantar Heel Spur". In contrast, the exostosis at the insertion of the Achilles tendon is called "Dorsal Heel Spur". The latter exostosis develops less often and is asymptomatic in a higher percentage of patients. A combination of both spurs is possible. Bilateral manifestations can be observed in many cases. The overall prevalence is estimated between 8% and 10% [28,54]. Data on the gender ratio vary in a large range [42]. Patients are usually older than 40 years. Most spurs have a length of 4 to 6 mm; however, larger spurs are possible. No correlation exists between the length of the spur and the extent of the clinical symptoms. Typical symptoms consist of a stinging and sometimes extensive pain under the heel, which may extend or radiate into the lower leg. Usually, gait and mobility are markedly impaired. A typical symptom is the localized pain at the medial and distal aspect of the tuber calcanei.

Chronic damage or continuous microtrauma to the insertion of the plantar aponeurosis and the small foot muscles plays - due to increased strain - an important role in the pathogenesis. The increased strain may be a result of foot deformity, obesity or

Correspondence: Oliver Micke, Klinik für Strahlentherapie und Radioonkologie Franziskus Hospital, Kiskerstraße 26, D-33615 Bielefeld, Germany. Tel.: +49 521 5891801. Fax: +49 521 5891804. E-mail: omicke@benign-news.de

(Received 30 August 2005; accepted 31 March 2006)

ISSN 0284-186X print/ISSN 1651-226X online
DOI: 10.1080/02841860600731935

extensive sports activities [38,54]. The chronic damage is followed by a decreased elasticity of the insertional cartilage. Gaps in the impaired cartilage are invaded by mesenchymal cells, which form scar tissue. After new vessels have developed, the scar slowly ossifies, which can lead to the growing of bony spurs [47].

The treatment generally follows the principles of therapy for osteoarthritis: decreasing weight burden by means of orthopedic shoes or insoles, local infiltration with corticoid crystal suspensions and local anaesthesia. Systemic non-steroidal anti-inflammatory agents (NSAIDs), iontophoresis, microwave and ultrasound applications are common treatment modalities. Different surgical techniques are also in use [2,7]. Although radiotherapy (RT) has long been known for excellent results in heel spurs and other musculo-skeletal degenerative and inflammatory entities [41], the decision for RT is still regarded as "last resort" approach to treat refractory cases.

The aim of this retrospective clinical cohort study was to analyse prognostic factors for long-term treatment success following low-dose RT for painful heel spurs, in order to identify those patients who may primarily benefit from RT and to find the optimal concept for dose/fractionation and treatment unit.

Material and methods

Patients

The clinical data of 502 patients irradiated for painful heel spurs between 1990 and 2002 at four cooperating German radiotherapy (RT) institutions (Weiden, Suhl, Herne and Wiesbaden) were collected. There were 337 female and 165 male patients with a median age of 58 years, ranging from 22 to 84 years. Four hundred and fourteen patients received a single RT series, 88 patients a second RT series after a median of three months.

Heel Spurs

A total of 544 painful heel spurs was treated (268 left, 276 right feet). All lesions were radiographically detectable. Three hundred and eighty one patients (75.9%) had received prior treatments: local analgesic injections, orthopedic insoles, non-steroidal anti-inflammatory drugs and physiotherapy. In 121 cases (24.1%) RT was the primary treatment. The indications for RT were clinical symptoms: pain in typical locations and functional deficit with markedly decreased range of pain free motion.

Treatment

In 341 patients (67.9%), RT was performed twice a week via a single 6 – 10 MV photon field, in 161 patients (32.1%) three times a week via a single 175-kV x-ray field. With 6 MV, ten fractions of 0.5 Gy were applied in 100 patients, five to six fractions of 1.0 Gy were applied in 140 patients. With 10 MV, five fractions of 1.0 Gy were applied in 101 patients. In all patients treated with 175 kV x-rays, six fractions of 1.0 Gy were applied. Treatment portals were planned with the help of a treatment simulator and included the whole calcaneus with the insertion of the plantar fascia and the Achilles tendon. Patients treated with a second RT series received the same single and total dose as in the first RT series. Clinical outcome was assessed by means of the widely established and accepted "von Pannewitz" score (pain free, substantially improved, slightly improved, and unchanged) at the end of radiotherapy and at the time of assessment [36]. Events were defined as (1) slightly improved or unchanged pain after therapy, or (2) recurrent pain sensations during follow-up period. During follow-up visits, acute or chronic side effects were recorded.

Follow-up

Follow-up was completed in November 2004 with a median duration of 26 months (range: 1 to 103 months). All patients were regularly followed up in the radiotherapy departments. The follow-up data were obtained by clinical examination and history taking of patients in the radiotherapy department as well as by questionnaire and telephone interview. There were 11 cases, where RT was helpful, but no further information was achieved. These cases were censored as one month, which means that the end of RT was the only examination. If RT did not help at all, patients were coded as an event with a time of 0 months.

Statistics

Event-free probabilities were estimated and graphically represented as time-to-event curves by means of the Kaplan-Meier method. Influence of cofactors was assessed with the help of Mantel's log-rank test for censored survival data. Variables that were significant in the univariate analyses were entered into the multivariate analysis.

The Cox proportional hazards model was used for multivariate analysis to assess independence of the pain situation from prognostic factors by specification of adjusted hazard ratios. We entered all significant variables into the multivariate model in a single step by using the forced-entry method.

Variable evaluation and selection was based on Wald statistics. All p-values resulted from two-sided statistical tests, with values of $p \leq 0.05$ being considered statistically significant. For processing and statistical analysis of all data, the SPSS/PC Software package, version 12.0 (SPSS GmbH, Munich, Germany), was used.

Results

Overall, 393 patients were event-free during the follow-up period. With a total number of 109 events, 8-year event-free probability was 60.9% according to Kaplan-Meier (Figure 1).

Univariate analyses

Event-free probabilities of patients with one/two series (414/88) were 69.7%/32.2% ($p < 0.001$); $>58/\leq 58$ years (236/266), 81.3%/47.9% ($p = 0.001$); high voltage/orthovoltage (341/161), 67.9%/60.6% ($p = 0.019$); pain anamnesis ≤ 6 months/ >6 months (308/194), 76.3%/43.9% ($p = 0.001$); single dose 0.5/1.0 Gy (100/401), 86.2%/55.1% ($p = 0.009$); without/with prior treatment (121/381), 83.1%/54.9% ($p = 0.023$); men/women (165/337), 61.2%/61.5% ($p = 0.059$).

A complete overview of all univariate analysed factors and event-free probabilities is given in Table I.

Multivariate analysis

The multivariate Cox regression analysis with inclusion of the number of treatment series, age, photon energy, pain history, single dose and prior treatments revealed patients with only one treatment series ($p < 0.001$), an age >58 years ($p = 0.011$) and therapy with high voltage photons ($p = 0.050$) to be significant prognostic factors for pain relief. Specifically, as the expected number of treatment series was an independent prognostic factor: compared with the reference group of patients with one series, patients with two treatment series had a significantly worse prognosis (adjusted hazard ratio = 2.41; $p < 0.001$). This means that the estimated risk of pain existence or recurrence following radiotherapy is 2.41 times greater for a patient with two treatment series than for a patient with only one series (Figure 2). Furthermore, age was an independent prognostic parameter in the multivariate model: compared to the reference group of patients older than 58 years, patients ≤ 58 years had a significantly worse prognosis (adjusted hazard ratio = 1.71; $p = 0.011$) (Figure 3). And at last, patients with orthovoltage had a significantly worse prognosis than patients with high voltage in the multivariate model (adjusted hazard ratio = 1.51; $p = 0.050$) (Figure 4).

In contrast to the univariate analyses, pain anamnesis, dose regime and prior treatment were not of independent significant importance, but at least a borderline significance was present ($p < 0.15$). In Table II, the results of the multivariate analysis are represented.

Discussion

There is a long tradition for radiotherapy of benign degenerative lesions [6,24,33,37,39,41,55]. RT of benign diseases accounts for about 8% to 10% of all RT procedures in Germany [50]. Painful disorders in the locomotor system [41] represent as much as 70% of these indications.

The excellent pain response of patients with heel spurs after RT is confirmed by numerous studies. In these studies, the effectiveness of radiotherapy under orthovoltage as well as under megavoltage conditions is described [1,6,10,14,20,22,26,31,33–36,39,41,42,45,46,48,49,55]. The improvement rate ranged between 65% and 100%. An overview is given in Table III.

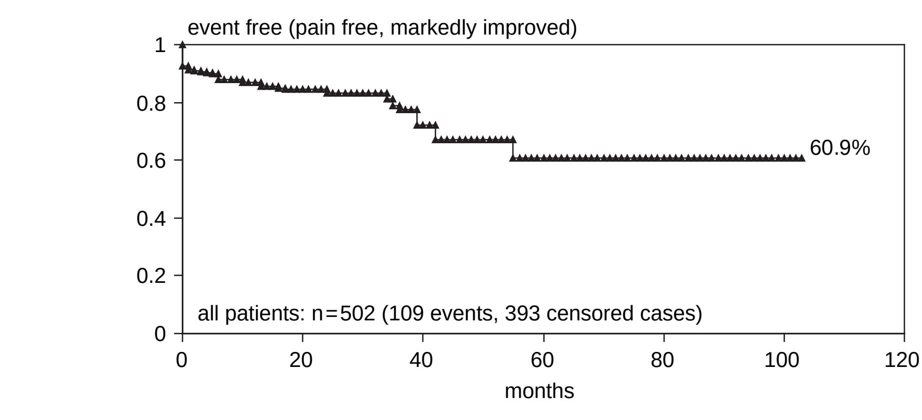

Figure 1. Kaplan-Meier curve for pain control of all patients (393 censored cases).

Table I. Univariate analyses of prognostic factors.

Variables	Number of patients	Event free probability (follow-up)	p-value
number of series			
two vs. one	88 vs. 414	32.2% (103 months) vs. 69.7% (103 months)	<0.001
age			
≤58 years vs. >58 years	266 vs. 236	47.9% (103 months) vs. 81.3% (103 months)	0.001
photon energy			
ortho voltage vs. high voltage	161 vs. 341	60.6% (103 months) vs. 67.9% (63 months)	0.019
pain anamnesis			
>6 month vs. ≤6 month	194 vs. 308	43.9% (86 months) vs. 76.3% (103 months)	0.001
dose regime (single dose)			
1.0 Gy vs.0.5 Gy	401 vs. 100	55.1% (103 months) vs. 86.2% (63 months)	0.009
prior treatment			
with vs. without	401 vs. 100	54.9% (103 months) vs. 83.1% (63 months)	0.023
gender			
female vs. male	337 vs. 165	61.5% (103 months) vs. 61.2% (63 months)	0.059

Unfortunately, the description of the patient groups and possible influencing factors is imprecise in some reports. Moreover, a number of different evaluation scores were used in the past.

Overall, it can be said that after a fast initial pain relief, the beneficial effect lasts up to several years. With a follow-up of 103 months, in our study the event-free probability (no residual pain or good pain relief) in accordance with Kaplan-Meier was 60.9%. Only few other studies have been able to report long-term results [34,42].

In patients with only one treatment series, the event-free probability was significantly higher than in patients with two series. Probably this is due to a negative selection of these patients. Response after the first treatment course is an important prognostic factor. Similar results were described by other authors [10,34,46].

Pretherapeutic age was a prognostic factor for the duration of the event-free period in univariate and multivariate analyses. Comparable data could not be found in the literature. It can be speculated that a changed nociception and pain behaviour during older age is responsible for these findings [9]. Biological studies showed that oxidative burst formation is impaired in the aged [4]. Eventually, the significantly better results in patients older than 58 years remain unclear.

In patients treated with 6–10 MV photons, the event-free probability was significantly better than in patients treated with 175 kV photons. Comparable data could not be found in the literature. Probably this is caused by a better and more homogeneous dose distribution achieved by using megavoltage units compared to orthovoltage conditions.

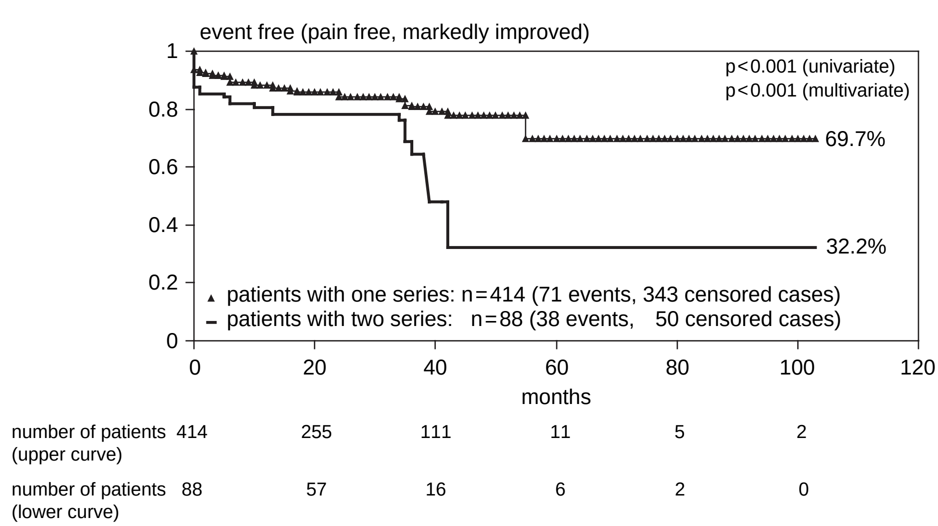

Figure 2. Univariate analysis (log-rank) for pain control related to number of treatment series (upper curve: 1 series [343 censored cases]; lower curve: 2 series [50 censored cases]).

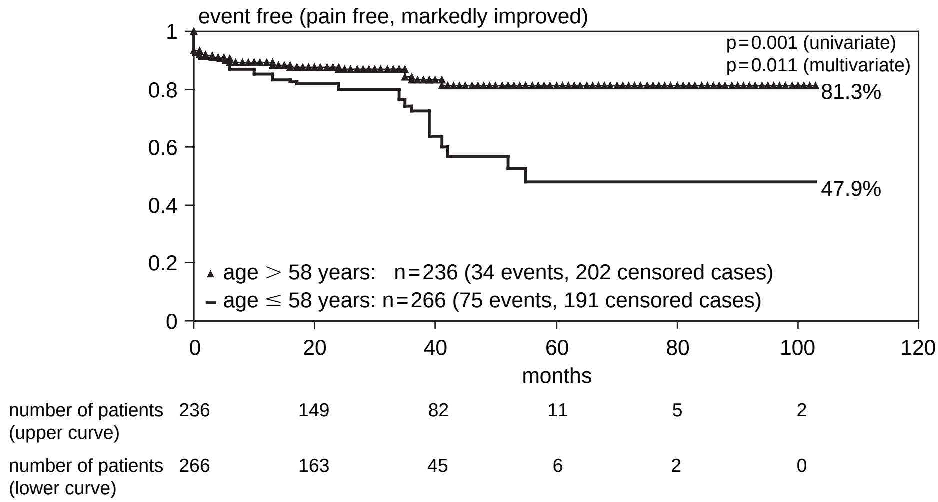

Figure 3. Univariate analysis (log-rank) for pain control related to age of patients (upper curve: >58 years [202 censored cases]; lower curve: ≤58 years [191 censored cases]).

In the prospective study by Seegenschmiedt et al., different RT dose regimens were evaluated [49]: In 72 cases, a total dose of 12 Gy was applied (two series of 6 × 1 Gy over two weeks), 50 patients received 10 × 0.3 Gy, and 48 cases 10 × 0.5 Gy. The best response was achieved with a total dose of 5 Gy delivered in single doses of 0.5 Gy. In our study, 86.2% of patients treated with this dose regime were event-free after five years. Higher doses with 3 × 1 Gy per week up to a total dose of 12 Gy did not contribute to the improvement of the response rate. In the long-term follow-up however, 5 Gy and 12 Gy proved to be better than a total dose of 3 Gy with single doses of 0.3 Gy. Single doses lower than 0.3 Gy are not recommended, as this dose is regarded as threshold for tissue alkalosis, which some authors see as the underlying cause for pain relief. Most authors recommend single doses of 0.3 to 0.5 Gy up to total dose of 3 to 6 Gy [34,42,49,53]. So far, no clear response rates have been observed with higher single or total doses [31,50,53].

Duration of pain before commencement of RT has been established as a prognostic factor for the event-free period in univariate analysis. Seventy six point three percent of our patients were event-free after a disease record of ≤6 months before radiotherapy, compared to 43.9% after a disease record of >6 months. These findings are also confirmed by Seegenschmiedt et al. [49].

A possible placebo effect of RT for pain treatment cannot be excluded. So far, there is no conclusive data available on the treatment of heel spurs. In one double-blinded study by Goldie et al. from the 1970s, a large variety of different degenerative skeletal diseases (among which were nine heel spurs)

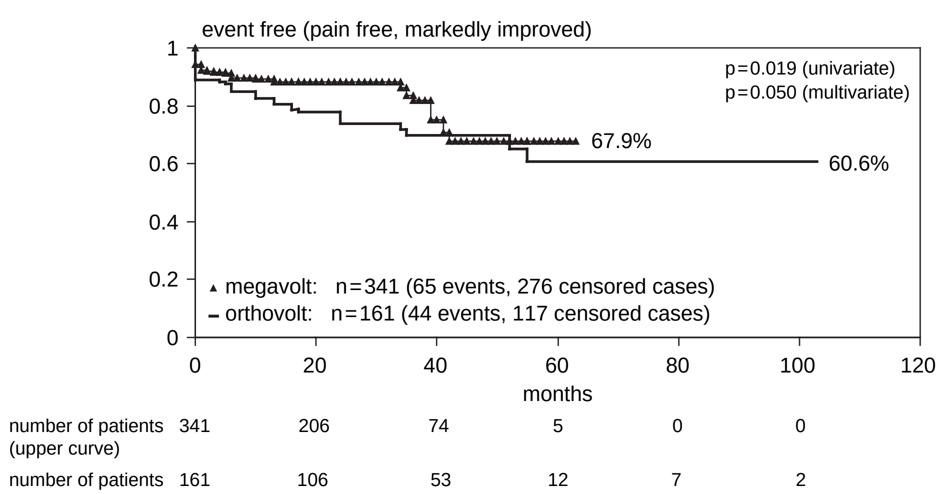

Figure 4. Univariate analysis (log-rank) for pain control related to photon energy (upper curve: megavolt [276 censored cases]; lower curve: orthovolt [117 censored cases]).

Table II. Multivariate analysis of prognostic factors.

Variables	Adjusted hazard ratio	95% confidence interval	p-value
number of series			
two vs. one*	2.41	1.62–3.60	<0.001
age			
≤58 years vs. > 58 years*	1.71	1.13–2.60	0.011
photon energy			
ortho voltage vs. high voltage*	1.51	1.0–2.28	0.05
pain anamnesis			
>6 month vs. ≤6 month*	1.42	0.95–2.10	0.085
dose regime			
1.0 Gy vs. 0.5 Gy*	1.7	0.86–3.35	0.127
prior treatment			
with vs. without*	1.57	0.91–2.71	0.107

* reference catagory.

were treated and analysed. Response rates for treated and untreated patients were 68% and 64%, respectively. Effectiveness of RT was considered questionable [11]. However, the study was rightly criticised for its inadequate study design, the marked flaws in outcome evaluation and the questionable results [30]. Overall, data on spontaneous pain regression in heel spurs are scarce. In general, the rates of spontaneous pain relief reported in literature range widely between 10% and 50% [31]. Furthermore, it should be taken into account, that the majority of patients are extensively pretreated. Therefore spontaneous pain regression is very unlikely [31,34].

These data also contrast with recent retrospective and prospective studies (Table III). A double-blinded study using sham irradiation might be able to answer this question. Moreover, a comparison of RT with competing treatments such as shock-wave therapy (lithotripsy) is still lacking [12]. For the latter, a long-term improvement in 2/3 of all patients has been reported [25,51]. For these treatment modalities, prospective comparative studies need to be conducted.

The precise pathophysiological mechanisms of pain relief after RT are still not well defined. Arthritis models using rabbits revealed an anti-inflammatory effect with decreasing synovitis after irradiation [52]. Older studies describe an influence on the vascular endothelium with improved tissue perfusion, destruction of inflammatory cells (in particular lymphocytes) with release of cytokines and proteolytic

Table III. Overview of pertinent literature.

Author	Patients	Heels	Type of radiotherapy	Response-rate (%)	CR (%)	PR (%)	NC (%)
Richarz (1924) [39]	5	5	OV	100	80	20	
Pannewitz (1933) [36]	88	88	OV	92			
Cocchi (1943) [6]	6	6	OV	83	33	50	
Mitrov (1967) [33]	1520	1520	OV	88	50	38	12
Zschache (1972) [55]	49	49	OV	86	12	74	14
Mantell (1978) [26]	17	26	240-300 kV	65	53	12	35
Basche (1980) [1]	102	102	120 kV	90	32	58	10
Sautter-Bihl (1993) [41]	15	15	HV	80	60	20	20
Schäfer (1995) [42]	18	21	Cobalt-60	67	58	8	33
Seegenschmiedt (1996) [49]	141	72 Pat 12 Gy / 98 Pat 3-5 Gy	200-250 kV	100/ 95	67 72	33 23	0 5
Oehler (2000) [35]	212	258	OV	88	81	7	12
Koeppen (2000) [22]	673	673	250 kV	78	13	65	22
Schreiber (2000) [48]	70	87	6 MV	86	67	29	14
Heyd (2001) [14]	105	127	6 MV	88	46	42	12
Glatzel (2001) [10]	141	161	175 kV	89	63	26	11
Schlehuber (2001) [45]	63	63	6 Mv	67	33	34	33
Mücke (2003) [34]	117	136	6 MV	90	75	15	10
Schneider (2004) [46]	141	161	OV	89	18	64	18
Kiffer (2004) [20]	29	29	MV	89	65	24	11
PCS Painful heel [31]	7947		HV, MV, OV, Co-60	70			15

enzymes, modulation of the vegetative nervous system, altering of the tissue pH and increased membrane permeability [27,52,53]. Other studies showed that there are also effects of low-dose ionising radiation on the molecular and cellular level involving adhesion molecules, cytokine expression and inflammation cascade [15,16,19,32,40]. Recent studies have given evidence that low-dose radiation may have an inhibitory effect on respiratory burst formation of neutrophilic granulocytes [29,43]. Most likely, irradiation does not act through a single mechanism but through a complex interaction of different effects.

Radiation side effects did not occur in any of our patients. This corresponds to the reported absence of chronic or acute adverse effects in the literature. Some authors describe an initial increase of pain symptoms after the first dose fractions. This is attributed to a transient local increase of acidosis [17,44].

Some colleagues from specialities other than radiotherapy are reluctant to recommend RT due to concerns about potential damage to gonads or tumour induction. However, so far no increased tumour rate has been reported in the literature for the chosen dose range [8,21,23,41].

In a literature review by Kim et al. [21] and Brady [3], no osteosarcoma is described after a fractioned application of 30 Gy over three weeks. Johansson et al. reported that the mean absorbed dose in red marrow is estimated at zero for patients in whom only distal parts of extremities were irradiated [18]. It may be useful to recall the epidemiological evidence that the attributable carcinogenic lifetime risk is considerably smaller at older age than earlier in life [5,8]. The applied gonad dose during the treatment of heel spurs is comparable to that of diagnostic imaging [13]. If standard radiation protection measures are taken (minimum field size, gonad shields etc.), the risk of RT in this subpopulation of mostly elderly patients can almost be neglected. Younger patients should be treated only in very exceptional cases and after careful evaluation of the potential risk compared with the expected benefit. The risks of pharmacological treatments such as NSAIDs must be also taken into account.

Conclusion

Overall low-dose RT is a very effective treatment for painful heel spurs both with orthovoltage and megavoltage units. No side effects have been observed. RT should not be regarded as a "last resort" treatment, and we recommend that the RT treatment should begin during the first six months of symptoms. Controlled prospective studies should assess the effect of RT by comparison with sham treatments to assess the possible role of placebo effects.

This paper is dedicated to Professor Manfred Strietzel in Rostock, one of Germany's renowned researchers on radiotherapy of benign diseases.

References

[1] Basche S, Drescher W, Mohr E. Ergebnisse der Röntgenstrahlentherapie beim Fersensporn. Radiobiol Radiother 1980;21:233–6.

[2] Boike Am, Snyder AJ, Roberto PD, Tabbert WG. Heel spur surgery. A transverse plantar approach. J Am Podiatr Med Assoc 1993;83:39–42.

[3] Brady LW. Radiation induced sarcomas of bone. Skeletal Radiol 1979;4:72–8.

[4] Braga PC, Sala MT, Dal Sasso M, Mancini L, Sandrini MC, Annoni G. Influence of age on oxidative bursts (chemiluminescence) of polymorphonuclear neutrophil leukocytes. Gerontology 1998;44:192–7.

[5] Broerse JJ, Snijders-Keilholz A, Jansen JT, Zoetelief J, Klein C, Seegenschmiedt MH. Assessment of a carcinogenic risk for treatment of Graves ophthalmopathy in dependence on age and irradiation geometry. Radiother Oncol 1999;53: 205–8.

[6] Cocchi U. Erfolge und Misserfolge bei Röntgenbestrahlung nichtkrebsiger Leiden. Strahlentherapie 1943;73:255–84.

[7] Dailey JM. Differential diagnosis and treatment of heel pain. Clin Podiatr Mes Surg 1991;8:153–66.

[8] Damber L, Larsson LG, Johansson L, Norin T. A cohort study with regard to the risk of haematological malignancies in patients treated with x-ray for benign lesions in the locomotor system. I. Epidemiological analyses. Acta Oncol 1995;34:713–9.

[9] Gagliese L, Melzack R. Age-related differences in the qualities but not the intensity of chronic pain. Pain 2003; 104:597–608.

[10] Glatzel M, Bäsecke S. Radiotherapy of the painful plantar heel spur. Benig News 2001;2:18–9.

[11] Goldie I, Rosengren B, Moberg E, Hedelin E. Evaluation of the radiation treatment of painful conditions of the locomotor system. Acta Radiol Ther Phys Biol 1970;9:311–22.

[12] Gross MW, Sattler A, Haake M, Schmitt J, Hildebrandt R, Muller H, et al. Die Wertigkeit der Strahlenbehandlung im Vergleich zur extrakorporalen Stoßwellentherapie (ESWT) beim Supraspinatussehnensyndrom. Strahlenther Onkol 2002;178:314–20.

[13] Hess F. Strahlentherapie gutartiger Erkrankungen. In: Scherer E, Hrsg. Strahlentherapie-Radiologische Onkologie. Berlin: Springer Press; 1980. p. 354–69.

[14] Heyd R, Strassmann G. Radiotherapy in the management of inflammatory calcaneal heel spurs: Results of a prospective study. In: Seegenschmiedt MH, Makoski HB, Hrsg. 15. Kolloquium Radioonkologie/ Strahlentherapie. Radiotherapie von gutartigen Erkrankungen. Altenberge: Diplodocus-Verlag; 2001. p. 173–83.

[15] Hildebrandt G, Seed MP, Freemantle CN, Alam CA, Colville-Nash PR, Trott KR. Mechanisms of the anti-inflammatory activity of low-dose radiation therapy. Int J Radiat Biol 1998;74:367–78.

[16] Hildebrandt G, Jahns J, Hindemith M, Spranger S, Sack U, Kinne RW, et al. Effects of low dose radiation therapy on adjuvant induced arthritis in rats. Int J Radiat Biol 2000;76: 1143–53.

[17] Hornykiewitsch Th. Physikalisch-chemische und histochemische Untersuchungen über die Wirkung der Röntgenstrahlen. Strahlentherapie 1952;86:175–206.

[18] Johansson L, Larsson LG, Damber L. A cohort study with regard to the risk of haematological malignancies in patients treated with x-ray for benign lesions in the locomotor system. II. Estimation of absorbed dose in the red bone marrow. Acta Oncol 1995;34:721–6.

[19] Kern P, Keilholz L, Forster C, Seegenschmiedt MH, Sauer R, Herrmann M. In vitro apoptosis in peripheral blood mononuclear cells induced by low-dose radiotherapy displays a discontinuous dose-dependence. Int J Radiat Biol 1999;75:995–1003.

[20] Kiffer J, Lynch R, Porter I. RE: F Schwarz et al.-are single fractions of radiotherapy suitable for plantar fasciitis? Australas Radiol 2004;484:529–30.

[21] Kim JH, Chu F, Woodard HQ, Melamed MR, Huvos A, Cantin J. Radiation induced soft tissue and bone sarcoma. Radiology 1978;129:501–8.

[22] Koeppen D, Bollmann G. Ein Beitrag zur Dosiswirkungsbeziehung bei der Röntgentherapie des Fersensporns. Strahlenther Onkol 2000;176 (Suppl 1):91.

[23] Levitt SH. Secondary malignancies after radiotherapy. In: Dunst J, Sauer R, Hrsg. Late sequelae in oncology. New York: Springer Press; 1995. p. 279–89.

[24] Lindner H, Freislederer R. Langzeitergebnisse der Bestrahlung von degenerativen Gelenkerkrankungen. Strahlentherapie 1982;158:217–23.

[25] Maier M, Steinborn M, Schmitz C, Stabler A, Kohler S, Pfahler M, et al. Extracorporal shock wave application for chronic plantar fasciitis associated with heel spurs: Prediction of outcome by MRI. J Rheumatol 2000;27:2455–65.

[26] Mantell BS. Radiotherapy for painful heel syndrome. Br Med J 1978;2:90–1.

[27] Mantell BS. The management of benign conditions. In: Radiotherapy clinical practice. London: Butterworths Press; 1986. p. 384–99.

[28] Mau C, Mau H. Fersenbeinsporne. In: Hohmann G, Hackenbroch M, Lindemann K, Hrsg. Handbuch der Orthopädie. Stuttgart – New York: Thieme Press; 1992. p. 987–92.

[29] Micke O, Haidenberger A, Auer T, Egger S, Seegenschmiedt MH, Hengster P, et al. Irradiation causes biphasic neutrophilic granulogy phagocytic function. Strahlenther Onkol 2005;181:313–8.

[30] Micke O, Seegenschmiedt MH. German Working Group on Radiotherapy in Germany. Consensus guidelines for radiation therapy of benign diseases: A multicenter approach in Germany. Int J Radiat Oncol Biol Phys 2002;52:496–513.

[31] Micke O, Seegenschmiedt MH. Radiotherapy in painful heel spurs (plantar fasciitis)-results of a national patterns of care study. Int J Radiat Oncol Biol Phys 2004;58:828–43.

[32] Micke P, Blaukat A, Micke O. Effect of cobalt-60 irradiation on bradykinin B2 receptor expression on human HF-15 cells. EXCLI Journal 2033;2:52–7.

[33] Mitrov G, Harbov I. Unsere Erfahrungen mit der Strahlentherapie von nichttumorartigen Erkrankungen. Radiobiol Radiother 1967;8:419.

[34] Muecke R, Schoenekaes KG, Micke O, Seegenschmiedt MH, Berning D, Heyder R. Low dose radiotherapy for painful heel spur-retrospective study of 117 patients. Strahlenther Onkol 2003;179:774–8.

[35] Oehler W, Hentschel B. Niedrigdosierte analgetische Radiotherapie von Arthrosen. Ärztebl Thür 2000;11:92–5.

[36] Pannewitz G, von. Die Röntgentherapie der Arthritis deformans. In: Holfelder H, Holthausen H, Jüngling O, Martius H, Schinz HR, Hrsg. Ergebnisse der medizinischen Strahlenforschung. Leipzig: Thieme Press; 1933. p. 61–126.

[37] Plettner P. Cited by: Schreiber A, Zollinger H. Entzündungen /Fersenbeinsporne. In: Hohmann G, Hackenbroch M, Lindemann K, Hrsg. Orthopädie in Klinik und Praxis. Stuttgart-New York: Thieme Press; 1985. p. 441–5.

[38] Prichasuk S, Subhadrabandhu T. The relationship of pes planus and calcaneal spur to plantar heel spur. Clin Orthop 1994;306:192–6.

[39] Richarz A. Die Röntgenbehandlung der Epikondylitis und Kalkaneodynie. Fortschr Röntgenstr 1924;32:460.

[40] Roedel F, Kamprad F, Sauer R, Hildebrandt G. Funktionelle und molekulare Aspekte der antiinflammatorischen Wirkung niedrig dosierter Radiotherapie. Strahlenther Onkol 2002;178:1–9.

[41] Sautter-Bihl ML, Liebermeister E, Scheurig H, Heinze HG. Analgetische Bestrahlung degenerativer, entzündlicher Skeletterkrankungen. Dtsch Med Wschr 1993;118:493–8.

[42] Schaefer U, Micke O, Glashoerster M, Rube C, Prott FJ, Willich N. Strahlentherapeutische Behandlung des schmerzhaften Fersenbeinsporns. Strahlenther Onkol 1995;171: 202–6.

[43] Schaue D, Marples B, Trott KR. The effects of low-dose X-irradiation on the oxidative burst in stimulated macrophages. Int J Radiat Biol 2002;78:567–76.

[44] Scherer E. Biologische Grundlagen und neuere Ergebnisse der Entzündungsbestrahlung und der funktionellen Röntgentherapie. Strahlentherapie 1955;97:349–61.

[45] Schlehuber E, Lochhas G, Prott FJ, Scharding BJ, Scüller P, Micke O. Radiotherapy of periarthrosis humeroscapularis (PHS), epicondylopathia humeri (EPH) and painful heel spur with 6 MeV photons. Int J Radiat Oncol Biol Phys 2001;513 (Suppl 1):364.

[46] Schneider O, Stueckle CA, Bosch E, Gott C, Adamietz IA. Effectiveness and prognostic factors of radiotherapy for painful heel spurs. Strahlenther Onkol 2004;180:502–9.

[47] Schreiber A, Zollinger H. Entzündungen /Fersenbeinsporne. In: Hohmann G, Hackenbroch M, Lindemann K, Hrsg. Orthopädie in Klinik und Praxis. Stuttgart – New York: Thieme Press; 1985. p 441–5.

[48] Schreiber H, Böhnlein G. Strahlentherapie des schmerzhaften Fersensporns. In: Seegenschmiedt MH, Makoski HB, Hrsg. 10. Kolloquium Radioonkologie/ Strahlentherapie. Radiotherapie von gutartigen Erkrankungen. Altenberge: Diplodocus-Verlag; 2000. p. 186.

[49] Seegenschmiedt MH, Keilholz L, Katalinic A, Stecken A, Sauer R. Heel spur: Radiation therapy for refractory pain-Results with three treatment concepts. Radiology 1996;200: 376–83.

[50] Seegenschmiedt MH, Micke O, Willich N. Radiation therapy for nonmalignant diseases in Germany-Current concepts and future perspectives. Strahlenther Onkol 2004; 180:718–30.

[51] Sistermann R, Katthagen BD. Experience and results after 5 years using extracorporal shock waves to treat plantar heel spur – A follow-up after 36.9 months. Z Orthop 1998;136: 402–6.

[52] Steffen C, Mueller C, Stellamor, Zeitlhofer J. Influence of x-ray treatment on antigen-induced experimental arthritis. Ann Rheum Dis 1982;41:532–7.

[53] Trott KR. Therapeutic effects of low radiation doses. Strahlenther Onkol 1994;170:1–12.

[54] Williams PL. The painful heel. Br J Hosp Med 1987;38: 562–3.

[55] Zschache H. Ergebnisse der Röntgenschwachbestrahlung. Radiobiol Radiother 1972;13:181–6.