Reducing Intensity of Treatment

Low-Dose Radiation Therapy for Benign Painful Skeletal Disorders: The Typical Treatment for the Elderly Patient?

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Summary

Low-dose RT is a very effective treatment for the management of painful degenerative skeletal disorders in the elderly. Because of the delayed onset of analgesic effects, low-dose RT results in a significantly improved long-term efficacy in comparison with the results immediately after RT.

Purpose: To prospectively evaluate the short-term and long-term efficacy of low-dose radiation therapy (RT) for calcaneodynia, achillodynia, painful gonarthrosis, and painful bursitis trochanterica in elderly patients aged ≥70 years.

Methods and Materials: Between October 2011 and October 2013, patients aged ≥70 years with painful degenerative disorders of joints were recruited for a prospective trial. Single doses of 0.5 to 1.0 Gy and a total dose of 6.0 Gy per series were used. Pain was measured before and right after RT (early response) with a 10-point visual analogue scale. Additionally, pain relief was measured with the 4-point pain scale according to “von Pannewitz” immediately on completion of RT and during follow-up. We defined a good response as complete pain relief and markedly improved.

Results: A total of 166 evaluable patients with a mean age of 76.6 years (range, 70-90 years) with calcaneodynia (n = 51), achillodynia (n = 8), painful gonarthrosis (n = 80), and painful bursitis trochanterica (n = 27) were recruited. The mean visual analogue scale value before treatment was 6.38 and immediately upon completion of RT was 4.49 (P < .001). Concerning the von Pannewitz status immediately on completion of RT, 6 patients were free of pain, 56 were much improved, 47 reported slight improvement, and 57 experienced no change. After a median follow-up of 29 months, 109 patients could be reached for evaluation of follow-up results. Thirty-three patients were free of pain, 21 had marked improvement, 18 had some...

Conflict of interest: none.
Introduction

In economically developed countries there is a tremendous increase in life expectancy, causing a permanent aging of populations with a corresponding increase in chronic diseases. Over the past 10 years the proportion of the general world population made up by those aged 65 years or more has increased from 16.6% to 20.7%, and the average age rose from 41 to 43 years. This aging of the population is associated with increases in morbidities and an increasing need for medical and nursing care, representing a clear global health challenge (1, 2).

In particular people in Germany today can expect to live longer than ever before. Because of the demographic development in Germany and the other European countries, there is a marked increase in the number of persons in the higher age groups, particularly in the group aged >70 years, and the group aged >80 years will quadruple over the next 20 to 40 years.

These dramatic changes will lead to an increasing number of patients with age-associated chronic disorders (1, 2). For many then, senior living includes carefully managing chronic conditions to stay healthy. Painful skeletal disorders are probably the number one condition that people aged ≥65 years contend with, and they can lead to lower quality of life. Although skeletal pain can discourage the elderly from being active, it is important to work with their treating physicians to develop treatment plans that can help maintain senior health.

Among the many well-known treatment options, such as surgery, nonsteroidal anti-inflammatory drugs, and physiotherapy, low-dose irradiation may also be used to achieve pain and functional improvement. Compared with other treatment options it is noninvasive, not very cost intensive, and is excellently tolerated in this multi-morbid patient population.

Every year more than 30,000 patients in Germany are treated for benign painful skeletal disorders with the use of ionizing radiation applied in approximately 300 radiation therapy (RT) facilities (3-7). More than 50% of these patients are adults aged ≥70 years. The aim of these treatments is and will be the preservation or recovery of various quality of life aspects (eg, by prevention of or reduction of pain and/or improvement of formerly disabled physical functions).

Nonmalignant indications for RT constitute approximately 10% to 30% of all patient treatments in most academic, public, and private RT facilities in Germany. Improvement, and 37 experienced no change. Therefore, a good response immediately on completion of RT could be achieved in 62 of 166 patients, and with the follow-up in 54 of 109 patients (P=.001).

Conclusions: Low-dose RT is a very effective treatment for the management of painful degenerative disorders of joints in the elderly. Low-dose RT offers a low-risk, genuinely conservative, noninvasive therapeutic alternative for elderly patients. © 2016 Elsevier Inc. All rights reserved.

Over the past decade various patterns of care studies focused on the general and various specific aspects of these diseases and their RT treatment conditions and concepts in Germany (3-10).

Meanwhile a considerable number of contemporary clinical trials have been carried out and published (11-25). The largest group of patients with nonmalignant disorders and indications for the use of RT are those with painful joint disorders (6-8). However, there are no clinical studies focusing especially on elderly patients treated for benign painful skeletal disorders with low-dose RT.

Methods and Materials

The aim of this prospective analysis was to evaluate the short-term and long-term efficacy of low-dose RT for painful degenerative skeletal disorders in patients aged ≥70 years.

Between October 2011 and October 2013, patients aged ≥70 years with calcaneodynia, achillodynia, painful gonarthrosis, and painful bursitis trochanterica were recruited for this prospective register study.

Radiation therapy was performed with both linear accelerator and orthovoltage conditions. Single doses of 0.5 to 1.0 Gy and a total dose of 6.0 Gy per series were used.

Pain was measured before and right after RT (early response) with a 10-point visual analogue scale (VAS) (0, no pain; 10, strongest pain) (26). Additionally, pain relief was measured with the 4-point pain score according to “von Pannewitz” (VPS) (complete pain relief, markedly improved, slightly improved, unchanged) immediately upon completion of RT and during follow-up (8). Within this context, we defined a good response as complete pain relief and markedly improved.

The assessment of the long-term efficacy was carried out by a telephone survey.

Statistics

All data were stored and analyzed using the SPSS statistical package 15.0 (SPSS, Chicago, IL). Descriptive statistics were computed for continuous and categorical variables. The statistics computed included means and standard deviations of continuous variables, and frequencies and relative frequencies of categorical factors. Testing for differences in continuous and categorical variables within the groups was accomplished by the Wilcoxon signed rank test. Testing for differences in continuous variables between the groups was accomplished by...
the Mann-Whitney U test, and in categorical variables between groups with the Fisher exact test, as appropriate. All P values were 2-sided statistical tests, and values of P < .05 were considered to be statistically significant.

**Results**

**Patients**

Overall 166 evaluable patients (108 female, 58 male; mean age 76.6 years [range, 70-90 years]) with calcaneodynia (n = 51), achillodynia (n = 8), painful gonarthrosis (n = 80), and painful bursitis trochanterica (n = 27) were recruited for this prospective trial. An overview of patient characteristics is given in Table 1.

Only 35 patients (21.1%) had a pain history of 6 months or less before radiation treatment.

**Treatment**

In 67 patients RT was performed with the linear accelerator; 99 patients received orthovoltage RT. In 137 patients RT was performed with $12 \times 0.5$ Gy, in 39 patients with $6 \times 1.0$ Gy. In 152 patients RT was performed with 1 series, in 14 patients with 2 series in case of insufficient remission of pain after 3 months.

**Visual analogue scale**

The mean (range) VAS value before treatment was 6.38 (3-10) and directly at the end of RT was 4.49 (0-10) ($P < .001$). A complete overview of the pain assessment before and after RT split by diagnoses is given in Table 2.

**VPS status immediately upon completion of RT**

Concerning the VPS status immediately upon completion of RT, 6 patients (3.6%) were free of pain, 56 (33.7%) were much improved, 47 (28.3%) reported slight improvement, and 57 (34.3%) experienced no change.

**VPS status at follow-up**

After a median (range) follow-up of 29 (3-39) months, 109 patients could be reached for evaluation of follow-up results. Thirty-three patients (30.3%) were free of pain, 21 (19.3%) had marked improvement, 18 (16.5%) had some improvement, and 37 (33.9%) experienced no change. We also found that only a minority of 13 patients (11.9%) used other alternative therapies (shock waves, injections, surgery) during the time of follow-up.

**Comparison of VPS status**

A good response immediately upon completion of RT could be achieved in 62 of 166 patients (37.3%), and at follow-up in 54 of 109 patients (49.6%) ($P < .001$). A complete overview of treatment response divided by treated disorders is given in Table 3.

**Comparison of results for different entities**

An overview of the treatment results of the different diagnoses is presented in Table 4. In general there was better effect of RT for the enthesiopathies in comparison with gonarthrosis.

**Table 1** Patient characteristics regarding diagnoses, distributions of age, gender, and pain intensity before RT

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>n</th>
<th>Age (y), mean (range)</th>
<th>Gender (female/male)</th>
<th>VAS value before RT, mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcaneodynia</td>
<td>51</td>
<td>74.5 (70-87)</td>
<td>40/11</td>
<td>6.69 (3-10)</td>
</tr>
<tr>
<td>Achillodynia</td>
<td>8</td>
<td>72.4 (70-76)</td>
<td>1/7</td>
<td>5.81 (3.5-7)</td>
</tr>
<tr>
<td>Gonarthrosis</td>
<td>80</td>
<td>78.8 (70-90)</td>
<td>50/30</td>
<td>6.32 (3-10)</td>
</tr>
<tr>
<td>Bursitis trochanterica</td>
<td>27</td>
<td>75.2 (71-88)</td>
<td>18/9</td>
<td>6.19 (3-9)</td>
</tr>
<tr>
<td>All patients</td>
<td>166</td>
<td>76.6 (70-90)</td>
<td>109/57</td>
<td>6.38 (3-10)</td>
</tr>
</tbody>
</table>

**Table 2** Pain assessment before and directly at the end of RT, for all patients and divided by diagnoses

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>VAS value before RT, mean (range)</th>
<th>VAS value directly at completion of RT, mean (range)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcaneodynia</td>
<td>6.69 (3-10)</td>
<td>4.05 (0-9)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Achillodynia</td>
<td>5.81 (3.5-7)</td>
<td>4.18 (0.5-6)</td>
<td>.027</td>
</tr>
<tr>
<td>Gonarthrosis</td>
<td>6.32 (3-10)</td>
<td>4.74 (0-10)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Bursitis trochanterica</td>
<td>6.19 (3-9)</td>
<td>4.49 (0-10)</td>
<td>.001</td>
</tr>
<tr>
<td>All patients</td>
<td>6.38 (3-10)</td>
<td>4.49 (0-10)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

**Table 3** Percentage patients with a good response to RT directly at the end of RT and during follow-up, for all patients and divided by diagnoses

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Good response at completion of RT, % (n)</th>
<th>Good response at follow up, % (n)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcaneodynia</td>
<td>62.7 (32/51)</td>
<td>89.5 (17/19)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Achillodynia</td>
<td>12.5 (1/8)</td>
<td>100 (3/3)</td>
<td>.102</td>
</tr>
<tr>
<td>Gonarthrosis</td>
<td>28.7 (23/80)</td>
<td>27.9 (17/61)</td>
<td>.822</td>
</tr>
<tr>
<td>Bursitis trochanterica</td>
<td>37.0 (10/27)</td>
<td>69.2 (18/26)</td>
<td>.002</td>
</tr>
<tr>
<td>All patients</td>
<td>37.3 (62/166)</td>
<td>49.6 (54/109)</td>
<td>.001</td>
</tr>
</tbody>
</table>

Abbreviations: RT = radiation therapy; VAS = visual analogue scale.
Number of series and single dose

Results regarding the influence of number of series and the single dose are shown in Table 5.

Further results

Further significant differences between the groups (fractionation, number of series, radiation unit, pain duration before RT, radiation unit, application of alternative therapy methods during the observation period) were not be found. No side effects of radiation treatment have been observed, in particular no radiation-induced malignancies.

Discussion

The above results of our prospective analysis confirm the results of recently published retrospective and prospective randomized studies, with a good analgesic effect of low-dose RT for patients with calcaneodynia, achillodynia, painful gonarthrosis, and painful bursitis trochanterica (6, 10-12, 15, 16, 19-25).

We demonstrated that even this old and very old population has an excellent benefit from low-dose radiation treatment.

The precise pathophysiologic mechanisms of pain relief after RT are still not well defined. Recent radiobiological experiments show that low doses of radiation have anti-inflammatory efficacy based on the modulation of a multitude of inflammatory pathways and cellular components. This includes immune components like endothelial cells, mono- and polymorphonuclear leukocytes, and macrophages, and an influence on the vascular endothelium with improved tissue perfusion, destruction of inflammatory cells (in particular lymphocytes) with release of cytokines and proteolytic enzymes, modulation of the vegetative nervous system, altering of the tissue pH, and increased membrane permeability. Most likely, irradiation does not act through a single mechanism but through a complex interaction of different effects (27).

We observed a significantly improved long-term efficacy in comparison with the results immediately after RT. This could be due to the delayed clinical onset of effects, which is most likely due to the above-mentioned radiobiological mechanisms.

We observed better long-term results in comparison with the results immediately after RT in patients with calcaneodynia, achillodynia, and bursitis trochanterica. This may be due to the delayed clinical onset of effects, due to the late onset of the above-mentioned radiobiological mechanisms. However, patients with gonarthrosis did not experience this delayed onset of effect. Most likely this is because gonarthrosis is an irreversible pathologic process with progressive cartilage damage that cannot be influenced by low-dose RT, which is limited to the acute inflammatory activation of the disease.

A few previously published double-blind studies from the 1970s did not find an advantage in using RT for painful

### Table 4

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Δ VAS</th>
<th>P</th>
<th>Good response at completion of RT (%)</th>
<th>P</th>
<th>Good response at follow-up (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcaneodynia</td>
<td>-2.64</td>
<td>.172</td>
<td>62.7</td>
<td>.016</td>
<td>89.5</td>
<td>.787</td>
</tr>
<tr>
<td>Achillodynia</td>
<td>-1.63</td>
<td>.512</td>
<td>12.5</td>
<td>.001</td>
<td>27.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Calcaneodynia</td>
<td>-2.64</td>
<td>.002</td>
<td>28.7</td>
<td>.001</td>
<td>89.5</td>
<td>.787</td>
</tr>
<tr>
<td>Gonarthrosis</td>
<td>-1.58</td>
<td>.589</td>
<td>12.5</td>
<td>.328</td>
<td>27.9</td>
<td>.031</td>
</tr>
<tr>
<td>Calcaneodynia</td>
<td>-1.63</td>
<td>.057</td>
<td>37.0</td>
<td>.074</td>
<td>69.2</td>
<td>.111</td>
</tr>
<tr>
<td>Bursitis trochanterica</td>
<td>-1.70</td>
<td>.093</td>
<td>28.7</td>
<td>.304</td>
<td>69.2</td>
<td>.429</td>
</tr>
<tr>
<td>Achillodynia</td>
<td>-1.63</td>
<td>.662</td>
<td>37.0</td>
<td>.422</td>
<td>69.2</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.

### Table 5

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Δ VAS</th>
<th>P</th>
<th>Good response at completion of RT (%)</th>
<th>P</th>
<th>Good response at follow-up (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>One series (n=152)</td>
<td>-2.03</td>
<td>.512</td>
<td>35.9</td>
<td>.165</td>
<td>48.9</td>
<td>.776</td>
</tr>
<tr>
<td>Two series (n=14)</td>
<td>-1.54</td>
<td>.084</td>
<td>21.4</td>
<td>.165</td>
<td>54.5</td>
<td>.175</td>
</tr>
<tr>
<td>12 × 0.5 Gy (n=137)</td>
<td>-2.12</td>
<td>.008</td>
<td>41.8</td>
<td>.076</td>
<td>53.3</td>
<td>.175</td>
</tr>
<tr>
<td>6 × 1.0 Gy (n=39)</td>
<td>-1.01</td>
<td>.057</td>
<td>20.7</td>
<td>.076</td>
<td>29.4</td>
<td>.175</td>
</tr>
</tbody>
</table>

Abbreviations as in Table 1.
of the population (8).

As expected, side effects from low-dose RT are insignificant. Directly after radiation the joint or enthesis might be slightly more painful, but this effect normally disappears in the first weeks after radiation. After a patient’s third to fourth decade, the carcinogenic risk of RT for benign diseases may decrease to that of general risk for cancer in the normal population. The reported lifetime risk of cancer induction is approximately 0.2% with low-dose joint irradiation, the main risk being induction of leukemia. However, the risk decreases with increasing age (8, 31, 32). Hence, in contrast to younger patients, low-dose RT in elderly patients can be used as a first treatment option too, because the carcinogenic risk can be nearly neglected. Clearly, most radiation-induced malignancies have a latency of 15 to 30 years to develop, which will not play a role compared with the life expectancy of the population (8).

On the other hand, surgical and other invasive procedures are often accompanied by complications and may bear a major economic burden in these multi-morbid elderly patients (7, 9).

Compared with the RT of malignancies, whereby the radiation treatment may be compromised by multimorbidity and multidrug medication, this is not a problem in low-dose RT for benign disorders because of the noninvasivity and the low toxicity profile (7).

Single doses of 0.5 to 1.0 Gy, total doses of 3.0 to 6.0 Gy, and 2 or 3 fractions per week with orthovoltage or megavoltage techniques are recommended. Generally, the target volumes for the different enthesopathies encompass the complete involved insertion zone together with the nearby bony and muscular and soft tissue structures. For painful arthrosis it is necessary to include the articular cartilage, the neighboring bone, and the entire synovium, as well as the joint-surrounding muscles and the periarticular connective tissue. In case of persisting pain or insufficient pain relief 6 to 12 weeks after the first RT series, a second RT series may be recommended (32).

Conclusion

Low-dose RT is a very effective treatment for the management of painful degenerative disorders of joints and entheses in the elderly. Because of the delayed onset of analgesic effects, low-dose RT results in a significantly improved long-term efficacy in comparison with the results immediately after RT. In view of the aging population and the corresponding increase in painful degenerative disorders of joints and entheses, low-dose RT offers a low-risk, genuinely conservative, noninvasive therapeutic alternative for elderly patients.

References


