# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Interventional procedure consultation document

# Radiation therapy for early Dupuytren's disease

In Dupuytren's disease, connective tissue in the palm of the hands thickens. This causes nodules (small, hard lumps) to form under the skin of the palm. Over time, the nodules can extend and form cords of tissue. These cords can shorten and cause the fingers to bend permanently towards the palm. Radiation therapy for early Dupuytren's disease involves directing low energy X-rays at the affected tissue with the aim of stopping the disease progressing. Treatment can be repeated in some patients.

The National Institute for Health and Care Excellence (NICE) is examining radiation therapy for early Dupuytren's disease and will publish guidance on its safety and efficacy to the NHS. NICE's interventional procedures advisory committee has considered the available evidence and the views of specialist advisers, who are consultants with knowledge of the procedure. The advisory committee has made draft recommendations about radiation therapy for early Dupuytren's disease.

This document summarises the procedure and sets out the draft recommendations made by the advisory committee. It has been prepared for public consultation. The advisory committee particularly welcomes:

- comments on the draft recommendations
- the identification of factual inaccuracies
- additional relevant evidence, with bibliographic references where possible.

**Note that this document is not NICE's formal guidance on this procedure. The recommendations are provisional and may change after consultation.**

The process that NICE will follow after the consultation period ends is as follows.

- The advisory committee will meet again to consider the original evidence and its draft recommendations in the light of the comments received during consultation.

- The advisory committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.

For further details, see the Interventional Procedures Programme process guide, which is available from the NICE website.

Through its guidance NICE is committed to promoting race and disability equality, equality between men and women, and to eliminating all forms of discrimination. One of the ways we do this is by trying to involve as wide a range of people and interest groups as possible in the development of our interventional procedures guidance. In particular, we aim to encourage people and organisations from groups who might not normally comment on our guidance to do so.

In order to help us promote equality through our guidance, we should be grateful if you would consider the following question:

Are there any issues that require special attention in light of NICE's duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations between people with a characteristic protected by the equalities legislation and others?

Please note that NICE reserves the right to summarise and edit comments received during consultations or not to publish them at all where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would otherwise be inappropriate.

Closing date for comments: 23rd September 2016

Target date for publication of guidance: December 2016

# 1 Draft recommendations

1.1 Evidence on the efficacy and safety of radiation therapy for early Dupuytren's disease is inadequate in quantity and quality. Evidence on efficacy is difficult to interpret because of uncertainty about the natural history of Dupuytren's disease. Evidence on safety does not show any major safety concerns although there is a theoretical risk of malignancy. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

1.2 Clinicians wishing to do radiation therapy for early Dupuytren's disease should:

- Inform the clinical governance leads in their NHS trusts.
- Ensure that patients understand the uncertainty about the procedure's efficacy, the unpredictability of progression of early Dupuytren's disease, and that there is a theoretical risk of malignancy in the long term after any type of radiation therapy. Clinicians should provide patients with clear written information. In addition, the use of NICE's information for the public is recommended.
- Audit and review clinical outcomes of all patients having radiation therapy for early Dupuytren's disease (see section 7.1).

1.3 NICE encourages further research into radiation therapy for early Dupuytren's disease in the form of randomised controlled trials comparing the long-term efficacy of radiation therapy with the natural history of the disease. It may update the guidance on publication of further evidence. Studies should include details of patient selection, stage of disease progression, duration and types of treatment, patient-reported outcomes, and long-term efficacy and safety data.

# 2 Indications and current treatments

2.1 Dupuytren's disease is a benign fibroproliferative disorder of the fascia of the hand and fingers. Its aetiology is unknown. It is characterised by connective tissue thickening in the palm of the hand, forming nodules. These nodules are thought to progress to form cords, which cause difficulty in extending the fingers. Symptoms include reduced range of motion, reduced hand function

and pain. It most commonly affects the fourth and fifth fingers. Most patients are affected in both hands. Not all patients have progressive disease, and the natural history of the disease is not well understood.

2.2 Treatments aim to restore hand function and prevent progression. These include needle aponeurotomy (percutaneous needle fasciotomy) in earlier disease, and open surgical correction (fasciotomy or fasciectomy) in later disease when secondary changes to tendons and joints have developed. Limited fasciectomy is the most commonly used open surgical treatment. Dermofasciectomy is used for advanced cases. A non-surgical treatment using injectable collagenase clostridium histolyticum is also sometimes used.

# 3 The procedure

3.1 The aim of this procedure is to prevent or postpone disease progression, and reduce the need for surgical intervention. The mechanism of action of radiation therapy is uncertain, but it is thought to affect the development and growth rate of fibroblasts in the palmar fascia.

3.2 Radiation therapy is delivered to the nodules and cords that have formed in the hands. The usual regimen is 30 Gy in 10 fractions, consisting of 2 phases of 15 Gy in 5 fractions with a gap of 6–12 weeks between the 2 phases. Alternatively, 21 Gy may be given in 7 fractions on alternate days over 2 weeks.

# 4 Efficacy

This section describes efficacy outcomes from the published literature that the committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the interventional procedure overview.

4.1 In a randomised controlled trial (RCT) of 129 patients (198 hands), in which both groups had radiation therapy, objective symptom assessment (number and consistency of cords and nodules, and degree of extension deficit) showed regression of Dupuytren's disease at 1-year follow-up in 56% (53/95) of hands treated with 30 Gy of radiation and in 53% (55/103) of hands treated with 21 Gy ($p<0.01$ for the before-after change in both groups; no statistically significant difference between groups). The symptoms remained stable in a further 37% (35/95) of hands treated with 30 Gy of radiation and a further 38% (39/103) of hands treated with 21 Gy (no statistically significant difference between groups). Overall disease progression rate at 1 year was 8% (16/198). New nodules were reported in 6% (11/198) of hands, new cords in 4% (7/198) and increased flexion deformity in 6% (12/198).The same trial reported that subjective symptom assessment (not otherwise defined) showed statistically significant regression of Dupuytren's disease at 1-year follow-up in 65% (41/63) of patients in the group treated with 30 Gy of radiation, and 53% (35/66) of patients treated with 21 Gy ($p<0.01$ for the within group change; level of statistical significance between groups not reported). The condition remained stable in a further 30% (19/63) of patients in the 30 Gy group and a further 41% (27/66) of patients in the 21 Gy group (level of statistical significance between groups not reported).

4.2 In a case series of 206 patients treated with 32 Gy of radiation, which collected self-reported questionnaire data at a median follow-up of 40 months, symptoms regressed in 45% (93/206) of patients and there was no further disease progression (including in patients with regression) in 80% (165/206) of patients.

4.3 In a case series of 135 patients (208 hands) treated with 30 Gy of radiation, clinical evaluation after a median follow-up of 13 years showed complete relief of symptoms in 16% (14/87) of patients, good relief in symptoms in 18% (16/87), minor relief in 32% (28/87), unchanged symptoms in 14% (12/87) and progression of symptoms in 20% (17/87). In the same case series, clinical evaluation after a median follow-up of 13 years showed regression of the disease in 10% (20/208) of hands, stable disease in 59% (123/208) of hands and progression in 31% (65/208) of hands.

4.4 In a case series of 33 patients (60 treated sites), which collected self-reported survey data after a median follow-up of 31 months, the disease progressed at any location within or outside the radiation therapy treatment field in 61% (20/33) of patients. In-field progression occurred in 23% (14/60) of sites but 4 sites were successfully re-irradiated with final local control in 83% (50/60) of sites. In the same study, the symptoms improved or remained stable in 93% of sites (relative numbers not given).

4.5 In the RCT of 129 patients (198 hands) treated with 30 Gy or 21 Gy of radiation, 3% (4/129) of patients needed hand surgery for disease progression within 1 year of follow-up. In the case series of 135 patients (208 hands), 20% (42/208) of hands needed surgery within a median follow-up of 13 years. In the case series of

33 patients, 6% (2/33) of patients needed surgery within a median follow-up of 31 months.

4.6 In the case series of 206 patients, the mean (± standard deviation) score for satisfaction with the therapy (measured with a visual analogue scale from 0 [not satisfied] to 10 [extremely satisfied]) was 7.9±2.7 points (n=198 patients) at a median follow-up of 40 months. In the case series of 33 patients, 94% (31/33) of patients considered radiation therapy successful (defined by patient report indicating whether patients felt that radiation therapy had been successful or not) at a median follow-up of 31 months.

4.7 The specialist advisers listed the following key efficacy outcomes: absence of progression, time to recurrence or progression to a functionally significant contracture, and rates of subsequent surgery.

4.8 Thirty four commentaries from patients who had experience of this procedure were received, which were discussed by the committee.

# 5 Safety

This section describes safety outcomes from the published literature that the committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the interventional procedure overview.

**Acute toxicity**

5.1 Dry skin or redness was reported in 38% (76/198) of hands in a randomised controlled trial (RCT) of 129 patients treated with 30 Gy or 21 Gy of radiation within a 4-week follow-up.

5.2 Dry desquamation was reported in 5% (10/198) of hands and wet desquamation in 2% (3/198) of hands in the RCT of 129 patients treated with 30 Gy or 21 Gy of radiation within a 4-week follow-up.

5.3 Extensive erythema was reported in 6% (12/198) of hands in the RCT of 129 patients treated with 30 Gy or 21 Gy of radiation within a 4-week follow-up. Erythema was reported in 20% (42/206) of patients in a case series of 206 patients treated with 32 Gy of radiation within a 4-week follow-up.

5.4 Pronounced swelling was reported in 2% (3/198) of hands in the RCT of 129 patients treated with 30 Gy or 21 Gy of radiation within a 4-week follow-up.

5.5 Tenderness was reported in 3% (2/60) of sites in a case series of 33 patients.

**Chronic toxicity**

5.6 Overall chronic toxicity events occurred in 16% (15/95) of hands treated with 30 Gy of radiation and in 11% (11/103) of hands treated with 21 Gy within 3 months and in 4% (4/95), and 5% (5/103) of hands treated with 30 Gy or 21 Gy respectively within 12 months of radiation therapy, in the RCT of 129 patients. Most of these events were skin dryness, increased desquamation, mild skin atrophy or slight subcutaneous fibrosis needing topical treatment (type of treatment not stated).

5.7 Dry skin was reported in 20% (41/206) of patients in the case series of 206 patients treated with 32 Gy of radiation, in more than 4 weeks of follow-up. Desquamation was reported in 2% (5/206) of patients in the same case series of 206 patients. Dry skin and

increased desquamation were reported in 23% (47/208) of hands in a case series of 135 patients within a median follow-up of 13 years.

5.8 Lack of sweating was reported in 4% (8/206) of patients in the case series of 206 patients treated with 32 Gy of radiation within a median follow-up of 40 months.

5.9 Skin atrophy was reported in 3% (7/206) of patients in the case series of 206 patients treated with 32 Gy of radiation, in more than 4 weeks of follow-up. In the same study, telangiectasia was reported in 3% (6/206) of patients, in more than 4 weeks of follow-up. Mild skin atrophy with occasional telangiectasia was reported in 7% (14/208) of hands in the case series of 135 patients within a median follow-up of 13 years.

5.10 Alteration of heat and pain sensation was reported in 4% (8/198) of hands in the RCT of 129 patients treated with 30 Gy or 21 Gy (minimum follow-up of 1 year). Sensory affection was reported in 2% (4/206) of patients in the case series of 206 patients treated with 32 Gy of radiation, in more than 4 weeks of follow-up. Erythema was reported in 2% (5/208) of patients in the case series of 135 patients at up to 1 year.

5.11 Weakness (subjective 10–20% reduction in strength) was reported in 3% (2/60) of sites in the case series of 33 patients within a median follow-up of 31 months.

5.12 Reduced nail health was reported in 3% (2/60) of sites in the case series of 33 patients within a median follow-up of 31 months.

5.13 Hyperpigmentation was reported in 3% (2/60) of sites in the case series of 33 patients within a median follow-up of 31 months.

5.14 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers did not list any new anecdotal adverse events. They considered that the following were theoretical adverse events: radiation-induced malignancy and adverse surgical outcome due to poor wound healing in irradiated skin.

# 6 Committee comments

6.1 The committee noted that, despite the recommendations in the previous guidance for audit, and encouragement for further research, data collection since the guidance was published had been disappointing.

6.2 The committee noted the large number of supportive comments received from patients who have had the procedure.

6.3 The committee noted that a review of the use of radiotherapy for benign conditions published by the Royal College of Radiologists in 2015 recommended that only patients whose disease has progressed within the last 6−12 months should be treated.

# 7 Further information

7.1 This guidance requires that clinicians doing the procedure make special arrangements for audit. NICE has identified relevant audit criteria and is developing an audit tool (which is for use at local discretion). This tool will be available when the guidance is published.

7.2 For related NICE guidance, see the NICE website.

7.3 This guidance is a review of NICE's interventional procedure guidance on radiation therapy for early Dupuytren's disease.

Tom Clutton-Brock
Chairman, interventional procedures advisory committee
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