Role of Radiation Therapy in Dupuytren’s Disease

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Disclosures

- No conflict of interest.
Objectives

- General overview of Dupuytren’s Disease
  - History
  - Anatomy
  - Etiology
  - Staging
- Role of radiation therapy in treatment of Dupuytren’s
- Success rate of radiation treatments
- Treatment options for disease recurrence
What is Dupuytren’s Disease?

- A superficial, spontaneously occurring, benign disorder involving the connective tissue of the hands and feet
- Disease specifically attacks palmar and plantar fascia
- Incurable and often debilitating to patients in the advanced stages of the disease
- Usually progresses slowly, sometimes taking years for symptoms to manifest
- Without therapy, approximately 50% of patients will show disease progression in 5 years
Also Know As....... 

- Dupuytren’s Contracture (contracted disease stage)
- Palmar Fibromatosis (palm)
- Morbus Dupuytren (palm)
- Plantar Fibromatosis (foot)
- Morbus Ledderhose (foot)
Presentation

- Early stage presentation includes palpable nodules, pitting of the skin, and the presence of a rope-like cords
- Burning, itching, pressure, and possibly pain
- Late stage presentation includes contractures of digits
- Typically affects
  - 4\textsuperscript{th} and 5\textsuperscript{th} digits the palm
  - 1\textsuperscript{st} and 2\textsuperscript{nd} digits of the foot
Early Stage Dupuytren’s Disease

Photo credit http://en.wikipedia.org/wiki/Dupuytren's_contracture
Late Stage Dupuytren’s Disease

Cords

3rd, 4th, and 5th digit contracture
Early Stage Ledderhose Disease
Late Stage Ledderhose Disease

History of Dupuytren’s Disease

- It was believed that Dupuytren’s Disease originated with the Vikings over 1,100 years and was spread throughout Northern Europe through their travels.
- Recent finding of a 3000 year old mummy Egypt

History of Dupuytren’s Disease

- First described by Swiss physician Felix Platter 1614 as a deformity of the flexor tendon
- In 1777 Henry Cline noted the involvement of the palmar fascia
- French anatomist Baron Guillaume Dupuytren delivered an anatomic and pathologic lecture on permanent retractions of the “flexed fingers” in 1831
Incidence of Dupuytren’s

- Age, gender, geography, and ethnicity influence Dupuytren’s prevalence worldwide
- Highest incidences can be found in Middle and Northern Europe, with few incidences reported in Asia, India and Africa
- The incidence in the United States is estimated to be 1% based on physician and/or surgical treatment, but may be upwards of 7% when including patient reported early symptoms
- This roughly equates to 3 cases per 10,000 US adults

Etiology of Dupuytren’s

- The nature of the disease is not clearly understood
- Genetic predisposition
  - Northern European Descent
    - Germany, Scotland, England, Scandinavia
- Gender and age
  - More men than women are affected
  - Presentation usually occurs in individuals over 40, with peak incidences in the 50’s and 60’s
  - Disease progression closely associated with nodule formation before age 50 and strong family history
Associated Risk Factors

The following conditions have been associated with Dupuytren’s Disease:

- Morbus Ledderhose
- History of keloids
- History of alcoholism
- Use of nicotine
- Diabetes Mellitus
- Epilepsy
- Hand trauma or inflammation
- Garrod’s Pads (knuckle pads)
Hand Anatomy Review

- Metacarpophalangeal Joint (MIP)
- Proximal Interphalangeal Joint (PIP)
- Distal Interphalangeal Joint

Photo credit http://www.dupuytrens.me.uk/dupuytrens.html
Joints Affected by Dupuytren’s
Plantar Fascia

Anatomy of the Sole of the Foot

Photo credit http://www.motionworkspt.com/content/running-past-plantar-fasciitis
Disease Course of Dupuytren’s

- **Stage 1: Proliferative Stage**
  - Increased number of fibroblasts are present in the subcutaneous tissue between the skin and tendons
  - Nodule formation occurs producing skin protrusion

- **Stage 2: Involution Stage**
  - Increased number of myofibroblasts present
  - Normal fascial vertical bands in connective tissue become diseased resulting in pit and cord formation

- **Stage 3: Residual Stage**
  - Collagenous fibers dominate connective tissue
  - Cords are more pronounced, shorten and cause contraction
Disease Course of Dupuytren’s

Dupuytren’s Contracted Hand
Clinical Presentation

- Clinical presentation can be evaluated based on a grading or staging system.
- Grading system is a more generalized progression based on nodule or cords and contraction.
- Staging System is more specific to the Total Flection Deformity or the total number of degrees a digit is contracted.
- The metacarpophalangeal and proximal interphalangeal joints are referenced for the Dupuytren’s Staging System.
Clinical Presentation

Progression of Dupuytren’s Disease

- Nodule
- Cords
- Flexion Contracture of Left Ring Finger

Grade 1
Grade 2
Grade 3

Dupuytren’s Contracture
Dupuytren’s Disease

Photo credit http://www.lakeoswegoplasticsurgery.com/hand/hand_dupuytrens_signs_symptoms.html
Staging of Dupuytren’s

- **Stage 1**: 0° - 45°
- **Stage 2**: 45° - 90°
- **Stage 3**: 90° - 135°
- **Stage 4**: 135° - 180°

Photo credit Charles Eaton, Florida Hand Center
# Treatment Options by Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Contracture</th>
<th>Description</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>0 degrees</td>
<td>Nodules/cords</td>
<td>Radiation Therapy</td>
</tr>
<tr>
<td>N/1</td>
<td>0-10 degrees</td>
<td>Slight contracture</td>
<td>Radiation Therapy</td>
</tr>
<tr>
<td>1</td>
<td>11-45 deg.</td>
<td></td>
<td>Hand Surgery Needle Aponeurotomy, Collagenase Injection</td>
</tr>
<tr>
<td>2</td>
<td>46-90 deg.</td>
<td></td>
<td>Hand Surgery Needle Aponeurotomy, Collagenase Injection</td>
</tr>
<tr>
<td>3</td>
<td>91-135 deg.</td>
<td></td>
<td>Hand Surgery Needle Aponeurotomy</td>
</tr>
<tr>
<td>4</td>
<td>&gt;135 deg.</td>
<td></td>
<td>Hand Surgery Needle Aponeurotomy</td>
</tr>
</tbody>
</table>

[http://www.dupuytren-online.info/dupuytren_stages_therapies.html](http://www.dupuytren-online.info/dupuytren_stages_therapies.html)
Staging of Dupuytren’s

<table>
<thead>
<tr>
<th>Stage</th>
<th>Deformity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No lesion</td>
</tr>
<tr>
<td>N</td>
<td>Palmar nodule without presence of contracture</td>
</tr>
<tr>
<td>1</td>
<td>TFD between 0° and 45°</td>
</tr>
<tr>
<td>2</td>
<td>TFD between 45° and 90°</td>
</tr>
<tr>
<td>3</td>
<td>TFD between 90° and 135°</td>
</tr>
<tr>
<td>4</td>
<td>TFD greater than 135°</td>
</tr>
</tbody>
</table>

Original staging of DD introduced by Tubiana [30]. Total flexion deformity (TFD) is measured with a goniometer at the metacarpophalangeal, proximal, and distal interphalangeal joints.

Objective of Radiation Therapy

- Slow or prevent the progression of early stage Dupuytren’s Disease
- Radiosensitive fibroblast and myofibroblast are targeted
- Alleviate discomfort caused by nodules or cords on palms and soles
  - Inflammation
  - Tightness
- Viable alternative to the “wait and see” approach, which often results in disease progression requiring collagenase injections and/or invasive hand surgery
Radiotherapy Dose Regimes

- Varying total doses from 12Gy to 30Gy given at 2Gy to 3Gy per fraction
- Currently widely accepted dose regime:
  - 21Gy delivered in 7 fractions
    - 3Gy x 7 delivered within 2 weeks
  - 30Gy delivered in 10 fractions
    - 3Gy x 5 fractions (6-12 week break) repeat 3Gy x 5 fractions
- Radiation retreatment (no published data)
  - Radiation Oncologist preference
## Radiotherapy Dose Regimens

<table>
<thead>
<tr>
<th>Overall Disease Status @ last FU (≥ 5 yrs)</th>
<th>Control (n = 87)</th>
<th>RT 21Gy (n = 165)</th>
<th>RT 30Gy (n = 163)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission</td>
<td>37 (47%)</td>
<td>120 (73%)</td>
<td>127 (78%)</td>
</tr>
<tr>
<td>Stable Disease</td>
<td>54 (62%)</td>
<td>45 (27%)</td>
<td></td>
</tr>
<tr>
<td>Progression</td>
<td></td>
<td></td>
<td>36 (22%)</td>
</tr>
<tr>
<td>p &lt; 0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

( final evaluation August 31, 2006 )

Radiotherapy Treatment Options

- **Orthovoltage Treatment**
  - 120-150kv photons prescribed to appropriate depth
  - Bolus
  - Uninvolved areas of palm or sole protected by lead placed on skin
  - Lead aprons for patient protection

- **Electron Treatment**
  - 6MeV or 9Mev prescribed to appropriate depth
  - Bolus
  - Custom or standard cerrobend cutouts
Dupuytren’s Treatment Planning

- Patient undergoes an extensive physical exam of palm or foot
- Mapping is done to outline nodules and or cords
- Margin of approximately 1-2 cm are given
- Immobilization of hand or foot occurs
- Planning CT scan is done to assess extent of disease
- Treatment energy and use of bolus material is determined
MRIs Can be Helpful

Photo credit www.homepage.nispeed.ch/piben/radiologie/mrimages/ledderhose.jpeg
Palm and Sole Mapping

- Radiation Oncologist performs physical exam of palms
- Cord and nodules are carefully outlined

Photo credit Perez Brady Principles and Practice of Radiation Oncology, 6th ed
Treatment Fields

- Treatment fields reflect distal/proximal margin of 1-2 cm and lateral margin of 1 cm.

Photo credit University of Erlangen, Germany
Treatment Fields

Photo credit http://www.dupuytren-online.info/
Hand Immobilization

Photo credit Perez Brady Principles and Practice of Radiation Oncology, 6th ed
Foot Immobilization

Photo credit VCU Health System
Orthovoltage Treatment Hand

Photo credit http://www.dupuytren-online.info/
Orthovoltage Treatment Foot

Photo credit http://www.dupuytren-online.info/
Electron Treatment Hand

Photo credit  http://www.dupuytren-online.info/
Dupuytren’s Disease Case Study

- 47 y.o. Caucasian male presents with Dupuytren’s disease of bilateral palms and Morbus Ledderhose of the left foot
- Physical exam reveals 3 small nodules on right hand, 2 small nodules on left hand, and a 1cm x 1cm nodule on left foot.
- Pt reported history of disease as being 18 months
- Family history significant Dupuytren’s disease
- Pt reported trauma to affected areas caused by exercise
Bilateral Palms

Photo credit VCU Health System
Treatment Planning

- Includes a treatment planning CT to determine depth of disease aiding in choice of appropriate energy

Photo credit VCU Health System
Treatment Setup Palms

Photo credit VCU Health System
Left Foot

Photo credit VCU Health System
Treatment Setup Palm Lt Foot

Photo credit VCU Health System
Radiation Therapy Outcomes

- Effective in delaying the progress of Dupuytren’s in 75% of Stage N/N1 treated cases
- Hand function is preserved (surgery delayed)
- No reports of “second malignancy” from treatments
- Does not interfere with future surgery
- Treatment toxicity mostly acute
  - Moderate to pronounced erythema
  - Dry desquamation
  - Moderate edema
Before and After

Photo credit http://www.dupuytren-online.info/
When Dupuytren’s Progresses

- Beyond Stages N and N/1, radiation therapy is not a treatment option (does not reverse contraction beyond 10 degrees)
- Treatment options for Stages 1 and beyond include
  - Collagenase Injections
  - Needle Aponeurotomy
  - Hand Surgery
    - Fasciectomy (Total, Partial, or Nodule)
    - Segmental Aponeurectomy
Injectable Collagenase

- Most effective for Stages 1 and 2
- Collagenase injected into affected cords followed by finger manipulation to rupture cord
- Reduce joint contracture within 0-5 degrees of full extension
- Recurrence rate 35% in three years

Needle Aponeurotomy

- Done in physicians office under local anesthesia
- 25 gauge needle used to pierce affected cord at multiple levels
- Finger then extended to pull the edges of perforated cord apart for full contracture release
- Shorter recovery than surgery
Surgery

- Traditional “gold standard”
- Requires anesthesia
- More complete and reliable joint release
- Requires hand therapy and limited activity during recovery

Photo credit Dr. Genesis Young
They Are Among Us!
Famous People with Dupuytren’s
Famous People with Dupuytren’s

[Image of Margaret Thatcher waving]

photo credit http://truebluespirit.com/blog/2013/09/29/margaret-thatcher-iron-lady/
Famous People with Dupuytren’s
Famous People with Dupuytren’s
Famous People With Dupuytren’s
NOT Dupuytren’s Disease

Photo credit http://nj1015.com/dennis-malloys-dupuytren-contracture-hand-nsfw-video/
Take Aways.....

- There is no cure for Dupuytren’s Disease
- Radiation therapy offers hope for early stage, but additional research is still needed (dose regimens, retreatment options)
- It’s probably coming to a clinic near you!
  - Ease of set-up and treatment
  - Aging population
  - Better informed patients and their families
  - Non-invasive; promising results
Questions???

Thank you!
Acknowledgements

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References