The role of radiotherapy in desmoids.

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What are desmoids?

Synonyms:
- desmoid tumor
- desmoid fibromatosis
- aggressive fibromatosis

Desmoids are rare:
- \(~0.03\%\) of all neoplasms
- \(<3\%\) of all soft tissue tumors
- 2–4 new cases per million per year

Types:
- Spontaneous (>90%)
  - mainly extremities and abdominal wall, but can be seen anywhere
- Associated with FAP (Gardner syndrome; 5-10%)
- Familial infiltrative fibromatosis, hereditary desmoid disease (~1%)
  - extremely rare, associated with APC mutations
Pathology can be difficult

Can look like scar tissue

Pathology can be difficult

Tumors are usually beta-catenin positive

Many chromosomal changes have been documented. mutations in codon 45F are associated with a poor prognosis

(A) Classic fibroblastic, spindle cell morphology of a desmoid tumor (hematoxylin and eosin, x200); (B) desmoid tumor with the characteristic expression of $\beta$-catenin (endothelial cells as negative control, x200).
What is the typical desmoid patient?

Slightly more females than males
    sometimes related to pregnancy and traumas

Typically between 10 and 40 years of age
Clinical presentation

Usually a painless lump

Phases of growth and progression, stabilization, and sometimes spontaneous regression

It never metastasizes, but it frequently recurs locally.
Prognostic factors for local recurrence

Are there “good’ and are there “bad” desmoids?

What features predict the future of a desmoid patient?
Prognostic factors for local recurrence

Age <37 years
Size > 7cm
Extra-abdominal disease
Macroscopic residual disease after surgery

Salas S et al. JCO 2011;29:3553-3558
Therapy for desmoids

Do nothing as long as reasonably possible

Weigh the balance between the trauma of surgery and the progression of the disease.

If treatment is necessary: radical surgery
Therapy for desmoids

The University of Texas M.D. Anderson Cancer Center desmoid tumor treatment flow chart.

Lev D et al. JCO 2007;25:1785-1791
WORKUP

- All patients should be managed by a multidisciplinary team with expertise in sarcoma
- H&P including evaluation for Gardner's Syndrome
  (See NCCN Guidelines for Colorectal Cancer Screening)
- Appropriate imaging of primary site with CT or MRI as clinically indicated

Resectable → (DESM-2)

Biopsy^{b,c} →

Unresectable or surgery would be unacceptably morbid → (DESM-3)
NCCN guideline

Desmoid Tumors (Aggressive Fibromatosis)

PRIMARY TREATMENT

Unresectable or surgery would be unacceptably morbid

⇒ Definitive RT<sup>fg</sup>
or Systemic therapy<sup>1</sup>
or Radical surgery to be considered if other modalities fail
or Observation

FOLLOW-UP

⇒ Evaluation for rehabilitation (OT, PT)
⇒ Continue until maximal function is achieved
⇒ H&P with appropriate imaging
every 3-6 mo for 2-3 y, then annually

⇒ Progression or Recurrence,
See Primary treatment recommendations
NCCN Guideline for Desmoid Tumors (Aggressive Fibromatosis)

**PRIMARY TREATMENT**

- **Observation**
  - Stable → Continue observation
  - Progression → See Treatment pathway below

- **Resectable**
  - Treatment
    - Surgery or RT and/or Systemic therapy
      - R0 or Complete radiographic response → Observation or Consider postoperative RT if large tumor
      - R1 or Minimal residual disease → Consider resection or RT, if no prior RT or Observation
      - R2 or Gross residual disease → Definitive RT or Systemic therapy or Radical surgery to be considered if other modalities fail or Observation

**FOLLOW-UP**

- Evaluation for rehabilitation (OT, PT)
  - Continue until maximal function is achieved
  - H&P with appropriate imaging every 3-6 mo for 2-3 y, then annually

- Progression or Recurrence, See Primary treatment recommendations
General guideline
General guideline

do nothing: watch and wait
General guideline

act: surgery

do nothing: watch and wait
General guideline

do nothing:
watch and wait

act:
surgery

act:
RT

do nothing:
watch and wait
General guideline

decision making: always together
Role of radiotherapy in desmoids

Radiotherapy in combination with surgery; RT before or after surgery

Or definitive radiotherapy without surgery
(Neo-) adjuvant radiotherapy

Important question: is this the first operation (primary disease) or is this a recurrence?

The more recurrences a patient has suffered, the stronger the indication for (neo-) adjuvant RT.

NCCN guideline: consider RT in
   large tumors
   R1 resection

Note: this will be a decision for a relatively young patient with a benign disease.
Desmoids are rare, surgery is the most important part of management

=> Not so many papers on RT in desmoids
Optimizing Treatment of Desmoid Tumors

Optimizing Treatment of Desmoid Tumors


Local control

1965-1994
1994-2005
The value of RT in both periods:

- a gain in local control by a factor of 2
The value of RT in both periods:

a gain in local control by a factor of 2

But the absolute gain is becoming smaller:
less patient benefit from RT because of better surgery
ROLE OF RADIOTHERAPY IN THE MANAGEMENT OF DESMOID TUMORS

IRIS GLUCK, M.D., KENT A. GRIFFITH, M.P.H., M.S., J. SYBIL BIERMANN, M.D.,
FELIX Y. FENG, M.D., DAVID R. LUCAS, M.D., AND EDGAR BEN-JOSEF, M.D.

Surgery only
RT only
Surgery + RT

Selection???
The impact of radiotherapy in the treatment of desmoid tumours. An international survey of 110 patients. A study of the Rare Cancer Network
Brigitta G Baumert
External-Beam Radiotherapy for Pediatric and Young Adult Desmoid Tumors

Michael S. Rutenberg, MD, PhD, 1 Daniel J. Indelicato, MD, 1,5* Jacquelyn A. Knapik, MD, 3 Joanne P. Lagmay, MD, 2 Christopher Morris, MS, 1 Robert A. Zlotecki, MD, PhD, 1 Mark T. Scarborough, MD, 4 Charles P. Gibbs, JR, MD, 4 and Robert B. Marcus, JR, MD 5

A report on 30 patients < 30 years old

<table>
<thead>
<tr>
<th>Characteristic (no. of patients)</th>
<th>5-year local-regional control (%)</th>
<th>15-year local-regional control (%)</th>
<th>P-value</th>
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<td>Previous treatment</td>
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<td>Surgery (17)</td>
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<td>None (12)</td>
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<td>Preoperative radiotherapy (1)</td>
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<td>Micro positive (6)</td>
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<td>Micro negative (8)</td>
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<td>Unresected tumor (16)</td>
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<td>Radiotherapy dose</td>
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<td>&lt;55 Gy (16)</td>
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<td>≥55 Gy (14)</td>
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LONG-TERM OUTCOMES FOR DESMOID TUMORS TREATED WITH RADIATION THERAPY

B. Ashleigh Guadagnolo, M.D., M.P.H., Gunar K. Zagars, M.D., and Matthew T. Ballo, M.D.

Department of Radiation Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX

Actuarial local control for all 115 patients.
41 of 115 patients treated by RT only
17% CR
68% long term local control

>56Gy no better local control but more complications
Results of a phase II pilot study of moderate dose radiotherapy for inoperable desmoid-type fibromatosis—an EORTC STBSG and ROG study (EORTC 62991–22998)

44 pts; RT 28 x 2Gy = 56Gy
27 females and 17 males; median age 39 years, median follow-up 5 years

3 years local control: 81.5%
CR 14%
PR 36% \[\text{clinical benefit 91%}\]
SD 41%

If progressive; most recurrences <3 years

20 patients;
49 events before RT, 2 events after RT,
FU after RT longer than before RT
The way **not** to go

Radiation therapy in the treatment of desmoid tumours reduces surgical indications

H.A. Rüdiger a,b,*, S.Y.K. Ngan c, M. Ng c, G.J. Powell a, P.F.M. Choong a

Radiotherapy only (no surgery)
- 20% CR
- 20% PR
- 55% growth arrest (SD)
- 5% PD

Message: less surgery and more radiotherapy

Comment: far more experience with surgery than with RT only
In conclusion

Desmoids are benign but locally aggressive

Watch and wait as long as reasonably feasible

If treatment is necessary preferably surgery

But if surgery mutilates too much: RT
Thanks for your attention

Mt Everest