

Original Article

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The analgesic effect of low-dose radiotherapy in treating benign musculoskeletal painful disorders using different energies: A retrospective cohort study

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Abstract

Introduction: This retrospective cohort study tries to determine if there is a correlation between the effectiveness of low-dose radiotherapy (LDRT) in treating painful inflammatory or degenerative musculoskeletal disorders (MSDs) and the applied radiotherapy energy.

Patients and Methods: Between September 2019 and January 2020, a total of 91 patients with either painful inflammatory or degenerative MSDs were treated with LDRT. The inclusion criteria were patients older than 40 years with either painful inflammatory disorders of the wrist or ankle joints. All patients were treated with a single dose of 0.5 Gy and a total dose of 6.0 Gy (2 to 3 fractions weekly). Patients were divided into two groups. Orthovolt group was treated with 200 Kv, 15 mA and 1 mm copper filtration with different tubes according to the site to treatment using direct fields. The second group included patients treated with Linac machines with opposing fields using energies between 6 and 18 MV. The pain was evaluated before and on the last day of treatment and 4–6 months later using the Numerical Rating Scale.

Results: 91 patients compatible with the inclusion criteria were identified with a median of 60 years. The median duration of symptoms was 6 months. 46% of patients were males, and 54% were females. The Orthovolt group included 49% of the patients and the Megavoltage group 51%. Most of the patients (98%) were previously treated with other methods such as local corticosteroid injection, painkillers or physiotherapy. At the end of the treatment, 60% of the patient's showed subjective pain relief and only 6% had a complete response. The follow-up conducted 4 to 6 months after the treatment showed that 65% of patients had a complete response and 8% had an improvement. The comparison between both studied groups shows that the used energy does not affect the response either at the end of the treatment or at the second control. The relationship between the aetiology and the early and late responses shows no difference in the early response but a better late response in patients suffering from inflammatory diseases with a *p*-value of 0.015. The response according to the treated location shows that patients with osteoarthritis of the ankle joint have a worse response in comparison to other examined joints and plantar fasciitis.

Conclusion: LDRT is an effective analgesic treatment option for both inflammatory and degenerative MSDs. There is no difference in response according to the used energy, and most of the patients show late responses 4 to 6 months after the treatment.

Introduction

The analgesic effect of low-dose radiotherapy (LDRT) in treating painful musculoskeletal disorders (MSDs) is well known.^{1,2} In the last few decades, the mechanism of action as well as the optimal therapeutic dose and fractionation regimen are the main topics under investigation.^{3–5} Germany is considered as one of the leading countries in this field and has a long tradition of treating benign MSDs with LDRT. The German Society of Radiation Oncology published the first treatment guideline in the ninetens of the last century, which was updated lastly in 2018.⁶ Several studies have investigated LDRT aiming to understand and prove their analgesic effect.^{7–9} The applied doses and the used technique, including target volumes, treated fields, and energy spectrum, differ between these studies and were continuously optimised in the last few decades, keeping up with the rapid progress of the radiotherapy machines and techniques.

This retrospective cohort study tries to declare if there is a correlation between the effectiveness of LDRT in treating painful inflammatory and degenerative MSDs and the used radiotherapy energy.

Patients and Methods

Between September 2019 and January 2020, a total of 91 patients with either painful inflammatory or degenerative MSDs were treated with LDRT. These patients were routinely treated in our department with the Orthovolt unit because of the implementation of a new Orthovolt machine where the patients were treated during the renovation period with Megavoltage Linear accelerator (Linac).

The inclusion criteria were patients older than 40 years with either painful inflammatory disorders such as epicondylitis humeri or plantar fasciitis or degenerative osteoarticular disorders of the wrist or ankle joints. The duration of the symptoms should be 1 month or longer. Patients with a previous history of malignant disease were also included after the exclusion of local or systemic recurrences by clinical and radiological examinations, including MR tomography and bone scintigraphy. Previously irradiated patients or those who were treated with other conservative methods such as ultrasound, local injections, laser therapy and electrotherapy, were also allowed to be included.

The exclusion criteria included patients treated with different energies in the same course. The pain aetiology is regarded as other medical conditions such as rheumatic or vascular diseases. Musculoskeletal proliferative diseases such as Morbus Ledderhose or Morbus Dupuytren and Inflammatory or degenerative disorders affecting small joints such as metacarpophalangeal, interphalangeal and metatarsophalangeal joints, or large joints like shoulder, knee and hip joints were also excluded. Patients desiring to have children in the first 2 years after the treatment or those who did not complete the radiotherapy course or missed follow-up were not allowed to be involved in the study.

The medical history, clinical examination and radiological investigations including an X-ray of the affected region were conducted. All patients were treated with the same fractionation, a single dose of 0.5 Gy, and a total dose of 6.0 Gy (two to three fractions weekly). The pain was evaluated before and on the last day of treatment then 4 to 6 months later using the Numerical Rating Scale, Verbal Rating Scale and modification of von-Pannewitz score as following complete pain relief, partial response and unchanged or worsening the pain conditions.

Patients with eligible criteria were divided into two groups. The first one included those who were treated with the Orthovolt unit (T-200 System, Firma Wolf-Medizintechnik GmbH, St. Gangloff, Thuringia) with the following parameters, 200 Kv, 15 mA, 1 mm copper filtration with different tubes according to the site to treatment using direct fields. The second group included patients treated with Linac machines (TrueBeam generation 2-7, Varian Medical Systems, Palo Alto, CA, USA) with opposing fields using energies between 6 and 18 MV according to the treated area with previous CT simulation. The collected data were statistically analysed using SPSS program version 25 (SPSS Inc., Chicago, IL, USA) with the assumption of the null hypothesis that there is no difference between both groups treated with different energies.

This retrospective analysis was conducted following the ethical standards of clinical research and compatible with the Helsinki Declaration of 1975 and the subsequent revisions. The internal institutional approval and patient agreement in the form of written consent were obtained.

Results

A total of 91 patients with painful inflammatory and degenerative MSDs are compatible with the inclusion criteria. The median age

Table 1. Patient characteristics

		Count	n %
Gender	Male	42	46.2
	Female	49	53.8
Previous treatment	Yes	89	97.8
	No	2	2.2
Type of energy used in the treatment	Orthovoltage	46	50.5
	High voltage	45	49.5
Need for further treatment after the radiotherapy	No	69	75.8
	Yes	22	24.2
Medical treatment including NSAID	No	23	25.3
	Yes	68	74.7
Ultrasound treatment	No	70	76.9
	Yes	21	23.1
Orthopaedic insoles	No	42	46.2
	Yes	49	53.8
Local analgesic injection	No	74	81.3
	Yes	17	18.7
Previous radiotherapy	No	81	89.0
	Yes	10	11.0
Another treatment	No	63	69.2
	Yes	28	30.8
Aetiology	Inflammatory	77	84.6
	Degenerative	14	15.4

was 60 years, and the median duration of symptoms was 6 months. The male patients represent 46%, and the female patients were 54%. 49% of the patients were treated with the Orthovolt unit, and 51% were treated with a linear accelerator. 98% were previously treated with other methods including local corticosteroid injection, pain killers such as NSAID, physiotherapy and other options. The patient's characteristics are summarised in Table 1.

Most of the patients (70%) suffered from an inflammatory heel spur or plantar fasciitis. Patients with epicondylitis humeri represent 17% of the studied patients. The classification of patients according to the treated region is illustrated in Figure 1.

At the end of the treatment, 60% of the patients showed subjective improvement of the pain and only 6% had a complete response. The delayed assessment which was conducted 4 to 6 months after the treatment showed 65% of patients a complete response and 8% an improvement. The treatment response is illustrated in Figures 2 and 3.

The Mann-Whitney U test was used to compare the treatment response between both studied groups, which resulted in retaining the Null hypothesis and proving that the used energy does not affect the response either at the end of the treatment or at the second control.

The same statistical test was used to compare the early and late response according to the disease aetiology, which shows no difference in the early response and better late response of patients suffering from inflammatory diseases with a *p*-value of 0.015. Figure 4.

Another statistical analysis with Kruskal-Wallis test was used to compare the response according to the treated location and

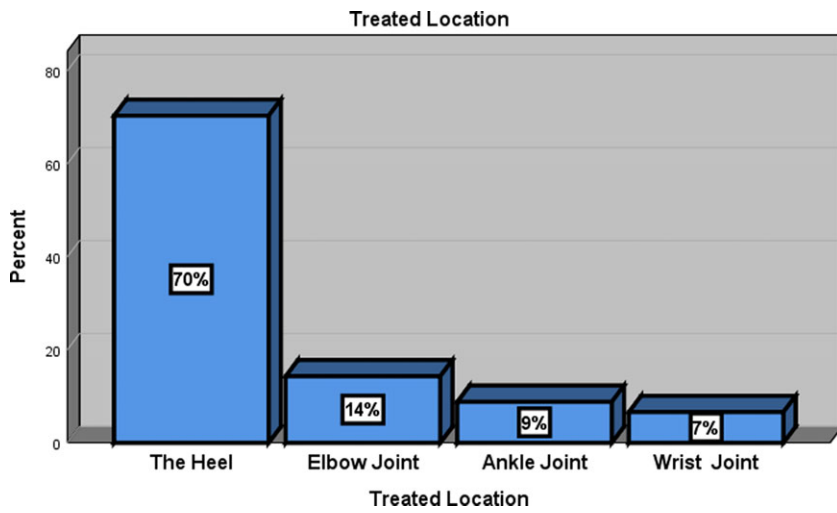


Figure 1. Classification of patients according to the treated region.

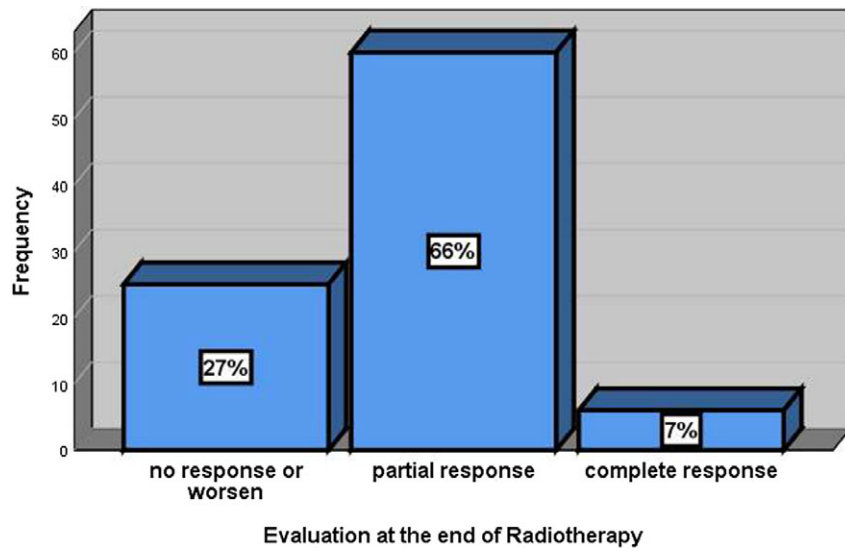


Figure 2. Evaluation of treatment response at the end of the treatment.

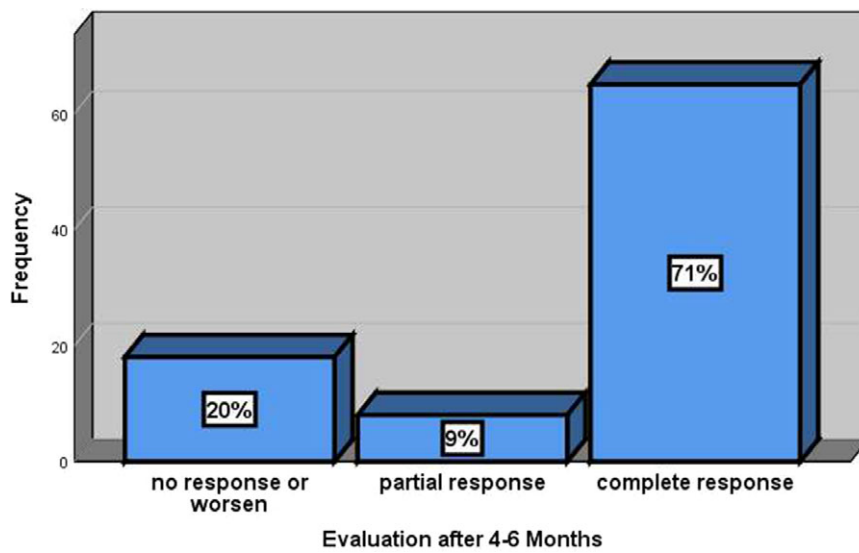


Figure 3. Evaluation of the late treatment response.

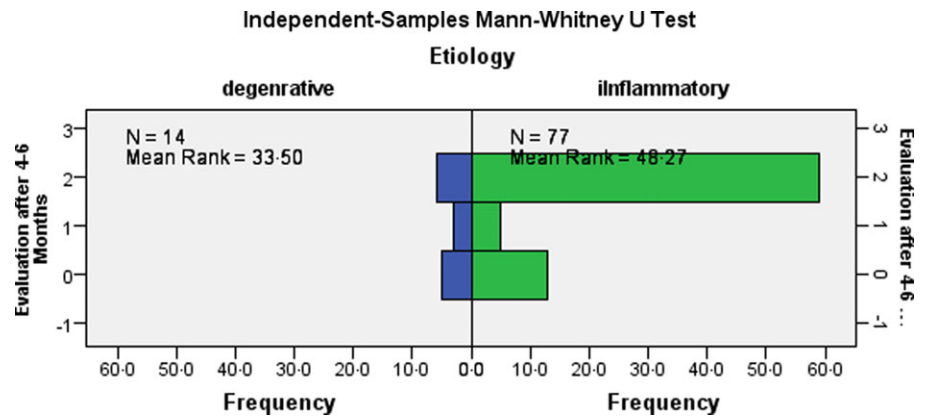


Figure 4. Comparison between the early and late response according to disease etiology. Note: (0 = no response or pain worsening, 1 = partial response, 2 = complete pain relief).

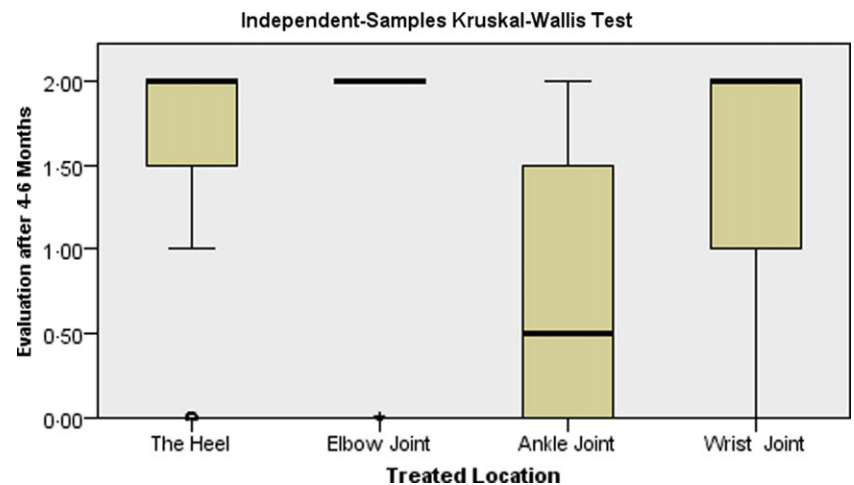


Figure 5. Comparison of response according to the treated location. Note: (0 = no response or pain worsening, 1 = partial response, 2 = complete pain relief).

showed that patients with osteoarthritis of the ankle joint have worse responses otherwise, there was no difference in response between the other treated sites (Figure 5).

Comparing the responses at the end of the treatment and 4 to 6 months later using the Wilcoxon signed-rank test resulted in a significant difference with p -value 0.000 favouring the late response.

There were no immediate or delayed side effects associated with the treatment.

Discussion

The analgesic effect of LDRT in treating inflammatory and degenerative MSDs is well known since the beginning of the 20 century.¹ Several studies have been conducted to investigate this effect using different single and total doses, variable techniques and energies.¹⁰⁻¹² The mechanism of action of LDRT is not yet completely clarified. It is assumed that LDRT stimulates a complex anti-inflammatory process by inhibiting the leucocyte accumulation, transfer and differentiation to macrophages. It also decreases the production of inflammatory-inducing cytokines and nitric oxide, which regulates the vascular permeability after any mechanical and chemical irritation of tissues resulting in the suppression of the inflammatory cycle.^{6,13,14}

The optimal dose and fractionation were also under investigation with a widely accepted single dose of 0.5 to 1.0 Gy and a total dose of 3 to 6 Gy in one or two courses.^{6,15-18} The Orthovolt machines producing X-ray with low energies (kilovolt) were routinely used in treating

benign skin and MSDs until the end of the last century.¹⁹⁻²¹ The reason for that standard of care was not only to reduce the costs and to spare the expensive Linacs for treating malignant diseases but also because of the assumption that the low energetic spectrum of radiotherapy is more effective in healing superficial soft tissue diseases.²²

The use of linac in the treatment of benign diseases has steadily increased over the past few decades, in parallel with improvements in treatment capacities and reductions in treatment costs. The use of different radiotherapy energies was compared in the multianalysis of the national standard of care in treating plantar fasciitis done by Micke et al.²², which showed that there was no difference in response according to the used energy. Another prospective study that evaluated the analgesic effect of LDRT showed the same results.²³

Nevertheless, it is important to notice that the investigated samples in these studies were unequal, which can affect the statistical power. In several studies, plays the patient selection also a role in the final results, either by including only one MSD with a specific treatment area, or by broadening the selection criteria to include regions that physically require high energy, such as the large joints which preferably treated with Linac.²³

The effectiveness of LDRT in the previously conducted studies varies depending on the aetiology, treated location, severity of the diseases and eventually the duration of symptoms.²³⁻²⁵ In the case of plantar fasciitis and epicondylitis humeri, a response rate of up to 90% can be achieved.^{1,9,23} The therapeutic effect in the case of osteoarthritic lesions reached up to 75%.^{23,26}

Conclusion

LDRT is an effective analgesic treatment option for both inflammatory and degenerative MSDs with different success rates according to the site and nature of the pathological condition. There is no difference in response according to used energy, and most of the patients respond lately with a time frame of 4 to 6 months after the end of the treatment.

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Conflicts of Interest. All authors declare that they have no conflicts of interest.

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