ORIGINAL ARTICLE

Radiotherapy with soft X-rays in Dupuytren's disease – successful, well-tolerated and satisfying

M. Zirbs,[1,2] T. Anzeneder,[1] H. Bruckbauer,[3] H. Hofmann,[1] K. Brockow,[1] J. Ring,[1,2] B. Eberlein[1]

[1]Klinik und Poliklinik für Dermatologie und Allergologie am Biederstein, Klinikum rechts der Isar, Technische Universität München, Munich, Germany

[2]Christine Kühne Center for Allergy Research and Education (CK-CARE), München, Munich, Germany

[3]Hautarztzentrum Neufahrn, Neufahrn, Germany

*Correspondence: M. Zirbs. E-mail: michael.zirbs@lrz.tu-muenchen.de

Abstract

Background Up to present no curative treatment is known for Dupuytren's disease (DD). Surgery remains the most common treatment but lack of long-term efficacy and complications limit this therapeutic option.

Objective In a retrospective analysis, the results of radiotherapy with soft X-rays in the treatment of DD were evaluated.

Methods A total of 206 patients (297 affected hands) with DD were included. Radiation therapy was carried out with soft X-rays. A structured questionnaire considering patient and disease characteristics and effects of radiotherapy was evaluated after a median follow-up time of 40 months.

Results Ninety-three (45%) of the 206 treated patients were reported on a regression of symptoms after radiation. No further disease progression (including patients with regression) was present in 165 patients (80%). Satisfaction with the therapy was expressed with an average score of 7.9 points (visual analogue scale, 0 = not satisfied, 10 = extremely satisfied). Subjective therapeutic effects for 426 nodules and/or cords showed a reduction of 92 nodules and/or cords.

Conclusion In 206 DD patients further disease progression was stopped in most patients. Radiotherapy proved to be well-tolerated, successful and satisfying for the patients.

Received: 3 December 2013; Accepted: 21 July 2014

Conflicts of interest

The authors have no conflict of interest to declare.

Funding source

None declared.

Introduction

Dupuytren's disease (DD) is a benign, fibroproliferative disorder of the fascia of the hand and fingers. Its aetiology remains unclear and it seems to have a multifactorial background with several associations as genetic inheritance, smoking, alcohol, diabetes mellitus, hyperlipidaemia, localized trauma, vibration exposure and certain drugs like anti-epileptics.[1–3] Prevalence of DD ranges from 2% to 42% in the male population.[4,5] The male to female ratio is about 3–15 : 1 and the incidence in women and men increases with age.[2–7]

Dupuytren's disease presents clinically with cords and nodules on the palmar fascia and a mostly progressive and irreversible flexion of the fingers due to a contracture of the fascia.[3,7,8] In most cases, the fourth and fifth finger of the hand are affected.[8]

So far, no curative treatment is known. Restoration of the hand function and prevention of disease progression is the aim of therapeutic approaches.[7,9–11] Therapy includes surgical correction like open excision of the involved fascia (fasciectomy), open fasciotomy and needle aponeurotomy and non-surgical treatments such as injection of enzymes, radiotherapy, ultrasonic therapy, dimethyl sulphoxide, allopurinol, steroids, interferon-γ and vitamin E, mostly without proven efficacy or limited success.[11–17]

Surgery is currently the most common treatment of DD in late stages but especially for early stages of DD radiotherapy is an attractive treatment option.[7,10,11,18] As published data on this well-known treatment option are limited, we want to draw the attention on new aspects concerning treatment of DD with radiotherapy.

In a retrospective analysis, the results of radiotherapy in the treatment and in the prevention of disease progression of DD were evaluated.

Patients and methods

Patient's characteristics

In total, 355 patients with DD have been treated with radiotherapy between 1999 and 2008 at the Department of Dermatology and Allergy, Technische Universitaet Muenchen (Munich, Germany) and Hautarztzentrum Neufahrn (Germany). In 2009, 6 months after the last treatment, 355 questionnaires were sent to these patients. Of these, 206 patients returned the questionnaires and were included in this study [123 males (59.7%), 83 females (40.3%)]. Median age of all included patients was 62.9 years (63.05 years in males, 62.4 years in females). Our collective included 297 hands with DD. Bimanual involvement was found in 91 patients (44.2%), 115 patients (55.8%) had a unilateral involvement. The right hand was affected in 72 patients (62.6%) and the left hand in 43 patients (37.4%).

Radiotherapy

Following informed consent, radiation therapy was carried out with soft X-rays (Dermopan II, Siemens, Germany). We used 50-kV photons at 25 mA, a 1 mm aluminium filter and a 2 mm cellon filter. Radiation was led through a tube (diameter 4 cm) at a focus skin distance of 15 cm. 1 mm lead cutouts protected the uninvolved areas of the palm. A total dose of 32 Gy was applied, with an 8-week interval between the four courses of two fractions at two consecutive days with a single dose of 4 Gy. Consecutively, half-value depth was 15 mm.

Evaluation

All study participants answered a structured questionnaire (Appendix 1) considering family history, predisposing factors, occupation, disease characteristics, progression, treatments, effects, side-effects of the radiotherapy and the satisfaction with this treatment measured with a visual analogue scale (1 = not satisfied, 10 = very satisfied). Mean follow-up time was 44.7 months (3 years and 9 months). Median was 40 months (3 years and 3 months), range from 6 to 115 months. A summary of the patient's characteristics are shown in Table 1.

Statistical evaluation

Statistical evaluation was performed using the fourfold table test.

Results

Left- and right-handedness

One hundred and ninety-five patients (95%) were right-handed and seven patients (3.4%) were left-handed and no data were obtained in four patients (2.6%).

Table 1 Patient characteristics

	n	%
Patients, total	206	100
Males	123	59.7
Females	83	40.3
Median age of the patients (years)	62.9	
Males	63.05	
Females	62.4	
Affected hands, total	297	100
Unilateral	115	55.8
Bilateral	91	44.2
Right hand	72	62.6
Left hand	43	37.4
Right-handed	195	95
Left-handed	7	3.4
Positive family history of Dupuytren's disease	59	28.6
Most common clinical symptoms		
Nodules	235 hands	
Cords	234 hands	
High tension	128 hands	
Comorbidities		
Total	100	48.5
Morbus Ledderhose	18	8.7
Induratio penis plastica	13	6.3
Knuckle pads	18	8.7
Keloids	7	3.4
Cardiovascular disease	21	10.2
Diabetes mellitus	18	8.7
Liver-disease	4	1.9
Epilepsy	1	0.5
Occupational stress/manual exposure		
Heavy	23	11.2
Low/fine	30	14.6
None	135	65.5

Family history and predisposing factors

Fifty-nine patients (28.6%) reported of at least one family member with diagnosis of DD and no data were obtained in eight patients (3.9%).

Forty-nine patients (24%) suffered from at least one other dermatofibrosis (Morbus Ledderhose of the plantar fascia in 18 patients, induratio penis plastica in 13 patients, knuckle pads in 18 patients and keloids in seven patients) and no data were obtained from six patients (3%).

Forty-two patients (20.4%) reported on comorbidities: 21 (10.2%) of these had an affection of the cardiovascular system like hypertension or coronary heart disease. Liver diseases or functional dysregulation (γ-GT elevation, haemochromatosis, toxic liver disease) were found in four patients (1.9%). Diabetes mellitus was present in 18 patients (8.7%), epilepsy in one patient (0.5%).

Occupation

Fifty-six patients (27.2%) had manual occupations, 98 patients (47.6%) were in the service sector and 44 patients (21.4%) had academic jobs. No data were obtained in eight patients (3.9%).

Occupational stress

Twenty-three patients (11.2%) reported on regular and heavy occupational manual work, 30 patients (14.6%) on light manual work and 135 patients (65.5%) had no manual work load in their occupation or in their leisure time. No data were obtained in 18 patients (8.7%).

Pretreatments

Thirty-seven patients (18%) had received one or more treatments: hand surgery in 18 patients, needle fasciotomy in eight patients, local steroid injection in three patients; in single patient's oral intake of vitamines, shock-wave therapy, magnetic field therapy, massage with homeopathic cremes, therapy with systemic non-steroidal anti-inflammatory drugs, handgymnastics, massage and injections of non-medical practitioners.

Clinical symptoms

Most patients suffered from nodules (235 hands), cords (234 hands) and high tension in the involved palms (128 hands). Less often symptoms like pain and burning, trigger fingers or functional restrictions were stated. Two hundred and eighty-three nodules and cords were present in the right hands and 254 nodules and cords in the left hands.

One hundred and twenty-two patients (59.2%) showed a slow progressive activity of the disease, 23 (11.2%) had a slow progression in batches, 25 (12.1%) had a rapid progression and 14 (6.8%) a very rapid disease progression.

One hundred and thirty-nine patients [67.5%, no data in 67 patients (32.5%)] had a median of 20 months (range was 0–329 months or 27.5 years) as first recognition of DD and onset of the radiation therapy.

Radiation therapy

Ninety-three (45%) of the 206 treated patients were reported on a regression of symptoms after radiation. No further disease progression (including patients with regression) was seen in 165 patients (80%).

Satisfaction with the therapy was measured with a visual analogue scale and included 198 patients (no data for eight patients) and estimated as very good [average score of 7.9 points (SD 2.7 points], median of 9 points).

Subjective therapeutic effects for 426 nodes and/or cords showed a reduction of 92 nodules and/or cords.

Side-effects

Erythema of the treated area was reported in 42 patients (20.4%) and no data were available for 27 patients (13.1%). Dryness of the treated skin was present in 82 patients (39.8%) and no data were available for 15 patients (7.3%). Desquamation was reported in eight patients (3.8%).

Chronic side-effects that persisted more than 4 weeks after the end of the treatment were dryness of the skin (41 patients, 20%), skin atrophy (seven patients, 3%), lack of sweating (eight patients, 4%), teleangiectasia (six patients, 3%), desquamation (five patients, 2%) and sensory affection (four patients, 2%).

Therapeutic results depending on symptom duration prior to beginning of radiation therapy

Available data on symptom duration prior to radiation were present for 117 patients: Of these, 56 patients had a duration less or equal to 20 months and 61 patients had a duration of more than 20 months before therapy start. Significantly better improvement was found in patients with symptom duration of less than 20 months ($p<0.05$).

No difference in results was found with regard to symptoms or number of nodules and/or cords nor age of the patients.

Discussion

After a mean follow-up time of almost 4 years after radiation therapy with soft X-rays, a further progression of DD could be avoided in 80% of the study collective. Most patients were satisfied with the therapy (average score of 7.9 points of 10 points in the visual analogue scale). Dryness of the skin was the most common side-effect in about 40% of all patients.

Altogether radiotherapy in this cohort proved to be effective, safe and satisfying for the patients.

Generally, the aetiology of DD is still unclear and treatment remains a therapeutic challenge since its first description in the Lancet in 1834.[3]

The male to female ratio with 10 : 7 in our group showed more affected females than described in the literature with 10 : 2–10 : 6.[3–7] The median age with about 63 years corresponded to the available data.[2–7] As expected, we found a family history of DD in about one-third of all patients as a sign of the heritability of this disease as shown in several other studies.[19–21] Existence of other dermatofibrotic diseases was reported in about one-fifth of the collective corresponding to the previously published data.[2,22–24]

The observed comorbidities were as high as in the normal population and we could not confirm correlations described in other studies.[2,12,22,25]

Another discussed risk factor for DD is occupational and non-occupational stress or trauma of the hands.[1,26–28] Our data suggest no significant correlation as about 65% of the patients had no heavy manual work and only 56 patients (27.2%) had manual occupations. Bimanual affection as seen in our patients and described before is as well an argument against the workload or trauma hypothesis, because one hand is usually leading in manual activity, in our collective the right hand with 95%.[27,28]

The literature is divergent and discusses a three times higher risk at heavy occupational hand stress whereas other studies showed no correlation.[1,26–28] Still, it remains unclear whether traumatic hand lesions or traumatic stress on the hands might induce fibrotic palmar changes.[1,26]

The therapeutic management of DD is not concordant throughout the literature. Some authors still prefer the wait and see option especially in early stages when the disease often is apparently stable.[9,27] Progression in untreated DD hands is seen in about 50% of patients after a 6 years follow-up time.[29]

The intralesional injection of clostridial collagenase was recently described as safe and effective in non-surgical treatment of DD in early stages.[9,13,30,31] An 8-year follow-up of eight patients treated with collagenase injection showed a reoccurrence or progression of symptoms, however, in a less severe manifestation than the initial status.[32] Other data showed more benefit in a 3-year follow-up study in a larger DD population of over 600 patients.[30]

Surgical treatment including total, partial and selective fasciectomy and needle aponeurectomy remains the most common used treatment for DD in later stages.[7,9,33–35] Postoperative complication rates for DD are 17–50% and include tendon rupture, nerve or vessel injury, haematoma, wound infection, dystrophy and scar contraction.[7,10] Recurrence rates after surgical DD treatment range from 26% to 80% and may be associated with co-factors like disease severity, diabetes, alcohol abuse or epilepsy.[13,36] After all, surgical treatment still is the treatment of choice but it seems to be reserved for advanced DD levels with functional impairment.[7,33,34,37,38]

Radiation of DD has not been used to replace surgical treatment, it rather was an option for prevention of further disease progression especially in early-phase DD as its first therapeutic experiments before world war two.[39] On the basis of biological process of fibrogenesis involving radiation-sensitive targets like fibroblasts, lymphocytes, production of fibrotic growth factor and tissue growth factors, this treatment has a scientific rationale.[39]

The reviewed literature on radiation of DD varies in the application of radiation, follow-up time and definition of the clinical response to the treatment.

Good treatment results with an improvement of clinical symptoms have been described in 1959 by Schirren *et al.*, with the same radiation protocol as in our study. Schirren[40] found that higher doses did not show better response and total doses below 16 Gy did not have any effect. Another study by Keilholz[37] of 1996 with a follow-up time of 6 years, 96 patients and a daily fractionation of 5 × 3 Gy and a second circle 6–8 weeks later (cumulative dose of 30 Gy) showed an improvement of the clinical symptoms in 72% of the patients, a stop of progression in 17% and a progression in 11% of the patients. The same group presented the data with a 10 year follow-up in 99 patients and revealed a regression or stabilization of DD in 59% of the radiated areas. 22% of the patients had a progression and 19% of the patients developed new DD lesions in not irradiated areas.[41] A 13 year follow-up of the described collective with 135 patients reported of an improvement in 10% of patients, a stabilization in 59% of the patients and 31% of the DD patients had a disease progression. Furthermore, radiotherapy had no effect on complication rates in surgical treatment due to disease progression.[29] Long-term side-effects like skin atrophy and dry desquamation was observed in 32% of the patients.[29] There seems to be a tendency towards an increase in disease progression or reoccurrence with a longer follow-up time. However, still this long-term data prove efficacy to prevent disease progression of DD by radiotherapy.[37]

Seegenschmiedt *et al.*[38] performed a randomized clinical study to compare two radiation dose concepts. In this study with 129 patients, radiation was done with 120 kV at 20 mA. In one group, the patients received a total dose of 30 Gy by applying 10 × 3 Gy in 2 series (5 × 3 Gy) separated by an 8-week interval, the second group received a total dose of 21 Gy by applying 7 × 3 Gy in one series within 2 weeks. Follow-up at 12 months showed an improvement of symptoms in 56%, respectively, 53% (30 Gy group vs. 21 Gy group) of the patients, a stabilization in 37%, respectively, 38% and a progression in 7%, respectively, 9% of the patients.[38] Thirty-eight per cent of the patients developed erythema and dryness of the radiated skin areas, 6% had only an erythema, 6% a desquamation and 2% a prolonged oedema. After 3 months side-effects persisted in 13% of the patients and after 6 months in 5% of the patients. Altogether both radiation regimes were well tolerated and equally effective, whereas in the 21 Gy group the incidence of acute toxic side-effects was slightly higher than in the 30 Gy group.[38] Other radiation induced complications may be lymphatic occlusions, actinic nerve lesions and skin affections like dermatitis, sclerosis and necrosis, but still radiotherapy has proved to be quite safe in early-stage DD.[14,37]

The described rates and distribution of side-effects are about the same as we have seen in our study collective (acute: erythema 20.4%, dryness 39.8%, desquamation 3.8%; chronic: dryness 20%, skin atrophy 3%, lack of sweating 4%, angiectasia 3%, desquamation 2%, sensibility affections 2%).

The risk of cancer and other neoplasia is definetively given when applying ionizing radiation to human cells. We used in total a dose of 32 Gy which is low compared to doses given in oncologic treatments. Uninvolved skin was always protected by lead cutouts. It has been shown that doses of 30 Gy are not increasing the risk of neoplasia in radiated areas as shown by Betz *et al.*[29] (2010) after 13 years of follow up.

According to previous studies the risk of developing skin cancer is clearly related to the total dose applied showing that cumulative doses up to 30 Gy have a very low risk for neoplasia.[42] Cases of skin cancer in the treated area after radiotherapy of M. Dupuytren have not been published yet, even if this treat-

ment is performed since decades. Furthermore, the "Deutsche Dupuytren Gesellschaft" (German Dupuytren Society) published a cancer risk estimation after radiotherapy of M. Dupuytren together with the former GSF (Gesellschaft für Strahlenforschung, Neuherberg, Society for Radiation Research), now Helmholtz Zentrum München - Deutsches Forschungszentrum für Gesundheit und Umwelt (GmbH).[43] It shows that the risk is dependent on the patient's age and gender at the time of irradiation. With a median age of our patients of 63 years the calculated risk is clearly under 0.05%.

Comparing the results of radiation in our collective, we found a regression of symptoms in 45% of the patients which is in the range of the cited literature (7–56%).[29,37,41,44,45] 80% of our collective showed no further disease progression which corresponds to publications of the last years (14–98%).[29,37,41,44,45] Still, the different radiation protocols make it difficult to compare these studies.

Our data revealed a significantly higher improvement in patients with a symptom duration of less than 20 months. It has been described that early disease stages are treated more effectively which supports our findings.[29,41,44] In addition, treated DD hands had a lower recurrence rate after 10 years follow-up compared to the untreated, natural course of the disease.[41]

There are several limitations of the study. A control group to compare results and effects of the radiation is lacking. Due to the fact that all our patients were treated according to disease progression and lack of therapeutic alternatives, we do not have data of an untreated collective in this study.

There is always a bias with patients giving information on subjective symptoms in questionnaires.

Finally, satisfaction with radiation therapy was high and the treatment well-accepted. Due to often severe functional impairment leading to individual suffering and the high economic burden, treatment of DD is necessary and radiation therapy represents a safe and cost-effective treatment option for early-phase DD.[46]

Acknowledgement

The authors want to thank the Christine Kühne Center for Allergy Research and Education (CK-CARE) for support.

References

1 Burke FD, Proud G, Lawson IJ, McGeoch KL, Miles JN. An assessment of the effects of exposure to vibration, smoking, alcohol and diabetes on the prevalence of Dupuytren's disease in 97,537 miners. *J Hand Surg Eur* 2007; **32**: 400–406.
2 Degreef I, Steeno P, De Smet L. A survey of clinical manifestations and risk factors in women with Dupuytren's disease. *Acta Orthop Belg* 2008; **74**: 456–460.
3 Gudmundsson KG, Arngrimsson R, Sigfusson N, Bjornsson A, Jonsson T. Epidemiology of Dupuytren's disease: clinical, serological, and social assessment. The Reykjavik Study. *J Clin Epidemiol* 2000; **53**: 291–296.
4 Anthony SG, Lozano-Calderon SA, Simmons BP, Jupiter JB. Gender ratio of Dupuytren's disease in the modern U.S. population. *Hand (N Y)* 2008; **3**: 87–90.
5 Wilbrand S, Ekbom A, Gerdin B. The sex ratio and rate of reoperation for Dupuytren's contracture in men and women. *J Hand Surg Br* 1999; **24**: 456–459.
6 Ross DC. Epidemiology of Dupuytren's disease. *Hand Clin* 1999; **15**: 53–62, vi.
7 Loos B, Puschkin V, Horch RE. 50 years experience with Dupuytren's contracture in the Erlangen University Hospital–a retrospective analysis of 2919 operated hands from 1956 to 2006. *BMC Musculoskelet Disord* 2007; **8**: 60.
8 Rayan GM. Clinical presentation and types of Dupuytren's disease. *Hand Clin* 1999; **15**: 87–96, vii.
9 Rayan GM. Nonoperative treatment of Dupuytren's disease. *J Hand Surg Am* 2008; **33**: 1208–1210.
10 Bulstrode NW, Jemec B, Smith PJ. The complications of Dupuytren's contracture surgery. *J Hand Surg Am* 2005; **30**: 1021–1025.
11 Pess GM, Pess RM, Pess RA. Results of needle aponeurotomy for dupuytren contracture in over 1,000 fingers. *J Hand Surg Am* 2012; **37**: 651–656.
12 Syed F, Thomas AN, Singh S, Kolluru V, Emeigh Hart SG, Bayat A. In vitro study of novel collagenase (XIAFLEX(R)) on Dupuytren's disease fibroblasts displays unique drug related properties. *PLoS ONE* 2012; **7**: e31430.
13 Badalamente MA, Hurst LC. Enzyme injection as nonsurgical treatment of Dupuytren's disease. *J Hand Surg Am* 2000; **25**: 629–636.
14 Cordova A, Tripoli M, Corradino B, Napoli P, Moschella F. Dupuytren's contracture: an update of biomolecular aspects and therapeutic perspectives. *J Hand Surg Br* 2005; **30**: 557–562.
15 Hurst LC, Badalamente MA. Nonoperative treatment of Dupuytren's disease. *Hand Clin* 1999; **15**: 97–107, vii.
16 Braun-Falco O, Lukacs S. Dermatologische Röntgentherapie: Ein Leitfaden für die Praxis. Springer, Berlin Heidelberg GmbH, 1. Auflage, 5. Juli 1973.
17 Peter RU, Plewig G. Strahlentherapie dermatologischer Erkrankungen. Blackwell Wissenschafts-Verlag, Berlin, Wien, 1996.
18 Gilpin D, Coleman S, Hall S, Houston A, Karrasch J, Jones N. Injectable collagenase *Clostridium histolyticum*: a new nonsurgical treatment for Dupuytren's disease. *J Hand Surg Am* 2010; **35**: 2027-38e1.
19 Dal Cin P, Pauwels P, Poldermans LJ, Sciot R, Van den Berghe H. Clonal chromosome abnormalities in a so-called Dupuytren's subungual exostosis. *Genes Chromosome Cancer* 1999; **24**: 162–164.
20 De Wever I, Dal Cin P, Fletcher CD *et al.* Cytogenetic, clinical, and morphologic correlations in 78 cases of fibromatosis: a report from the CHAMP Study Group CHromosomes And Morphology. *Mod Pathol* 2000; **13**: 1080–1085.
21 Ling RS. The genetic factor in Dupuytren's disease. *J Bone Joint Surg Br* 1963; **45**: 709–718.
22 Brenner P, Krause-Bergmann A, Van VH. [Dupuytren contracture in North Germany. Epidemiological study of 500 cases]. *Unfallchirurg* 2001; **104**: 303–311.
23 Shaw RB, Jr, Chong AK, Zhang A, Hentz VR, Chang J. Dupuytren's disease: history, diagnosis, and treatment. *Plast Reconstr Surg* 2007; **120**: 44e–54e.
24 Heyd R, Dorn AP, Herkstroter M, Rodel C, Muller-Schimpfle M, Fraunholz I. Radiation therapy for early stages of morbus Ledderhose. *Strahlenther Onkol* 2010; **186**: 24–29.
25 Geoghegan JM, Forbes J, Clark DI, Smith C, Hubbard R. Dupuytren's disease risk factors. *J Hand Surg Br* 2004; **29**: 423–426.
26 Lucas G, Brichet A, Roquelaure Y, Leclerc A, Descatha A. Dupuytren's disease: personal factors and occupational exposure. *Am J Ind Med* 2008; **51**: 9–15.
27 Trojian TH, Chu SM. Dupuytren's disease: diagnosis and treatment. *Am Fam Physician* 2007; **76**: 86–89.
28 Yost J, Winters T, Fett HC, Sr. Dupuytren's contracture; a statistical study. *Am J Surg* 1955; **90**: 568–571.

29 Betz N, Ott OJ, Adamietz B, Sauer R, Fietkau R, Keilholz L. Radiotherapy in early-stage Dupuytren's contracture. Long-term results after 13 years. *Strahlenther Onkol* 2010; **186**: 82–90.
30 Peimer CA, Blazar P, Coleman S *et al.* Dupuytren contracture recurrence following treatment with collagenase *Clostridium histolyticum* (CORD-LESS Study): 3-year data. *J Hand Surg Am* 2013; **38**: 12–22.
31 Witthaut J, Jones G, Skrepnik N, Kushner H, Houston A, Lindau TR. Efficacy and safety of collagenase *Clostridium histolyticum* injection for dupuytren contracture: short-term results from 2 open-label studies. *J Hand Surg Am* 2013; **38**: 2–11.
32 Watt AJ, Curtin CM, Hentz VR. Collagenase injection as nonsurgical treatment of Dupuytren's disease: 8-year follow-up. *J Hand Surg Am* 2010; **35**: 534–539, 9 e1.
33 Coert JH, Nerin JP, Meek MF. Results of partial fasciectomy for Dupuytren disease in 261 consecutive patients. *Ann Plast Surg* 2006; **57**: 13–17.
34 van Rijssen AL, Gerbrandy FS, Ter Linden H, Klip H, Werker PM. A comparison of the direct outcomes of percutaneous needle fasciotomy and limited fasciectomy for Dupuytren's disease: a 6-week follow-up study. *J Hand Surg Am* 2006; **31**: 717–725.
35 Becker GW, Davis TR. The outcome of surgical treatments for primary Dupuytren's disease–a systematic review. *J Hand Surg Eur* 2010; **35**: 623–626.
36 Yi IS, Johnson G, Moneim MS. Etiology of Dupuytren's disease. *Hand Clin* 1999; **15**: 43–51, vi.
37 Keilholz L, Seegenschmiedt MH, Sauer R. Radiotherapy for prevention of disease progression in early-stage Dupuytren's contracture: initial and long-term results. *Int J Radiat Oncol Biol Phys* 1996; **36**: 891–897.
38 Seegenschmiedt MH, Olschewski T, Guntrum F. Radiotherapy optimization in early-stage Dupuytren's contracture: first results of a randomized clinical study. *Int J Radiat Oncol Biol Phys* 2001; **49**: 785–798.
39 Seegenschmiedt MH. Morbus Dupuytren/Morbus Ledderhose. In: Seegenschmiedt MH, Makoski H-B, Trott K-R, Brady LW, eds. Radiotherapy for Non-Malignant Disorders, Contemporary Concepts and Clinical Results. Springer, Berlin-Heidelberg-New York, 2008: 161–192.
40 Schirren CG. Röntgentherapie gutartiger und bösartiger Geschwülste, Morbus Peyronie, Dupuytrensche Kontrakturen. In: Jadassohn J, ed. Handbuch der Haut- und Geschlechtskrankheiten. Springer, Berlin-Göttingen-Heidelberg, 1959: 327–330.
41 Adamietz B, Keilholz L, Grunert J, Sauer R. [Radiotherapy of early stage Dupuytren disease. Long-term results after a median follow-up period of 10 years]. *Strahlenther Onkol* 2001; **177**: 604–610.
42 Landthaler M, Hagspiel HJ, Braun-Falco O. Late irradiation damage to the skin caused by soft X-ray radiation therapy of cutaneous tumors. *Arch Dermatol* 1995; **131**: 182–186.
43 Deutsche Gesellschaft für Radioonkologie (DEGRO). LEITLINIEN IN DER STRAHLENTHERAPIE, Strahlentherapie gutartiger Erkrankungen, Fachgruppenspezifische evidenzbasierte S2e-Leitlinie der Deutsche Gesellschaft für Radioonkologie, "Radiotherapie gutartiger Erkrankungen". [WWW document] 2013. URL http://www.dupyutren-online.de/downloads/Krebsrisiko_durchStrahlentherapie_des_MorbusDupuytren.htm.
44 Keilholz L, Seegenschmiedt MH, Born AD, Sauer R. [Radiotherapy in the early stage of Dupuytren's disease. The indications, technic and long-term results]. *Strahlenther Onkol* 1997; **173**: 27–35.
45 Seegenschmiedt MH, Olschewski T, Guntrum F. [Optimization of radiotherapy in Dupuytren's disease. Initial results of a controlled trial]. *Strahlenther Onkol* 2001; **177**: 74–81.
46 Maravic M, Landais P. Dupuytren's disease in France–1831 to 2001–from description to economic burden. *J Hand Surg Br* 2005; **30**: 484–487.

Appendix: I

Questionnaire for history and clinical symptoms of Dupuytren's disease

1. PERSONAL DATA

Name, Surname: _____

Date of birth: _____

2. GENERAL INFORMATION

A. Are there family members suffering from Dupuytren's disease?

Yes ☐ No ☐

B. Do you suffer from any of the following diseases?

Induratio Penis Plastica	☐	Morbus Ledderhose	☐
Knuckle pads	☐	Keloids	☐
Diabetes mellitus	☐	Epilepsy	☐
Liver diseases	☐	Cardiovascular diseases	☐

C. Have your hands been exposed to heavy work-load?

Yes (mostly rough hand movements) ☐

Yes (mostly fine hand movements) ☐

No ☐

D. Occupation: _____

E. Left-handed ☐ Right-handed ☐

3. DISEASE CHARACTERISTICS

A. First onset of clinical signs:

Month: _____Year: _____

B. Clinical signs

	Right hand		Left hand	
Pain/ burning sensation	No ☐	Yes ☐	No ☐	Yes ☐
Increased palm tension	No ☐	Yes ☐	No ☐	Yes ☐
Functional restrictions	No ☐	Yes ☐	No ☐	Yes ☐
Pain at rest	No ☐	Yes ☐	No ☐	Yes ☐
First skin changes	No ☐	Yes ☐	No ☐	Yes ☐
Palpable nodules	No ☐	Yes ☐	No ☐	Yes ☐
Palpable cords	No ☐	Yes ☐	No ☐	Yes ☐
Trigger finger	No ☐	Yes ☐	No ☐	Yes ☐
Flexion deformity	No ☐	Yes ☐	No ☐	Yes ☐
Other complaints	No ☐	Yes ☐	No ☐	Yes ☐

C. How was the progression of the disease?

Slowly progredient ☐ Slowly batch-wise ☐

Rapidly progredient ☐ Very rapidly progredient ☐

D. Did you receive other therapies?

_____

E. Has there been a regression of disease symptoms after treatment?

No ☐ Yes ☐

F. Could disease progression be stopped? Yes ☐ No ☐

G. Are you satisfied with the radiotherapy?

0 – 0 – 0 – 0 – 0 – 0 – 0 – 0 – 0 – 0 – 0

disappointed very satisfied

4. TREATMENT

A. Which of the following side-effects during the first 4 weeks after end of treatment did you notice?

1. Erythema No ☐ Yes ☐
2. Dryness No ☐ Yes ☐
3. Desquamation No ☐ Yes ☐

B. Are there any side-effects persisting for more than 4 weeks after end of treatment?

1. Dryness No ☐ Yes ☐
2. Skin atrophy No ☐ Yes ☐
3. Angiectasia No ☐ Yes ☐
4. Sensational affection No ☐ Yes ☐

5. GRAPHIC PRESENTATION

A. Which areas of the hands have been affected prior to therapy? *(Mark nodules as circles and cords as ovals)*

left hand **right hand**

B. Which areas of the hands are affected at the moment? *(Mark nodules as circles and cords as ovals)*

left hand **right hand**