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Long-term efficacy of radon spa therapy in rheumatoid arthritis—a randomized, sham-controlled study and follow-up

A. Franke, L. Reiner[1], H. G. Pratzel[2], T. Franke and K. L. Resch

Balneology and Rehabilitation Sciences Research Institute (FBK), Bad Elster, [1]In-patient rehabilitation hospital (Dr Ebel Fachklinik) Bad Brambach and [2]Institute of Medical Balneology and Climatology, Ludwig Maximilians University, Munich, Germany

Abstract

Objective. To quantify the efficacy of a series of baths containing natural radon and carbon dioxide (1.3 kBq/l, 1.6 g carbon dioxide/l on average) versus artificial carbon dioxide baths alone in patients with rheumatoid arthritis.

Subjects. Sixty patients participating in an in-patient rehabilitation programme including a series of 15 baths were randomly assigned to two groups.

Design. Pain intensity (100 mm visual analogue scale) and functional restrictions [Keitel functional test, Arthritis Impact Measurement Scales (AIMS questionnaire)] were measured at baseline, after completion of treatment and 3 and 6 months thereafter. To investigate whether the overall value of the outcomes was the same in both groups, the overall mean was analysed by Student's *t*-test for independent samples.

Results. The two groups showed a similar baseline situation. After completion of treatment, relevant clinical improvements were observed in both groups, with no notable group differences. However, the follow-up revealed sustained effects in the radon arm, and a return to baseline levels in the sham arm. After 6 months, marked between-group differences were found for both end-points (pain intensity: -16.9%, 95% confidence interval -27.6 to -6.2%; AIMS score: 0.57, 95% confidence interval 0.16 to 0.98). The between-group differences were statistically significant for both overall means (pain intensity, $P = 0.04$; AIMS, $P = 0.01$).

Conclusion. Marked short-term improvements in both groups at the end of treatment may have masked potential specific therapeutic effects of radon baths. However, after 6 months of follow-up the effects were lasting only in patients of the radon arm. This suggests that this component of the rehabilitative intervention can induce beneficial long-term effects.

KEY WORDS: Rheumatoid arthritis, Randomized controlled trial, Spa therapy, Radon, Long-term efficacy.

Rheumatoid arthritis (RA) is an inflammatory rheumatic disease for which there is neither prophylaxis nor cure. Treatment regimens are complex and include, besides disease-modulating and symptomatic drug therapy, specific exercises, physical and/or occupational therapy, surgery, rehabilitative treatment and orthopaedic aids, together with psychological care [1]. Most treatment concepts concern long-term disease management.

RA rehabilitation aims particularly to inhibit the inflammatory processes, to relieve pain, to preserve the remaining functions and to develop or stabilize compensatory functions and suitable coping strategies. Spa therapy is used as an integral part of physical therapy for RA [2].

The inert natural radioactive gas radon has been used since the beginning of the century in the treatment of rheumatic diseases. The most famous European health resort where radon is used therapeutically is Badgastein in Austria. Evidence from empirical experience and from clinical observational studies [3–6] suggests that radon has analgesic [7, 8], anti-inflammatory [9] and immune-stimulating [10, 11] effects. Patients' compliance with radon treatment is usually high. However, because of its intrinsic radioactivity the therapeutic use of radon is still controversial [e.g. 12, 13]. The dosages used in radon therapy are very small. Hofmann [14] compared target organ doses in medical X-ray diagnosis with those

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Correspondence to: A. Franke, Balneology and Rehabilitation Sciences Research Institute (FBK), Lindenstrasse 5, 08645 Bad Elster, Germany.

of several radon treatment schemes used at Badgastein. For instance, the dose equivalents for an X-ray examination of the lumbosacral spine are typically about 40 mSv and almost twice as much as this for computed tomography, whereas a typical series of thermal baths in Badgastein results in a cumulative exposure of 0.8 mSv to the skin, which receives the highest organ-specific dose. Although there are differences in radiation quality, exposure time and the distribution of radiation, the organ doses are similar for the two exposure modes, and therefore the radiation hazards may also be supposed to be similar [14].

We undertook a study of the efficacy of baths with natural spring water containing radon and carbon dioxide in comparison with baths containing artificially produced carbon dioxide at the same concentration as in the spring water, but without radon. The evaluation of efficacy was based on the hypotheses that: (1) the complex treatment regimen in our study (including the baths) is effective in relieving pain, in increasing mobility and in decreasing functional and psychosocial limitations; and (2) with radon–carbon dioxide baths but not with carbon dioxide baths (despite the comprehensive co-intervention) treatment effects are maintained for a clinically relevant period of time (long-term effects).

Methods

This study was designed to evaluate, under controlled conditions, the efficacy of baths with natural spring water containing, on average, radon 1.3 kBq/l and carbon dioxide 1.6 g/l *vs* artificially produced carbon dioxide baths of the same carbon dioxide concentration. Patients with classical or definite RA who were participating in a multi-modality in-patient rehabilitation programme of 4 weeks' duration in Bad Brambach were invited to enter the trial. The springs at this health resort, situated in the south-west of Saxony, Germany, contain both radon and carbon dioxide in therapeutic concentrations.

Patients and therapy

The setting for this study—an in-patient rehabilitation programme offered in a health resort—represents a therapeutic option of high treatment intensity (in comparison with out-patient physical therapy) for patients with mild to moderate disease activity but worsening overall health status. German health insurance companies agree to patients' participation, based on a medical certificate, if this treatment promises to stabilize the patients' living conditions with as little external support as possible.

Patients referred to the rehabilitation hospital were invited to participate if they met the inclusion and exclusion criteria. The inclusion criteria were based on the 1987 revised American College of Rheumatology (ACR) criteria for RA [15]. Patients receiving disease-remitting drugs must have started this treatment at least 6 months before the start of the study. Participation was restricted to patients younger than 75 yr.

Exacerbation of the inflammatory process requiring an injection of cortisone led to the exclusion of a patient. Further exclusion criteria included concomitant musculoskeletal diseases possibly affecting measurement of the outcome measures, i.e. advanced osteoarthritis, endoprosthesis of the hip or knee, spinal disc syndrome or muscular dystrophy. Patients with central nervous system diseases such as epilepsy or with systemic inflammatory diseases such as collagen diseases and gout, patients with general contraindications to immersion in water and patients with advanced malignancies were also excluded.

To enrol 60 patients, 84 patients who fulfilled the inclusion/exclusion criteria were asked to participate. Among those who refused, three patients did not agree with the study procedures, three were to stay in Bad Brambach for only 3 weeks, and 18 objected to exclusion from radon therapy if they were allocated to the control treatment.

The recruitment period was 16 months and ended in October 1996.

The treatment regimen is described in Table 1. The only systematic difference in treatment between the two groups was the therapeutic bath used: either radon–carbon dioxide water or artificially enriched carbon dioxide water.

Participants in the study were not restricted with regard to additional offers (leisure time sport, relaxation therapy), in order to maximize the patients' compliance. As expected, demand was similar in the two groups (Table 1). All patients continued to receive their regular drug treatment without any change in type or dose.

Randomization and blinding

After they had given informed consent, the patients were randomized into the treatment groups. The patients, therapists and investigator were unaware of group allocation.

A randomization list was generated by means of a random number table, and was used to produce one bar code card for each patient in the study. An automated device constructed for the purpose and activated by the patient's bar code card guaranteed the correct filling of the bath according to group assignment [16]. Because of relocation of the hospital during the course of the study, bath fillings had to be prepared manually for approximately two-thirds of the patients. This was done by a single therapist, who was instructed not to interfere with the patients otherwise or to disclose any patient's group allocation to any other person.

End-points

The outcome criteria of the study were focused on the patient-centred core symptoms in RA, i.e. pain and functional limitations.

Pain intensity. Pain intensity (PI) was measured on a visual analogue scale (VAS) from 0 mm = no pain to

TABLE 1. Components of therapeutic intervention during in-patient rehabilitation

Therapy	Absolute frequency in 4 weeks	
	Planned	Provided: median (25%, 75%)
Radon–carbon dioxide baths[a]	15 per patient, 20 min each, subsequent 30-min rest, between 10 and 12 a.m.	15 (15, 15) Min. 14, max. 15
Artificially generated carbon dioxide baths[b]	15 per patient, 20 min each, subsequent 30-min rest, between 10 and 12 a.m.	15 (15, 15) Min. 14, max. 15

Further treatment procedures not evaluated	Absolute frequency in 4 weeks		
		Provided: median (25%, 75%)	
	Planned	Radon group	Control group
RA-specific exercises and/or physiotherapy	10–12 30 min each	10 (9, 11)	10 (10, 11)
Classical massage	8–10 25 min each	8 (8, 9)	8 (8, 9)
Hydrogalvanic partial baths	6–8	7 (7, 8)	7 (7, 8)
Occupational therapy	On request	7.5 (0, 9)	8 (5, 10)
Leisure time sports	On request	1 (0, 11)	0 (0, 6)
Relaxation therapy	On request	0 (0, 2)	0 (0, 0)

[a]250 l, 35°C, on average 1.3 kBq/l, 1.6 g CO_2/l.
[b]250 l, 35°C, 1.6 g CO_2/l.

100 mm = pain as bad as it can be; VAS are regarded as reliable, valid and sensitive to changes [17, 18].

Keitel functional test. The Keitel functional test [19] was performed to evaluate limitations of functioning; its index (KFI) ranges from 0 to 100 points (100 = no functional limitations). Because of known diurnal variations, measurements were always taken at the same time of day. The validity and reliability of the KFI have been shown to be satisfactory [20, 21].

Arthritis Impact Measurement Scales. A validated German version of the Arthritis Impact Measurement Scales (AIMS), the MOPO (measurement of patient outcome) [22], was used to describe the physical and psychosocial consequences of RA. This questionnaire has been shown to have good reliability, validity, sensitivity and practicability [22]. Scores range from 0 to 10. However, in contrast to the original AIMS, a score of 10 represents good health status for the overall score as well as the subscales measuring mobility, physical activity, dexterity, household activity, social activity and activities of daily living. Only the pain, depression and anxiety subscales follow the convention of associating good health status with low scores. These three scales had to be transformed in order to summarize the AIMS (MOPO) overall score.

In addition, to describe disease activity the erythrocyte sedimentation rate (ESR; Westergren method), the serum concentration of C-reactive protein (CRP), pain frequency and morning stiffness (on rating scales) were recorded.

Short-term and long-term treatment effects were evaluated. Data were collected at admission, on completion of treatment and 3 and 6 months thereafter. Longitudinal changes were analysed within and between groups.

Analysis

The target sample size was 60 patients. This number yields a power of 90% to detect large differences in effect size between treatment groups according to Cohen [23] when one-sided α is limited to 0.05. One-sided hypothesis formulation seemed to be justified because there was considerable empirical evidence concerning the larger effects attainable with radon intervention [24]. Assuming moderate group differences and using 30 patients per group, the power of the trial would be 0.6.

All analyses were based on intention to treat as initially assigned. Data missing because of loss to follow-up were handled by means of the last-observation carry-forward approach. No interim analyses were done.

Measures that were distributed fairly normally were expressed as mean and S.D. and as mean change with the 95% confidence interval (CI). Measures with a discrete distribution were expressed as counts (k/n cases) and as odds ratios for improvement.

For all outcome measures, effect sizes were calculated according to Cohen [23].

To determine whether the overall value of the outcomes was the same in both treatment groups, the simple mean of repeated measurements was calculated. With equal intervals between successive observations (as in this study), this is considered to be closely related to the area under the curve [25]. Thereafter, between-group *t*-tests were performed for confirmatory analysis. Summary measures like the above simple mean are recommended by Matthews *et al.* [25] for the analysis

of serial measurements, provided they are meaningful (e.g. to quantify an 'overall treatment difference').

A sensitivity analysis was carried out to estimate the robustness of the results.

Multivariate analyses with the outcome criteria (see above) as dependent variables were used to test whether imbalance in prognostic factors between the two groups may have affected the results despite randomization. Predictive variables included were treatment group, sex, age, body mass index, socioeconomic status, disease duration, radiological damage and baseline scores describing disease activity such as pain, stiffness and laboratory measures.

For statistical analysis, SPSS 8.0 for windows (SPSS, Chicago, IL, USA) was used.

Course of the trial

The study was conducted according to a protocol that was approved by the ethics committee of the Ludwig Maximilians University, Munich, Germany. At the initial examination, sociodemographic and clinical characteristics and all baseline data were documented. After completion of treatment, all measures were taken again except for the AIMS (because of lack of comparability of the patients' situation at home with that in the hospital).

Follow-ups were carried out 3 and 6 months after the completion of treatment by means of a postal questionnaire. It addressed all measures suitable for self-assessment by the patients, including questions about modification of medication. Furthermore, patients were asked to report the actual ESR determined by their general practitioners. If necessary, patients were reminded by telephone to send back the questionnaire.

The patients' level of adherence to the treatment protocol was high (Table 1).

Results

Sample characteristics

Table 2 summarizes the characteristics of the treatment groups at baseline. Almost three-quarters of the study participants were women. For approximately two-thirds of the patients, X-rays revealed marked erosions of joints, cysts or lesions, or subluxation [26a, 26b]. Eighty per cent reported daily or continuous pain. Almost all patients suffered from morning stiffness lasting at least 1 h. Every second participant was retired or had retired early. Only 12 patients (20%) were actively employed at the beginning of the study. The age of the study participants ranged from 21 to 75 yr, the mean age at onset of RA was 48 yr, and the duration of disease ranged from 1 to 46 yr (median 6 yr). The mean body mass index was 25.7 kg/m^2 (S.D. = 3.7). The drug prescription profile varied markedly, and included disease-modifying anti-rheumatic drugs, non-steroidal anti-inflammatory drugs (NSAIDs), steroids and combinations (Table 2). Only 11 patients were not on continuous medication. The patients' basic medication was kept unchanged during the in-patient rehabilitation period. An attempt was made to maintain this medication during the follow-up period by informing the patients' general practitioners about their participation in the study. The short-term use of drugs on demand (exclusively NSAIDs) was not recorded.

Table 3 provides a descriptive summary of the main outcome measures at baseline and during the course of the study, according to group allocation. In the multiple regression models, the two treatment groups did not differ significantly at baseline (pain intensity, $P = 0.55$; KFI, $P = 0.89$; AIMS, $P = 0.32$).

Losses to follow-up

For one patient in the control group, no follow-up data were available for unknown reasons. After rehabilitation, her outcome measures showed only small restrictions in comparison with healthy persons. Three other patients returned their follow-up questionnaire incomplete (one subject from the control group after 3 months, and two subjects from the radon group after 6 months). The AIMS score was available for 59 of the 60 patients at both follow-ups.

Treatment effects

Both groups showed marked treatment effects at discharge (Table 3). Pain intensity was reduced by 14.9% (95% CI, 5.1 to 24.6%) in the radon group and by 11.8% (95% CI, 4.4 to 19.2%) in the control group. There was virtually no difference between groups (Table 4). The KFI improved more in the radon group than in the control group (Table 3), but the difference ($\Delta_{KFI} = 2.6$, 95% CI, -0.5 to 5.8) did not reach statistical significance ($P_{descriptive} = 0.09$).

Despite a decrease in treatment effects during the follow-up period, the radon group had better values 3 and 6 months after the end of rehabilitation compared with baseline, whereas the control group had already declined to values below the baseline level after 3 months (Table 3, Fig. 1). Lasting effects of small and moderate size, respectively, according to Cohen [23] were observed only in patients of the radon group (Fig. 2). Group differences increased continuously (Table 4). Whereas the AIMS score indicated superiority of the radon treatment at both 3- and 6-month follow-ups, this was true for pain relief only at 6 months.

For pain intensity, the overall treatment effect was 9.5% (95% CI, 2.1 to 16.9%) in the radon group and no effect was found (-0.7%; 95% CI, -6.1 to 4.8%) in the control group. A similar situation was observed for the AIMS score, which remained improved (0.40; 95% CI, 0.14 to 0.67) in the radon group compared with the control group (-0.11; 95% CI, -0.36 to 0.13).

The confirmatory analysis of the overall treatment differences ($\Delta_{pain\ intensity} = 10.1$ [95% CI, 0.9 to 19.3; $\Delta_{AIMS} = 0.52$; 95% CI 0.15 to 0.88) revealed significant superiority of the radon bath series over the sham treatment for both outcome criteria (Table 4). No side-effects were observed in either group.

TABLE 2. Patient characteristics of the treatment groups at baseline

Feature	Radon group ($n = 30$)	Control group ($n = 30$)	Total
Sex (F/M)[a]	22/8	24/6	46/14
Age (yr)[b]	58.1 (9.9)	58.6 (11.9)	58.3 (10.9)
Body mass index (kg/m^2)[b]	25.7 (3.3)	25.7 (4.0)	25.7 (3.7)
Duration of disease (yr)[b]	11.1 (12.2)	9.9 (9.8)	10.5 (11.0)
Occupational status[a]			
Working/sick leave/retired	8/7/15	4/5/21	12/12/36
Radiograph classification[a,c]	4/21/5	5/21/4	9/42/9
Medication[a]			
DMARDs	4	2	6
Steroids	1	1	2
NSAIDs	6	6	12
DMARDs + steroids	1	2	3
DMARDs + NSAIDs	8	8	16
Steroids + NSAIDs	1	3	4
DMARDs + steroids + NSAIDs	2	4	6
None	7	4	11

[a]Number of patients.
[b]Mean (S.D.).
[c]Dorso-palmar/plantar view of both hands and feet: no or insignificant erosion of joints; only slight decalcification/clear signs of erosion of joints; cysts, osseous lesions subluxation/atrophy, destruction of joints.

TABLE 3. Baseline measures [mean (S.D.) or absolute frequency] and mean changes with 95% confidence interval or improvement rates (compared with baseline measures) during the course of the study; $n = 30$ in each group unless indicated otherwise

Measure		Baseline	End of rehabilitation	3-month follow-up	6-month follow-up
Pain intensity	Radon	44.8 (25.0)	− 14.9 (− 24.6 to −5.1)	− 6.0 (− 16.5 to 4.5)	− 6.5 (− 17.8 to 4.8)[b]
	Control	38.6 (20.2)	− 11.8 (− 19.2 to −4.4)	4.8 (− 5.0 to 14.7)[b]	9.7 (2.0 to 17.4)[a]
Keitel functional index	Radon	70.5 (18.0)	5.2 (2.2 to 7.7)	–	–
	Control	71.1 (13.2)	2.3 (−0.4 to 5.1)	–	–
AIMS (MOPO) score	Radon	6.27 (1.33)	–	0.41 (0.06 to 0.75)	0.41 (0.06 to 0.74)
	Control	6.60 (1.10)	–	− 0.06 (− 0.34 to 0.23)[a]	− 0.18 (− 0.56 to 0.20)[a]
ESR (1st h, mm)	Radon	18.6 (15.8)	2.1 (−2.9 to 7.0)	5.2 (−0.7 to 11.0)[a]	3.3 (− 3.4 to 9.9)[c]
	Control	22.0 (15.6)	− 3.1 (− 7.9 to 1.7)	− 0.3 (− 7.2 to 6.5)[d]	1.2 (− 5.2 to 7.7)[d]
C-reactive protein (g/ml)	Radon	12.2 (14.4)	1.2 (− 2.0 to 4.4)	–	–
	Control	18.4 (17.0)	− 4.9 (− 10.1 to 0.3)	–	–
Pain frequency					
No pain/sporadic/	Radon	1/2/13/14			
daily/continuous	Control	2/3/18/7			
improvement of	Radon		47% (14/30)	37% (11/30)	57% (16/28)
$\geqslant 1$ category	Control		37% (11/30)	28% (8/29)	24% (7/29)
Morning stiffness					
None/$\leqslant$1h/	Radon	1/15/8/6			
$\leqslant$2 h/until noon	Control	4/16/7/3			
Improvement of	Radon		33% (10/30)	40% (12/30)	28% (8/29)
$\geqslant$1 category	Control		27% (8/30)	14% (4/29)	24% (7/29)

[a]$n = 29$.
[b]$n = 28$.
[c]$n = 27$.
[d]$n = 26$.

Sensitivity analysis

In 27 patients (11 of the radon group and 16 of the control group), drug consumption changed during the follow-up period. Therefore, a sensitivity analysis was carried out to estimate the influence of changes in medication during the follow-up period on the study results. A two-way analysis of variance was done using group allocation and changes in medication as independent factors (55 of 60 patients with complete information included). For both outcome criteria, neither a significant influence of changes in medication nor a significant interaction between the two factors was found at the 6-month follow-up. On the other hand, the differences between the treatment groups remained significant (Table 5). These results validated those of the confirmatory analysis.

Discussion

Perceived pain relief and increased joint mobility led to the common acceptance of radon treatment in musculoskeletal diseases in Central Europe, although the evidence for its efficacy was only empirical. Since 1990, however, controlled randomized trials using up-to-date

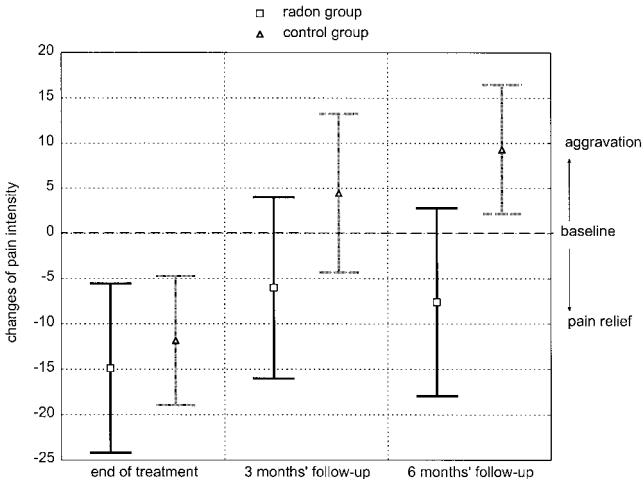

FIG. 1. Longitudinal mean changes in pain intensity and 95% confidence intervals for both treatment groups.

methods have been performed. Positive effects have been reported for tendomyopathy, osteoarthritis and ankylosing spondylitis [8, 27–29]. The present trial confirmed these effects for RA.

Basic research in the last two decades has revealed some of the potential therapeutic mechanisms of radon in the human organism. It has been suggested that it is the skin that is primarily responsible for the incorporation of radon [9]. Within its morphological structures, radiation may activate local processes that are similar to the effects of topical steroids [30]. In animal experiments it has been demonstrated that the accumulation of incorporated radon, enhanced by its lipophilia, stimulates the secretion of corticoids from the adrenal cortex [31]. The normalization of killer cell activity, which is reduced in rheumatic diseases, has been found under radon therapy [32]. At the cellular level, the forced generation of free radicals has been observed along the α-traces, resulting in increased activity of scavenger

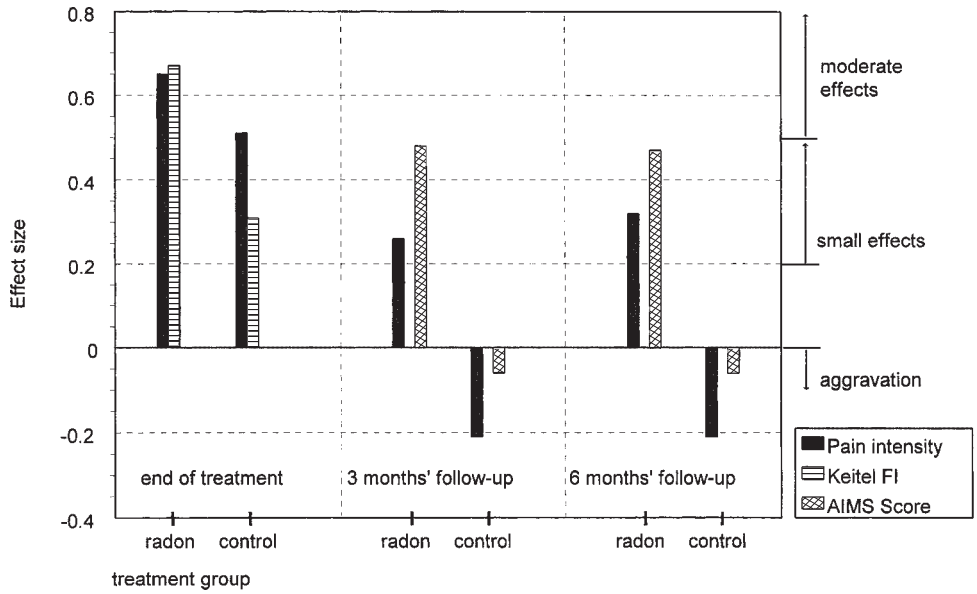

FIG. 2. Treatment effects of pain and functional capacity/disability. Effect sizes according to Cohen [23]. The KFI was assessed at baseline and after completion of treatment by the investigator; AIMS score was measured at baseline and at follow-ups by self-assessment.

TABLE 4. Between-group differences in longitudinal changes in outcome criteria

Measure	End of treatment	3-month follow-up	6-month follow-up	Overall mean
Pain intensity, Δm[a]	− 3.0 (− 13.0 to 7.0)	− 10.5 (− 21.8 to 0.9)	− 16.9 (− 27.6 to −6.2)	− 10.1, $P = 0.04$ (− 19.3 to −0.9)
Keitel functional index, Δm[a]	2.6 (− 0.5 to 5.8)			2.6, $P = 0.09$ (− 0.5 to 5.8)
AIMS score, Δm[a]		0.46 (0.10 to 0.82)	0.57 (0.16 to 0.98)	0.52, $P = 0.01$ (0.15 to 0.88)
ESR, Δm[a]	5.1 (− 1.6 to 11.9)	5.5 (− 3.3 to 14.3)	2.1 (− 7.0 to 11.1)	
Pain frequency, OR[b]	1.5 (0.5 to 4.2)	1.5 (0.5 to 4.6)	4.2 (1.3 to 13.0)	
Morning stiffness, OR[b]	1.4 (0.5 to 4.2)	4.2 (1.2 to 15.0)	1.2 (0.4 to 3.9)	

[a]Mean group difference (95% confidence interval) (treatment minus reference group).
[b]Odds ratio (95% confidence limits) of improvement rate (treatment *vs* reference group).

TABLE 5. Effect of changes in drug consumption during the follow-up period on the results of the trial (two-way analysis of variance; SS/MS: sum/mean of squares; DF: degrees of freedom)

Source of variation	SS	DF	MS	*F*	Significance
Pain intensity after 6 months (n = 53)					
Main effects					
Treatment group	4467.06	1	4467.06	7.16	0.010
Change in medication	45.50	1	45.50	0.07	0.788
Interaction					
Group × medication	234.61	1	234.61	0.38	0.543
Residuals					
Within observations	30571.44	49	623.91		
Total	35231.02	52	677.52		
AIMS score after 6 months (n = 55)					
Main effects					
Treatment group	6.22	1	6.22	6.68	0.013
Change in medication	0.02	1	0.02	0.02	0.894
Interaction					
Group × medication	1.35	1	1.35	1.45	0.234
Residuals					
Within observations	47.48	51	0.93		
Total	55.00	54	1.02		

enzymes such as superoxide dismutase. An increase in these enzymes may contribute to the improvement of symptoms of the disease, e.g. by inhibiting rheumatic inflammation [33]. The DNA repair capacity of the cell nucleus increases with small radiation doses, suggesting that disease-related DNA damage may be repaired more quickly and effectively [13, 34]. Both the response of the organism to the generation of free radicals and the increase in the DNA repair capacity represent adaptive, health-supporting reactions which may also offer increased protection against other, non-radiation induced, health-threatening influences [35, 36].

In this study, the radon spa therapy was part of a complex rehabilitation programme in an in-patient rehabilitation hospital. Random allocation of the patients seemed to be successful, since it resulted in groups that were comparable in their sociodemographic and disease features as well as in their initial status with respect to the outcome criteria. Because the specific spa treatment was the only systematic difference in treatment between the groups, it can be assumed to have been the cause for the differences observed.

The rehabilitation regimen was apparently effective with regard to pain relief and the improvement of functional capacity, but no relevant difference was found after completion of treatment. This result was not surprising because in both groups the rehabilitation programme focused on the specific problems of RA patients. The resulting marked improvements in both groups at the end of the treatment may have masked specific therapeutic effects of radon baths. However, between-group differences increased during the follow-up period in favour of the radon group, and long-term effects were observed only in the radon group, not least the significant group differences in the overall treatment effect. These findings agree with those of other trials [8, 27–29] and confirm the suggestion that radon baths induce beneficial long-term effects in rheumatic diseases, although the underlying mechanisms are not yet fully understood.

Regarding the outcomes in RA clinical trials, the last decade has been characterized by efforts to achieve better standardization of effect measures [37–44]. Recommendations have been published by the ACR and by the participants in the OMERACT conference(s) with the aim of improving the comparability of study results. Both the ACR [40] and the WHO/ILAR [41] core set of end-points included pain, patients' and physicians' global assessments and physical disability, as well as joint indices and acute-phase reactants.

To deal with the multiplicity of end-points that have been used in previous RA studies, it was recommended [47] either that a few high-quality outcome measures fulfilling the known validity criteria should be selected, or that various measures should be pooled into a single composite index. Although pooling single measures is considered to be a valid way [45] of increasing sensitivity to change and is favoured by various authors [e.g. 46–48], only a few RA studies [e.g. 46, 49] have used this approach.

In our study we limited the number of end-points to three validated outcome measures reflecting relevant patient-centred dimensions of chronic diseases: impairment and disability/activity [50]. Because the patients came from all parts of Germany and it would therefore have been impossible for the clinical investigator (L.R.) to carry out follow-up examinations, we chose outcomes that could be obtained by self-assessment by the patients. Self-reports of pain, functional capacity, activities of daily living and health-related quality of life obtained by means of validated scales and questionnaires such as the AIMS [51], the Health Assessment Questionnaire [52], the Functional Questionnaire Hanover (FFbH) [53, 54] and others are appropriate for the evaluation of rehabilitation programmes because they indicate the somatic, function-related and psychosocial effects of

interventions. Regarding the follow-ups in our study, the AIMS score was more sensitive to differences in effect than the visual analogue scale for pain.

Because the patients' typical living conditions could not be compared with their situation in the rehabilitation hospital (especially with respect to their psychosocial state and personal interactions), we decided not to assess the AIMS at the end of rehabilitation. Instead, the KFI, performed by the clinical investigator, was used to evaluate functional deficits. In contrast to the AIMS score, the KFI measures impairment rather than disability, yet correlates well with the AIMS physical function score [55]. This was shown in our sample; the observed correlation coefficients were $r = 0.80$ (Pearson) and $r = 0.76$ (Spearman).

In accordance with other studies in typical in-patient rehabilitation settings [54, 56], effect sizes after completion of treatment were moderate.

Considering that most patients had long-standing disease, that the duration of treatment was relatively short, and that the treatment had good tolerability, no side-effects and long-term benefits, this complex rehabilitation programme, including a series of radon baths, may be an interesting option for RA patients.

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