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Epicondylopathia humeri (EPH) and peritendinitis humeroscapularis (PHS): evaluation of radiation therapy long-term results and literature review

M. Heinrich Seegenschmiedt[a,b,*], Ludwig Keilholz[a]

[a]*Department of Radiotherapy, University of Erlangen-Nuremberg, Universitätsstraße 27, 91054 Erlangen, Germany*
[b]*Department of Radiation Oncology and Nuclear Medicine, Alfried Krupp von Bohlen und Halbach Hospital, D-45117 Essen, Germany*

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Abstract

Background: The effectiveness of radiotherapy (RT) for degenerative inflammatory disorders has been clinically documented in historical studies, but long-term follow-up and assessment with objective criteria are still not available.

Patients and methods: From 1986 to 1991, 200 consecutive patients with symptomatic epicondylopathia humeri (EPH, $n = 104$) and peritendinitis humeroscapularis (PHS, $n = 96$) were referred to our clinic. All patients were refractory to conventional therapy prior to irradiation. One hundred fifty-six patients with 192 sites (due to bilateral symptoms) received a full treatment course and were available for long-term follow-up, i.e. 83 patients with 93 elbows and 73 patients with 89 shoulders. The treatment response was evaluated with regard to pain symptoms grouped into five categories (pain at strain, pain at night, persistent pain during daytime, pain at rest and morning stiffness) and four grades (none, mild, moderate and severe) and with regard to established orthopedic scores (Morrey score and Constant and Murley score). The analysis was performed before and 6 weeks after RT and at last follow-up. All joints received two RT series applied in three weekly fractions (EPH, 6×1 Gy (total 12 Gy); PHS, 6×0.5 Gy (total 6 Gy)). The second RT series started 6 weeks after the first RT series. The minimum follow-up was 1 year for both groups and the mean follow-up reached 4 years (range 1–8 years).

Results: Fifty elbows (43 patients) and 44 shoulders (39 patients) achieved complete pain relief in all pain categories; 24 elbows and 28 shoulders substantially improved, i.e. had only minor symptoms. Thus, 74 elbows and 72 shoulders responded to RT. Nineteen elbows (17 patients) had surgery after RT due to persisting symptoms or subjective dissatisfaction; 17 shoulders (12 patients) were non-responders and five of those were operated on; seven elbows and one shoulder were completely free of pain after surgery. The mean Morrey score improved by 18 points (from 78 to 96) and the mean Constant and Murley score improved by 48 points (from 18 to 66). Two cases worsened according to the Morrey score and one case worsened according to the Constant and Murley score. Bi- and multivariate analysis revealed two factors with negative prognostic value on treatment outcome, i.e. EPH, long symptom interval prior to RT and long-term immobilization with plaster ($P < 0.05$) and PHS, long symptom interval prior to RT and lack of pain intensification during the first RT course ($P < 0.05$) were poor prognostic factors.

Conclusion: RT is highly effective for refractory EPH and PHS. Structured pain scores and quantitative orthopedic scores are important for evaluation. Prognostic factors for outcome can be established. Due to minimal side effects and low costs, RT represents an excellent treatment compared to conventional methods of treatment and surgery in the chronic disease. © 1998 Elsevier Science Ireland Ltd.

Keywords: Benign diseases; Epicondylopathia humeri; Peritendinitis humeroscapularis; Insertion tendonitis; Radiotherapy; Orthovoltage radiotherapy

1. Introduction

Epicondylopathia humeri and peritendinitis humeroscapularis are degenerative disorders of the connective tissue of the involved tendon insertion zones of shoulder and elbow. Epicondylopathia humeri (EPH) occurs with pain at the lateral (tennis elbow) or medial epicondylus (pitchers or golfers elbow). In some European countries chronic refractory EPH is regarded as an occupational illness. Historically the terms writers cramp [63], occupational neuralgia [5], tennis elbow or epicondylitis [31,32] have been used. The modern term epicondylopathia [10] signals a better under-

* Corresponding author.

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standing of the differential diagnosis; insertion tendonitis is also referred to in the modern literature. Patients are about 45 years old (range 30–55 years) [19]. Different causes of the disease are discussed, i.e. mechanical causes [31,32, 42,45,49], neuro-irritative causes at the elbow (arthrogenic factors) or spinal column (spondylogenous factors) [4,42,60,85] and functional neurogenic causes [9,67,80]. However, a morphological correlate is rarely to be found [78]. The ligamentum anulare syndrome, the tunnel syndrome of the n. radialis, the impingement syndrome of the olecranon and the cervical spine syndrome have to be clinically differentiated from the typical EPH.

The typical pain is triggered by (a) fine-tuned motions, (b) rough motions, e.g. butchers or carpenters [62], (c) extreme straining of the forearm or awkward movements in sports without training [15,34,41], (d) compression neuropathy [36], (e) mechanical irritations of the bursa of the capitulum radii [8] and (f) radial nerve entrapment syndrome [13,85]. Several clinical tests involving provocation of pain in the musculature of the forearm substantiate the diagnosis, i.e. the Talbot pressure test [69], the Coenen finger snapping test [12] and the Thomsen hand grip [70].

The periarthropathia humeroscapularis (PHS) embraces many disorders of the shoulder joint, i.e. peritendinitis or insertion tendinitis (infra- and supraspinal, subscapular and biceps longus muscles) and bursitis [44,77,84]. The peritendinitis has to be clinically differentiated from bursitis calcarea, (sub)total rupture of involved tendons, impingement syndrome and neurologic disorders of the brachial plexus. The typical clinical symptoms include (sub)acute inflammatory reactions of the connective tissue around the joint. They cause functional restrictions (preferentially abductional and rotational movements) and persistent pain symptoms and alter occupational activities during daytime and disturb the night rest. The working arm is mostly affected in connection with occupational, professional and sports activities indicating the possible mechanical causes, but other causes are also discussed. Consequently most professional and leisure activities are impaired and long-term absence from work and early retirement lead to high socioeconomic costs in both EPH and PHS.

Different treatments have been chosen for both disorders depending upon personal preference. Despite proven success of radiotherapy (RT) in former years, it is only used as last resort for refractory pain in EPH [11,20,23,28,30,35,37, 39,48,61] [64,76,77,83,86] and PHS [1,3,17,24–27,29,30, 33,47,48,51,64,71,86]. In recent decades ionizing radiation has been disregarded due to some critical reports about possible tumorigenesis. However, these reports are mostly related to cases treated for ankylosing spondylitis in young patients [7], which have been poorly documented and were not related to the applied RT dose and target volume. Thus, today local or systemic antiphlogistics are preferred for the treatment of EPH and PHS, but refractory patients cascade through several other treatments, e.g. ultrasound or acupuncture.

All 200 patients of this study underwent several therapies before RT, but they were considered to be refractory. The study was designed to assess the effect of RT in long-term outcome and analyze new quantitative methods of pain and functional assessment in these disorders.

2. Patients, materials and methods

2.1. Patient parameters

From 1986 to 1991, 200 consecutive patients with symptomatic EPH ($n = 104$) and PHS ($n = 96$) were referred to our clinic. All patients were refractory to conventional therapies prior to irradiation. One hundred fifty-six (78%) patients with 192 sites (due to bilateral symptoms) were included in this study because of full compliance with the prescribed treatment schedule and availability for long-term follow-up assessment. Forty-four patients were not available; 28 patients stopped treatment after the first treatment course due to satisfaction ($n = 20$) or dissatisfaction ($n = 8$) with treatment outcome, 11 patients refused long-term follow-up assessment and five patients were deceased at the time of final examination.

Eighty-five (82%) EPH patients and 73 (75%) PHS patients received two RT courses and completed all planned follow-up examinations. Due to bilateral symptoms a total of 93 elbows and 89 shoulders were evaluated, respectively. The related disease and pretreatment parameters are summarized in Table 1 . Besides age distribution, duration of symptoms and type of pain onset no significant differences were found between the EPH and PHS populations.

Among EPH patients, 45 had stopped or changed their professional activities, while 14 had already retired due to pain symptoms. Among PHS patients, 61 were severely disabled in their occupational activities. Sixty-eight EPH cases had been pretreated with three or more therapeutic measures, 21 cases had undergone two therapeutic attempts and in four cases only one type of therapy (all surgery) had been carried out. No PHS case had previously undergone surgery. Three PHS cases had been irradiated with 6 Gy each at 8, 10 and 15 years prior to the actual RT course. A total of 18 PHS cases had received three or more therapeutic measures.

2.2. Clinical assessment

The clinical examination aimed to exclude all other possible reasons of pain symptoms related to elbow and shoulder pain, e.g. cervical spine syndrome. Only patients with typical insertion tendinitis (EPH, PHS) were included in this study. Patients with generalized polyarthritis, local arthritis or conspicuous neurological conditions in affected arms were excluded. Patients were examined according to an interdisciplinary program prior to RT, 6 weeks after RT and at last follow-up in close cooperation with orthopedists.

Table 1
Disease and pretreatment parameters

Parameter	Epicondylopathia humeri (EPH) (N = 85; n = 93)	Peritendinitis humeroscapularis (PHS) (N = 73; n = 89)
No. patients/cases	85/93 elbows	73/89 shoulders
Age (years)		
Mean	45 ± 12	59 ± 15
Median	47	56
Range	30–75	33–84
Gender (female/male)	42/43	40/33
Distribution of working/support arm (cases)		
Right/left	57/20	38/19
Bilateral	8	16
Working/support arm	75/18	62/27
Duration of symptoms (months)		
Mean	15 ± 14	28 ± 24
Median	12	18
Range	6–86	3–204
Type of pain onset (cases) ((sub)acute/chronic)	41/52, pain symptoms triggered by: professional activities (n = 46), sport or leisure activities (n = 23), occurred spontaneously (n = 11), related to former trauma (n = 3)	32/41, pain symptoms were not triggered: mostly non-professionals without preferential sports or any leisure activities, no former trauma cases included
Pain localization[a]	Limited to elbow (n = 41), extension distally into forearm (n = 46)/hand (n = 42), extension proximally into shoulder (n = 27)	Limited to shoulder (n = 46), extension distally into upper arm/elbow (n = 31), extension proximally into nape (n = 12)
Pretreatment[a]	Local injections: steroids (n = 69), anesthetics (n = 46), NSAD (n = 35); oral steroids/NSAD (n = 74); immobilization procedures: plaster (n = 33), taping (n = 59); gymnastic and physical therapy (n = 81); acupuncture (n = 6); local surgery (n = 23); local radiotherapy (none)	Local injections: steroids (n = 62), anesthetics (n = 52), NSAD (n = 8); oral steroids/NSAD (n = 86); immobilization procedures (none); gymnastic and physical therapy (n = 82); acupuncture (n = 3); local surgery (none); local radiotherapy (n = 3)

[a]Several options possible.
NSAD, non-steroidal anti-inflammatory drugs.

Twenty-three EPH cases had conspicuous radiological findings prior to RT, i.e. insertion spur (n = 10), free ossifications at the lateral or medial epicondylus (n = 22) or triceps muscle insertion (n = 12), osteophytes (n = 4), or indirect signs of joint effusion (n = 1). Thirty-one PHS cases had conspicuous radiological findings, i.e. calcifications in the tendinous insertion zones. However, for both disorders the degree of pain symptoms was independent of the radiological findings.

The subjective pain symptoms were classified into five categories. While pain at strain (S) and morning stiffness (M) were regarded as acute pain symptoms, pain at night (N), pain at rest (R) and persistent pain during daytime (D) were regarded as chronic pain symptoms. In addition, in each pain category the intensity of pain was grouped into four grades according to the patient's subjective impression, i.e. no pain (0 points), mild pain (1 point), moderate pain (2 points) and severe pain (3 points). Thus, a total pain score was calculated according to the following formula

$$\sum = (n \times S) + (n \times M) + (n \times N) + (n \times R) + (n \times D)$$

with n = 0–3. This pain score was calculated prior to RT and after RT in long-term follow-up and was analyzed together with international orthopedic scoring systems of the elbow according to Morrey et al. [50] (M-score, Table 2) and of the shoulder according to Constant and Murley [14] (C-score, Table 3). For EPH, pain categories prior to RT were distributed as follows: pain at strain (n = 90, 97%), pain at night (n = 65, 70%), persistent pain during daytime (n = 60, 65%), pain at rest (R) (n = 63, 68%) and morning stiffness (n = 30, 32%). For PHS, a very similar distribution of pain categories was noted. Pain and reduced daily activities were regarded as subjective symptoms, while loss of strength and function were considered as objective findings within these scoring systems.

2.3. Radiotherapy

Affected elbows and shoulders were irradiated with patients in a comfortable sitting position for EPH patients and in a standing position for PHS patients. Radiation safety measures included gonad protection using a lead apron. The head and trunk were turned away from the side of the radiation source. All other radiotherapy details are compiled in Table 4. Gymnastic and/or physiotherapy and physical rest were recommended parallel to the RT course.

Table 2

Elbow scoring system (M-score) according to Morrey et al. [50]

Pain assessment (maximum 30 points)	Points
None	30
Slight, with continuous activity and no medication	25
Moderate, with occasional activity and some medication	15
Moderately severe, much pain and frequent medication	10
Severe, constant pain and markedly limited activity	5
Complete disability	0
Daily activities/function (maximum 12 points)	
Use back pocket	1
Rise from chair	1
Carry weight of 10–15 lbs	1
Dress	1
Perineal care	1
Wash opposite axilla	1
Pulling	1
Throwing	1
Eat with utensil	1
Comb hair	1
Do usual work	1
Do usual sports	1
Strength (maximum 15 points)[a]	
Flexion	5
Extension	4
Pronation	3
Supination	3
Motion (neutral zero method) (maximum 37 points)	
Extension from 90° to: (8 points)	
0–10°	8
11–30°	7
31–50°	5
51–70°	2
>70°	0
Flexion from 0° to: (17 points)	
0–30°	0
31–50°	3
51–70°	6
71–90°	9
91–100°	11
101–110°	13
111–120°	15
>120°	17
Pronation (6 points)	
<15°	0
15–30°	1
31–45°	2
46–60°	3
61–75°	4
76–90°	5
>90°	6
Supination (6 points)	
<15°	0
15–30°	1
31–45°	2
46–60°	3
61–75°	4
76–90°	5
>90°	6
Instability (maximum 6 points)	
Anterior/posterior (3 points)	
None	3
Mild	2
Moderate	1
Severe	0
Medial/lateral (3 points)	Points
None	3
Mild	2
Moderate	1
Severe	0

[a]Measurement by pondmeter with maximum 7.5 kg; original text version contains no information about the measurement procedure.

Table 3

Shoulder scoring system (C-score) according to Constant and Murley [14]

Pain assessment (maximum 15 points)	Points
None	15
Mild	10
Moderate	5
Severe	0
Daily activities/function (maximum 10 points)	
Full work possible	4
Unaffected sleep	2
Full recreation possible	4
Arm positioning (maximum 10 points)	
Up to the waist	2
Up to the xiphoid	4
Up to the neck	6
Up to the top of the head	8
Above the top of the head	10
Strength (maximum 25 points)	
Measurement by pondmeter in 90° arm abduction (i.e. lateral elevation)[a]	
Motion (neutral zero method) (maximum 40 points)	
Forward elevation flexion (10 points)	
0–30°	0
31–60°	2
61–90°	4
91–120°	6
121–150°	8
151–180°	10
Lateral elevation abduction (10 points)	
0–30°	0
31–60°	2
61–90°	4
91–120°	6
121–150°	8
151–180°	10
External rotation (10 points)	
Hand behind head	
with elbow held forward	2
with elbow held backward	2
Hand on top of head	
with elbow held forward	2
with elbow held backward	2
Full elevation from on top of head	2
Internal rotation (10 points)	
Dorsum of hand	
to lateral thigh	0
to buttock	2
to lumbosacral junction	4
to waist (3rd lumbar vertebra)	6
to 12th dorsal vertebra)	8
to interscapular region	10

[a]Modified international weight system, 0.5 kg = 1 point; original text version, 1 lbs (English weight measure, 0.454 kg).

Table 4
Radiation treatment prescription parameters for EPH and PHS

RT parameters	Epicondylopathia humeri radialis	Epicondylopathia humeri ulnaris	Peritendinitis humeroscapularis
Target volume	Radial epicondylus	Ulnar epicondylus	Whole shoulder joint
Treatment portal	Single portal (radial) (6 × 8 cm) AP arrangement	Single portal (ulnar) (6 × 8 cm) AP arrangement	Parallel opposed portals (10 × 15 cm) AP/PA arrangement
SSD (cm)	40	40	40
Dose reference point (cm)	0.5	0.5	Midplane dose (~5–6)
Energy level (kV/mAs)	120/20	120/20	250/15
Beam filtration	4 mm Al	4 mm Al	1 mm Cu
Prescribed RT schedule	6 × 1 Gy (1 series), 2–3 fractions/week	–	6 × 0.5 Gy (1 series), 2–3 fractions/week
Total prescribed dose	12 Gy (2 series)	–	6 Gy (2 series)
Prescribed treatment timing	1st series (within 2–3 weeks), 2nd series after a treatment break of 6 weeks		–

2.4. Evaluation

Minimum follow-up was 1 year for both groups and mean follow-up reached 4 years (range 1–8 years). Response to RT was assesses by comparing the M-score and the C-score prior to RT with corresponding scores in short- and long-term follow-up. In addition, the total pain score was evaluated; the complete disappearance of all pain symptoms and re-achievement of normal joint function was classified as complete response (CR), pain relief by more than 50% or reduction of all pain categories to a maximum of mild pain (1 point) with functional improvement was scored as partial response (PR) and pain relief ≤50% or reduction of pain categories to a maximum of moderate pain (2 points) with functional improvement was scored as minor response (MR). All cases without improvement in any of the pain categories or those who underwent surgery after RT were scored as non-responders (NR). The statistical description of all relevant subjective and objective patient and disease parameters included median, mean, standard deviation and range for continuous variables and absolute and relative values for categorical variables. Differences between frequencies of groups were analyzed with Fisher's exact test and the χ^2-test. Mean values of group frequencies were analyzed with Student's *t*-test. Dependencies of continuous variables were measured with Pearson's coefficient [2].

3. Results

3.1. Epicondylopathia humeri (EPH)

Forty-three of 85 (51%) EPH patients or 50 of 93 (54%) elbows achieved complete response and 19 (20%) cases experienced partial response, i.e. had only mild pain in individual or all pain categories. Thus, 69 (74%) cases yielded a very good or good response to RT. An additional 16 (17%) cases reached minor response (MR); only eight (8%) cases had no improvement (NR) or progressed during treatment and thereafter.

3.2. Peritendinitis humeroscapularis (PHS)

Thirty-five of 73 (48%) PHS patients or 44 of 89 (49%) shoulders achieved complete response in all pain categories. Twenty-three (26%) cases experienced partial response, i.e. had only mild pain in individual or all pain categories. Thus, 67 (75%) cases yielded a very good or good response to RT. An additional five (6%) cases reached a minor response and only 17 (19%) cases had no response or progressed during follow-up.

3.3. Development of individual pain categories

With regard to the individual pain categories a significant improvement was observed between the original findings prior to RT and the findings at last follow-up ($P < 0.05$). The separation between the two acute pain categories (pain at strain (*S*) and morning stiffness (*M*)) and the three chronic pain categories (pain at rest (*R*), pain at night (*N*) and persistent pain during daytime (*P*)) is reflected in the different correlations between these categories. For EPH cases, the chronic pain categories *N*, *R* and *P* were closely correlated between each other (all *R*-coefficients >0.6), but not with the acute pain categories *S* and *M* (Table 5). Very similar findings were observed for the pain development in long-term follow-up for PHS cases when compared to the initial findings ($P < 0.05$). Thus, these categories of pain symptoms can be used for a better differentiation of symptoms prior to and after RT. The complete response of the individual pain categories was much higher than the overall treatment response, which reflected the results of all pain categories. For EPH, 53 of 90 (59%) cases with pain at strain (*S*) became completely free of pain symptoms and accordingly 51 of 65 (79%) cases with pain at night (*N*), 49 of 58 (84%) cases with persistent pain during daytime (*D*), 51 of 64 (80%) cases with pain at rest (*R*) and 22 of 27 (81%) cases with morning stiffness (*M*) became completely free of pain symptoms. The response pattern for PHS patients was similar.

Response to RT could be predicted from the initial change of pain symptoms during the first RT course. For

Table 5
Correlation of pain categories prior to RT and at last follow-up (for EPH, $n = 85$)[a]

Pain categories	*S*	*N*	*R*	*D*	*M*
Pain at strain (*S*)	**1.000**	–0.045, 0.590	–0.176, 0.429	0.079, 0.544	–0.360, 0.294
Pain at night (*N*)	–	**1.000**	**0.622**, **0.645**	**0.758**, **0.695**	0.262, 0.467
Pain at rest (*R*)	–	–	**1.000**	**0.751**, **0.663**	0.467, 0.179
Persistent pain during daytime (*D*)	–	–	–	**1.000**	0.274, 0.546
Morning stiffness (*M*)	–	–	–	–	**1.000**

Correlation coefficients prior to RT are listed first and those at last follow-up are listed second in each cell.
All *R*-coefficients >0.6 (in bold) are regarded as highly correlated. The chronic pain categories *N*, *R* and *D* yield the highest correlations among each other.
[a]For patients with bilateral symptoms only values of the working arm were respected.

PHS, 21 of 41 (51%) cases with an initial pain intensification during the first RT series finally improved during the following weeks and in long-term follow-up only three (7%) non-responders were observed in this group; in contrast, only 12 of 48 (25%) cases with no intensified pain symptoms during the first RT series improved during the following weeks and in long-term follow-up 14 (29%) became non-responders ($P < 0.05$). A similar statistically significant result was obtained for EPH cases. This response pattern was a major reason for 28 patients to stop treatment after the first RT series, either due to subjective satisfaction ($n = 20$) or subjective dissatisfaction ($n = 8$) with the achieved treatment outcome.

3.4. Change of orthopedic scores

The changes of the Morrey score and the Constant and Murley score during follow-up are compiled in Table 6. For EPH cases the mean Morrey score improved by a total of 18 points (from 78 prior to RT to 96 at last follow-up) ($P < 0.05$). The improvement was mostly related to reduced pain (+11 points), better range of movement (+2 points) and improved daily functions (+4 points); strength (+1 point) and joint instability (±0) did not contribute to the improvement. According to the M-score only two cases worsened by 2 or 3 points and both received a salvage operation. All other cases had an improved M-score including all those patients who had claimed to have a dissatisfactory outcome. For PHS, the mean Constant and Murley score improved by a total of 48 points (from 18 prior to RT to 66 at last follow-up) ($P < 0.05$). The improvement was mostly related to reduced pain (+8 points), better range of movement (+18 points), improved daily functions (+11 points) and especially regained strength (+11 points); joint instability (±0) did not contribute to the improvement. According to the C-score only one case worsened by 23 points; he received no salvage operation in long-term follow-up.

3.5. Treatment failures

Seventeen (18%) EPH patients (19 elbows) and five (7%) PHS patients (five shoulders) had salvage surgery after RT during follow-up and were considered as non-responders. Salvage surgery was justified either due to persisting symptoms or due to dissatisfaction with outcome. After surgery nine EPH and one PHS case improved, while 10 EPH and four PHS cases experienced only slight or no improvement. The mean elapsed time from RT to the time of salvage surgery was short (mean 7 ± 6 months, median 6 months, range 0.5–24 months). In long-term follow-up only two EPH cases (relapse at 17 and 31 months) and three PHS cases (relapse at 18, 23 and 29 months) relapsed after a

Table 6
Change of mean Morrey elbow and Constant and Murley shoulder score during follow-up

Score categories (maximum points per category)	EPH ($N = 85$, $n = 93$)[a]		*P*-value	PHS ($N = 73$, $n = 89$)[a]		*P*-value
	Prior to RT	Last follow-up		Prior to RT	Last follow-up	
Pain (M, 30; C, 15)	17	27	*	3	11	**
Strength (M, 15; C, 25)	14	15	NS	6	17	**
Mobility of joint (M, 37; C, 40)	34	37	*	4	22	**
Instability of joint (M, 6; C, 0)	6	6	NS	–	–	–
Daily functions (M, 12; C, 20)	7	11	*	5	16	**
Total change of M-/C-score	78	96	**	18	66	**

NS, non-significant ($P>0.05$); M, Morrey Score; C, Constant and Murley score.
*Differences of the single M-score criteria pain, mobility of joint and daily functions prior to RT and at last follow-up are significant ($P < 0.05$).
**Differences of the total M-score and of the total C-score and differences of the single C-score criteria pain, strength, mobility of joint and daily functions prior to RT and at last follow-up are highly significant ($P < 0.01$).
[a]For patients with bilateral symptoms only values of the working arm were respected for the comparative statistical analysis.

mean period of 2 years. After a minimum follow-up of 4 years no relapse was observed in 41 of 93 (44%) EPH cases and 32 of 89 (36%) PHS cases with adequate follow-up.

3.6. Treatment toxicity

No acute or chronic radiation side-effects and no secondary malignancies were observed in short- and long-term follow-up, although the observation time may still be too short for long term events.

3.7. Prognostic parameters

With regard to complete pain relief (CR) as the end-point, the following parameters had negative prognostic impact in uni- and bivariate analysis of EPH: symptom duration prior to RT >12 months, immobilization with plaster, severe pain at night and during daytime and specific subjective and objective findings of the M-score ($P < 0.05$). In multivariate analysis, the only independent prognostic factors were duration of symptoms and immobilization with plaster ($P < 0.05$). For PHS, bi- and multivariate analysis revealed two factors with negative prognostic impact on treatment outcome, i.e. symptom duration prior to RT >12 months and lack of pain intensification during the first RT course ($P < 0.05$).

4. Discussion

Treatment of painful degenerative disorders like insertion tendinitis is not a foremost task of the radiooncologist who is specialized in treating malignant tumors, but represents an important clinical field of the therapeutic radiologist in some parts of the world. One US reference [55] which summarized a national survey on treatment policies for benign diseases did not support the use of RT for insertion tendinitis and argued that randomized studies failed to show a different response rate between irradiated and unirradiated groups [22,56,72]. In contrast, another reference book [17] and many studies in EPH [11,20,30,35,37,48,64,65,76, 77,83] (Table 7) and PHS [3,25,30,33,38,47,48,51,59,64,65, 73–75,83,86] (Table 8) have reported favorable results for RT of subacute and chronic painful disorders.

4.1. Biological aspects

Theoretical aspects of RT for benign diseases have been summarized by Trott [71], but he stated a lack of reasonable radiobiological data on assumed radiobiological targets and mechanisms [65]. While few experimental data explain the analgesic effects of ionizing radiation for degenerative/inflammatory disorders, many theories have been discussed [71], i.e. (a) the impact on tissue perfusion and vascular endothelia (perfusion theory), (b) the destruction or alteration of inflammatory cells, e.g. T-lymphocytes, release of cytokines, adhesion molecules and proteolytic enzymes (cellular fermentive theory), (c) the impact on the nervous system (neuro-regulatory theory) and (d) transformation of tissue acidosis to tissue alkalosis, a phenomenon assumed in the secondary stage of inflammation (electro-chemical theory). A critical issue which is brought up by patients and non-radiologists deals with potential hazards of tumorigenesis. However, in a recent review by Levitt [46] no concerns were addressed for exposure with low range ionizing radiation as applied in this series, but several theoretical and

Table 7
Literature review of radiotherapy of epicondylopathia humeri (EPH)

Clinical RT studies			RT technique		Clinical results (%)			
Author	Year	*N*	Single dose (Gy)	Total dose (Gy)	CR	PR	MR	NR
Cocchi	1943	22	1.2 versus 1.8	6.0 versus 9.0	48	21		48
Gärtner et al.	1988	70	0.75	3.75	59		41	
Hess and Bonmann	1955	56	2.0	6.0	54	35		11
Kammerer et al.[a]	1990	207 (79)	0.3 (1.0)	1.5 (4.0)	16 (16)	29 (30)	30 (25)	25 (29)
Kammerer et al.[a]	1990	103 (51)	0.3 (1.0)	3.0 (8.0)	29 (33)	32 (31)	26 (22)	13 (14)
Keim	1965	7	0.1–0.5	4.0	57		43	
Mantell	1986	30	2.0	10.0	40	7		53
von Pannewitz	1960	43	NS	NS	52	38		10
Sautter-Bihl et al.	1993	15	0.5–1.0	2.5–6.0	13	33	27	27
Wieland and Kuttig	1965	15	1.0	4.0	60	13	0	27
Zschache	1972	150	0.75–1.0	2.25–4.5	5	7	57	31
Own data[b]		93	1.0	12.0	50 (54)	19 (20)	16 (17)	8 (9)
[c]			2 series					

NS, not specified.
[a]Prospectively controlled non-randomized study.
[b]Patients with bilateral symptoms only values of the working arm were respected; numbers (percentage in brackets).
[c]Differences of the total M-score and single M-score criteria pain, mobility of joint and daily functions prior to RT and at last follow-up are statistically significant ($P < 0.05$).

Table 8
Literature review of radiotherapy of periarthropathia humeroscapularis (PHS)

Clinical RT studies			RT technique		Clinical results (%)			
Author	Year	*N*	Single dose (Gy)	Total dose (Gy)	CR	PR	MR	NR
Cocchi	1943	74	1.2 versus 1.8	6.0 versus 9.0	26	57		17
Gärtner et al.	1988	42	0.75	3.75	67		33	
Goldie et al.[a]	1970	70 (71)	1.5 (control)	4.5 (without RT)	74 (66)		26 (34)	
Hassenstein et al.	1979	233	0.5–1.0	3.0/6.0	43	31		26
Hess and Bonmann	1955	116	2.0	6.0	50	36		14
Keinert et al.	1972	145	1.0	4.0	50	46		4
Lindner and Freislederer	1982	42	1.0	4.0	17	59		24
Plenk[a]	1952	21 (17)	1.5 (control)	4.5 (without RT)	29 (47)	43 (41)		29 (12)
Sautter-Bihl et al.	1993	30	0.5–1.0	2.5–6.0	33	37		30
Valtonen et al.[a]	1975	26 (20)	1.0 (control)	3.0 (without RT)	31 (25)	27 (40)		42 (35)
Wieland and Kuttig	1965	33	1.0	4.0	55	36	0	9
Zschache	1972	546	0.75–1.0	2.25–4.5	6	83		11
Own data[b] [c]		89	0.5 2 RT series	6.0	44 (49)	23 (26)	5 (6)	17 (19)

[a]Prospectively controlled non-randomized study.
[b]Patients with bilateral symptoms only values of the working arm were respected; numbers (percentage in brackets).
[c]Differences of the total C-score and the single score criteria pain, mobility of joint and daily functions prior to RT and at last follow-up are statistically significant ($P < 0.05$).

practical aspects of this treatment should be well known and critically discussed with any patient.

4.2. Clinical results

The effectiveness of RT for EPH and PHS (Tables 7 and 8) has been described in many studies, but most of these reports provide inaccurate data on important clinical aspects, especially patient selection data, pretreatment analysis, treatment schedule, outlined target volume, specification of radiation dose and other possibly confounding factors. Most criteria for assessment of treatment response have been subjectively defined and are not sufficient for an objective evaluation procedure. In almost all studies long-term follow-up is lacking. According to modern standards of good clinical practice (GCP) for the conduct of clinical trials, these studies would fail in almost all aspects. This is especially true for the few randomized studies reported in the literature [22,56,72] which challenge the possible value of ionizing radiation for degenerative musculoskeletal disorders. Our study is different in several aspects of the aforementioned studies, i.e. it relies on clearly defined inclusion and exclusion criteria, incorporates a modern description of dose reference points and target volume, introduces and implements semiquantitative orthopedic scores [14,50] and provides an additional analysis of long-term outcome after at least 1 year of follow-up.

Although our study was conducted with a pretreated and negatively selected patient population, 54% of EPH and 49% of PHS cases achieved long-term complete response. The improvement of the individual pain categories (*N*, *D*, *R* and *M*) was, to some extent, even better, but pain at strain was the most critical pain category and yielded the least improvement for EPH and PHS. The orthopedic Morrey score (for EPH) and Constant and Murley score (for PHS) provided good quantitative measures for evaluation of joint functions and for verification of subjective improvement and objective findings. In our opinion, these two scores may be well used in all future controlled multicenter studies dealing with these two benign disorders.

The 20% failure rate of our study is not uncommon in the literature [25,29,47,64,82]. Failing patients display a multitude of unfavorable factors such as a long duration of symptoms >12 months prior to RT, complex pain score (high score values) and a long period of unsuccessful pretreatments prior to RT. Primary psychosomatic, secondary somatopsychic repercussions, socioeconomic aspects or possible gain from disease (occupational retraining or early retirement) may also influence the response [81]. It appeared conspicuous to us that some patients underwent surgery shortly after RT, although their symptoms had significantly improved according to orthopedic scores. Presumably expectations for RT were so high that an additional waiting for further improvement in treatment outcome seemed impossible and salvage surgery was sought as a last resort. However, long-term observation of 6–12 months is mandatory, as slow responders occurred in the EPH and PHS populations.

4.3. Treatment concept and technique

The ideal RT concept is still to be found. So far various RT treatment concepts have been applied with a multitude of different RT parameters, i.e. (a) single RT doses ranging from 0.3 to 2 Gy and total RT doses ranging from 1.5 to 12 Gy, (b) RT fractions applied two to three times per week or

even daily and (c) the number of RT series ranging from 1 to 4 (Tables 7 and 8). Most groups have used single doses ≥0.5 Gy and total doses ≥4 Gy. In the past, irradiation of degenerative disorders was performed with orthovoltage units [74,76,77], while clinical data with high energy photons (cobalt, cesium or linear accelerators) have rarely been reported [20,37,64,83]. Gärtner et al. [20] obtained better results with telecobalt as compared to orthovoltage applications. In contrast, Nestle et al. [52] achieved better results with telecobalt as compared to linac photons. However, photon energy may not be as important as appropriate target volume and treatment portal encompassing all critical structures. For example, at the elbow joint the selected reference point has to be about 0.5 cm below the skin surface at the level of the tendinous insertion plate. In contrast, at the shoulder joint the midplane dose is usually recommended. Thus, surface dose prescriptions, a formerly well accepted RT practice, should be completely abolished.

Our prescription of two RT series is an empirical concept, which was based on a historical concept of von Pannewitz [73,77]. He recommended single RT doses of 0.3–0.4 Gy, while we have chosen 0.5–0.7 Gy at the target points. Trott [71] assumed that the effectiveness of RT is probably decreased if single RT doses exceed 1 Gy. This may well explain the poor results of Goldie et al. [22] and Plenk [56], who applied a higher single RT dose of 1.5 Gy per fraction and a total RT dose of 4.5 Gy. For organizational reasons we applied three weekly fractions and a total of six fractions per series in order to complete the entire treatment series within a relatively short period of time. According to von Pannewitz [73,77] the best clinical results occurred when using several small fractions applied one or two times per week.

Kammerer et al. [35] compared two RT concepts for EPH prospectively, 0.3 Gy five times per week (1.5 Gy total dose) and 1 Gy twice per week (4 Gy total dose). No difference was noted after one or two RT series. Unfortunately the study lacked clear selection criteria for both treatment arms. Possible confounding factors between the two groups were not sufficiently compared and treatment outcome was only evaluated 6 weeks after RT, but not in long-term follow-up. Thus, so far no clear conclusions can be drawn from all published studies with regard to the optimal single and total RT dose and the exact RT treatment prescription (Tables 7 and 8). Future prospective (randomized) studies may provide better conclusions.

4.4. Long-term evaluation

Few studies [11,30,47,57,58,64] report on long-term outcome and relapses. As typical complaints may still persist and slowly change as late as 3–6 months after RT, we would recommend a minimum follow-up of at least 6–12 months for final evaluation of treatment outcome. In our study the 1-year success and failure rates corresponded well with long-term outcome. Thus, salvage surgery should not be performed within the first 6–12 months after RT. Only two EPH and three PHS patients complained of renewed pain symptoms in the same joint (relapse) 1–2 years after achieving complete pain relief. Other studies confirm this low relapse rate after initial complete response [11,30,47,57, 58,68]. A salvage operation for EPH or a second RT course for PHS may be applied for these relapses.

4.5. Prognostic factors

Duration of clinical history, pretreatment data, stage of disease and restriction of movement prior to RT influence treatment outcome [11,20,25,47,64,74,76,77]. The impact of symptom duration on treatment outcome has been confirmed in our study; both for EPH and PHS, a lower success rate was found in cases with long symptom duration, many prior therapies and long-term immobilization with plaster. Thus, future prospective studies should be stratified according to the symptom duration, e.g. <6 versus >6 months.

4.6. Short- and long-term side-effects

So far neither acute nor chronic side-effects have been detected in our patient population during available follow-up. However, a mean follow-up of 4 years is too short for development of secondary malignancies. No publication which has dealt with low dose radiotherapy for degenerative disorders like EPH and PHS has reported a tumor induction. According to a review [46] local side effects, injury to the gonads or tumorigenesis are very unlikely due to several reasons, i.e. (a) treatment of shoulder and elbow regions results in a cumulative gonad dose which is comparable to the dose for most X-ray procedures, (b) most patients were older than 50 years and this population is much less likely to develop secondary malignancies; nevertheless, tumorigenesis has to be mentioned in any informed consent as a possible but very unlikely event in long-term follow-up; (it may be more relevant after irradiation of lumbar spine for spondylarthritis ankylosans (M. Bechterew) and degenerative hip joint disease if a large volume of bone marrow is irradiated or especially during the radiosensitive adolescent age [30,40,53]) and (c) the application of appropriate radiation protection measures (restriction of the target volume, optimal RT portal, direction of photon beam and appropriate gonad and thyroid protection by lead apron) should contribute to a further reduction of radiation hazards and a better perception of the treatment by the patients.

4.7. Other therapies

Questionable etiology and pathogenesis make EPH and PHS management prone to polypragmasy including physical/physiotherapy, local or systemic analgetic and antiphlogistic medication (NSAD, steroids and anesthetics), immobilization procedures (taping, bandage and plaster) and surgical measures. Immobilization is often used for

the acute stage of EPH, but its potentially curative value is reduced if a chronic stage has been reached. Physical hyperemic combined with anti-inflammatory measures are likely to be effective, i.e. microwaves, iontophoresis, ultrasound, frictional and underwater massages as well as fango, while laser therapy is disputed [68]. Local infiltration with steroids is very popular, but may lead to teno- and osteonecrosis [66]. Application of NSADs may also induce considerable side effects [43,54]. While surgical procedures are rarely indicated for PHS, for the chronic stage of EPH Hohmann's operation and surgical methods derived therefrom are well established [31,32,85] as well as other surgical techniques [6,16,19,21,36,85]. According to the literature, the success of these measures corresponds to the long-term results of our study, but surgery is a partially mutilating and expensive therapy. Nowadays a full RT course consisting of medical exams in the beginning, in-between and at last follow-up, RT planning (table calculation) and 12 RT fractions (two RT series of six fractions) is very cheap (about 150 ECU for Germany) as compared to the many weeks or months of other treatments or surgery.

4.8. RT indication

RT should not be indiscriminately applied but is also more than a last resort for refractory chronic stage EPH and PHS. It should be applied only after interdisciplinary counseling and when conventional measures have been proven ineffective after 3 months follow-up. Along with the RT treatment we recommend avoiding severe strain (professional or sporting activities) and receiving state-of-the-art physiotherapy [18]. If patients are younger than 40 years, we would recommend undertaking a careful risk–benefit analysis together with the patient. As indications for RT are rarely determined by radiotherapists themselves but by other physicians, prior to RT a careful evaluation of other disorders with similar symptoms should always be performed [79]. In the acute stage of insertion tendinitis (EPH and PHS) it is useful to ask whether all other measures have been fully exhausted and which treatment the patient prefers. For the chronic stage of EPH there is still a choice between local surgery and RT. Both treatments can be used as salvage therapy for failures after each treatment.

5. Conclusions

RT of symptomatic refractory EPH and PHS is effective for the elimination or alleviation of refractory pain symptoms. All future studies should incorporate the following characteristics: (a) patients should be treated in a uniform fashion and should be evaluated for treatment response not only initially, but also in long-term follow-up (at least 1 year); (b) all subjective pain symptoms should be documented according to specific categories and grades which can be translated into a semi-quantitative pain score; (c) the established Morrey elbow and Constant and Murley shoulder scoring systems should be used as an additional measure to compare and correlate both subjective and objective response criteria; and (d) a prospective study design should be defined together with a list of inclusion and exclusion criteria. Due to the minimal time and personnel required and the minimal therapeutic risks, both the chronic refractory and subacute refractory stages (symptom duration >6 months) should be irradiated. Which RT dose and which fractionation are best suited for the acute and chronic stages of EPH and PHS must be examined in future prospective studies with clearly defined scores for evaluation.

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