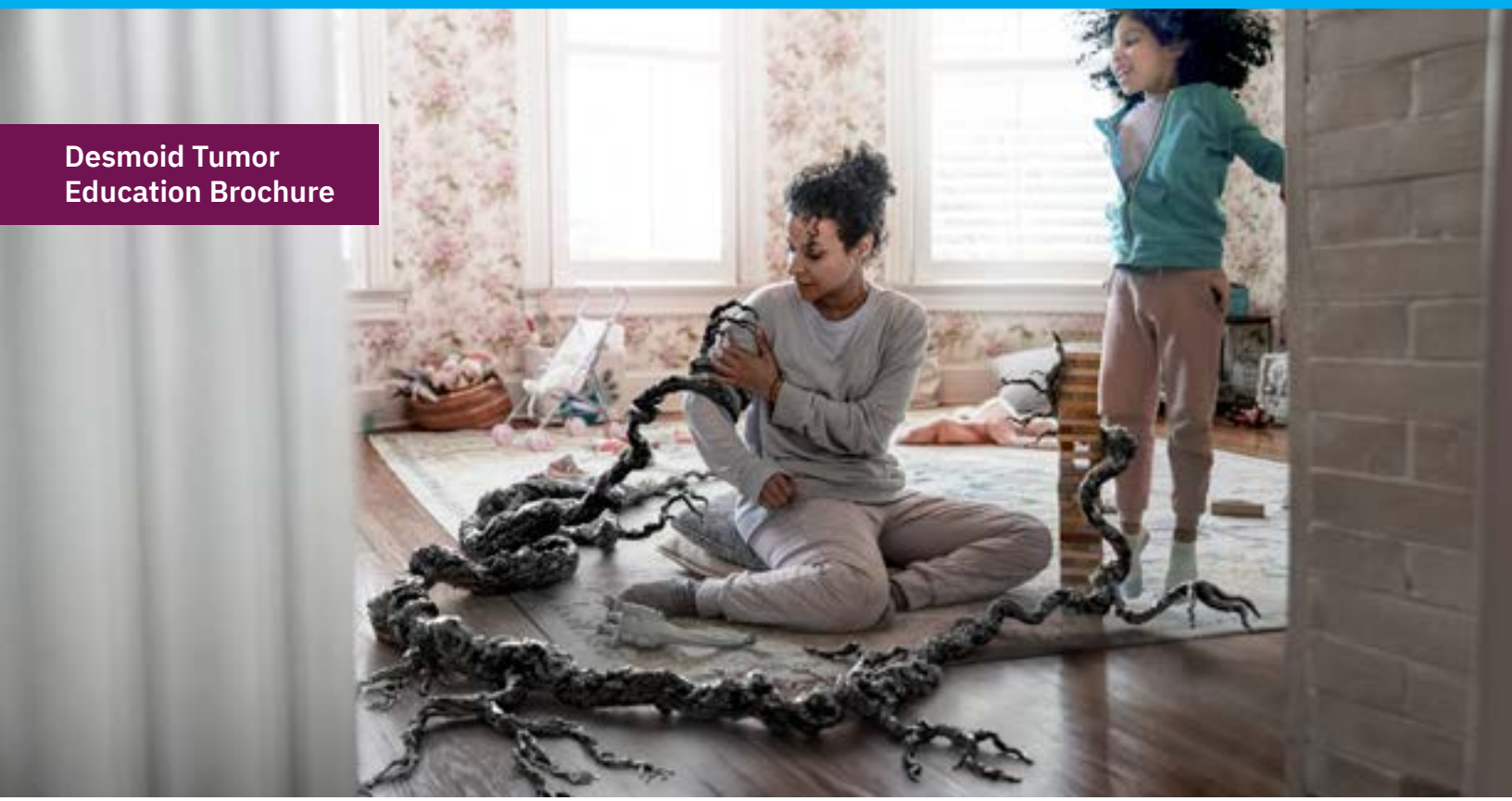
Desmoid Tumor Education Brochure



Rethink desmoid tumors

Don't underestimate these unpredictable tumors and their "tendril-like" growths

Information to help you diagnose, manage, and support patients with desmoid tumors

Navigate to a **specific topic**

- → About Desmoid Tumors
- → Diagnosis
- → Management
- → Patient Resources

Desmoid tumors can be locally invasive and painful, with **"tendril-like" growths that can threaten vital structures and compromise patients' function and quality of life**[1-3]

Approximately **30% to 40% of desmoid tumors are initially misdiagnosed** due to their rarity and histologic mimics[4]

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) and the Desmoid Tumor Working Group recommend an **initial evaluation and management by a multidisciplinary team** with expertise and experience in sarcoma[5,6]

There are currently **no FDA-approved treatment options** specifically indicated for desmoid tumors.[7] **In most tumor locations, surgery is no longer the recommended first-line treatment approach for desmoid tumors**[4,6]

Access desmoid tumor information & resources **DesmoidTumors.com/HCP** **Sign up for information**

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About Desmoid Tumors

Desmoid tumors are **locally aggressive,** potentially morbid tumors of the soft tissues, with a tendency to infiltrate surrounding structures.[1,4] Although they don't metastasize, desmoid tumors are associated with **local recurrence rates ranging from 24% to 77% after surgical resection**.[8,9]*

In rare cases when vital organs are impacted, they can be life-threatening.[2]

30% to 40% of desmoid tumors are initially misdiagnosed[4]

Incidence and Risk Factors

- ~1000 to 1650 annual cases in the United States[10-12]
- Most patients are diagnosed between 20 and 44 years of age[11]
- Female-to-male ratio is ~2-3:1[9,11,13]
- Recent pregnancy, injury, or surgery may increase risk[14,15]
- Patients with familial adenomatous polyposis (FAP) have ~850-fold higher risk of developing desmoid tumors than the general population[16]

Image reproduced with permission from Duan M, Xing H, Wang K, et al. A large and aggressive fibromatosis in the axilla: a rare case report and review of the literature. *Onco Targets Ther.* 2018;11:3179-3184.

Large desmoid tumor on left axillary

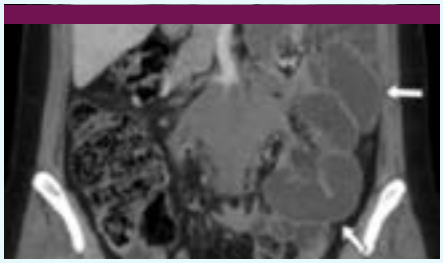


Image reproduced with permission from Braschi-Amirfarzan M, Keraliya AR, Krajewski KM, et al. Role of imaging in management of desmoid-type fibromatosis: a primer for radiologists. *Radiographics*. 2016;36(3):767-782.

Contrast-enhanced CT showing an unresectable desmoid tumor causing a bowel obstruction

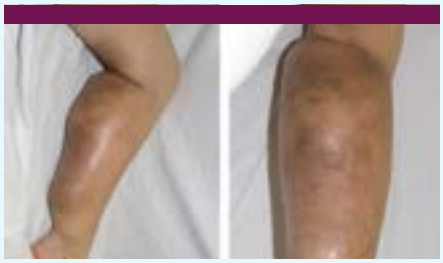


Image reproduced with permission from McDonald ES, Yi ES, Wenger DE. Best cases from the AFIP: extraabdominal desmoid-type fibromatosis. *Radiographics*. 2008;28(3):901-906.

Lateral and posterior images of a desmoid tumor on the left leg

Symptoms and Complications Related to Specific Tumor Sites

Symptomatology related to desmoid tumors varies based on where the tumors present.[17-19] According to a prospective cohort study, tumors in the **chest wall, upper limb, and head and neck** were associated with poor outcomes.[20]

Physical burdens are just the beginning. The pain severity and burden of disease can lead to anxiety and depression.[3,19]

TUMOR SITE	EST. FREQUENCY[18]	COMMON SYMPTOMS AND COMPLICATIONS
Intra-abdominal	**20%**	Compression may cause pain, cachexia, malaise, abdominal distention, or obstruction of the intestines or ureters[18,21,22]
Abdominal Wall	**16%**	Invasion of the bladder or compression of the fallopian tubes, causing them to become swollen and fluid-filled[21]
Lower Extremities	**16%**	Limited mobility, pain, muscle stiffness, or deformity[18,23]
Chest Wall	**15%**	Dyspnea, dysphagia, pleural invasion, rib or spinal involvement, bone erosion, and pain[18,21,24,25]
Upper Extremities	**14%**	Restricted mobility, muscle and ligament involvement, limb weakness, deformity, or pain[18,26]
Head and Neck	**8%**	Pain, neurologic deficit, proximity to vital structures—including mortality risk from vascular or airway restriction[2]
Other	**11%**	Symptoms and complications are dependent on the tumor location[17-19]

*Based on observational data, factors associated with local recurrence postsurgery include tumor location, age of the participant, and tumor size.[27]

Diagnosing Desmoid Tumors

A Multidisciplinary Approach Is Key

NCCN Guidelines® and the Desmoid Tumor Working Group recommend an initial evaluation and management by a multidisciplinary team with expertise and experience in sarcoma.[1,5,6]

A multidisciplinary team may include:

- Medical oncologist
- Sarcoma specialist
- Surgeon/surgical oncologist
- Radiologist and/or Radiation oncologist
- Primary care physician
- Pathologist
- Nurses
- Mental health professional

Evaluation for suspected desmoid tumors should include imaging and histopathologic assessment of biopsy tissue.[1,5,6] Genetic testing can help distinguish between sporadic desmoid tumors (85%-90%) and those arising in the context of FAP (10%-15%).[1,6]

Key Diagnostic Strategies

NCCN Guidelines recommend that a **CT/MRI scan and biopsy** be performed prior to determining any specific therapeutic interventions (surgery or systemic therapy) for progressive, morbid, or symptomatic desmoid tumors.[5] The Desmoid Tumor Working Group consensus guideline recommends **genetic testing for *CTNNB1* or *APC* mutations**.[6]

☑ CT/MRI scan ☑ Biopsy ☑ Genetic testing for *CTNNB1* or *APC* mutations

Imaging[6]

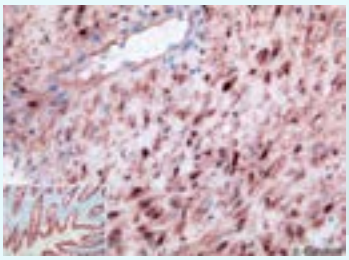
- MRI of abdominal wall and extra-abdominal desmoid tumors is typically recommended for initial diagnosis and postsurgical recurrence
- CT scan (with contrast) is often recommended for diagnosing intra-abdominal desmoid tumors and can be used to evaluate changes in tumor size

MRI scan showing a multifocal sporadic extra-abdominal desmoid tumor in the right calf. Surgery was not feasible in this patient's case due to the extensive multifocal involvement[28]

Image reproduced with permission from Braschi-Amirfarzan M, Keraliya AR, Krajewski KM, et al. Role of imaging in management of desmoid-type fibromatosis: a primer for radiologists. *Radiographics*. 2016;36(3):767-782.

Biopsy and Beta-Catenin Staining

- Immunostaining for beta-catenin and histopathologic assessment are important for diagnosis of desmoid tumors[29]
- Nuclear accumulation of beta-catenin is seen in 80% to 98% of sporadic desmoid tumor cases and 60% to 100% of FAP-associated desmoid tumor cases[6]



Immunohistochemistry of a desmoid tumor with beta-catenin staining[4]

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Managing Desmoid Tumors

There are currently no FDA-approved treatment options for desmoid tumors.[7] Management options include active surveillance, off-label systemic therapy options, surgery limited to specific tumor sites and locoregional therapies.[6] A multidisciplinary team that includes sarcoma specialists can help determine the best path forward for each patient.[17]

Current Management Options

Management strategy should be individualized based on morbidity, tumor location, pain, functional limitation, and persistent progression of disease.

Active Surveillance (also known as "watch and wait")[5,6]

For patients who have **desmoid tumors that are asymptomatic and not progressing or morbid, active surveillance may be an appropriate option**. The NCCN Guidelines recommend continued observation with MRI imaging or CT scan, initially every 3 months. Optimal frequency for imaging depends on the location of the tumor, risk of progression, and symptoms[5]

Systemic Therapy

Currently, there are no FDA-approved therapies specifically indicated for the treatment of desmoid tumors.[7] However, there are off-label therapy options. The Desmoid Tumor Working Group does not propose a definitive sequence due to the lack of comparative studies.[6] NCCN Guidelines list agents and regimens with activity in desmoid tumors[5]:

- **Tyrosine kinase inhibitors** (sorafenib [category 1]; imatinib, pazopanib [category 2A])
- **Chemotherapy** (methotrexate and vinblastine/vinorelbine, doxorubicin-based regimens [category 2A])
- **NSAIDs** (sulindac or other NSAIDs, including celecoxib for pain [category 2A])

These regimens do not have an NCCN Guidelines recommendation:

- **Antihormonals +/— NSAIDs** (tamoxifen with sulindac, or toremifene)

Surgery

In most tumor locations, surgery is **no longer the recommended first-line treatment option for desmoid tumors**.[4,6] Surgical resection is associated with **local recurrence rates** ranging from 24% to 77%, and due to the invasive nature of the tumor's "tendril-like" growths, clear margins may be difficult to identify.[8,9]* Resection needed for clear margins is often large and may require radical surgery, which can lead to functional impairment or morbidity[30]

Locoregional Therapy

Radiation therapy, cryoablation, and high-frequency ultrasound are sometimes used to help treat desmoid tumors.[4,6,31] Caution should be exercised as to use of radiotherapy for abdominal wall tumors and in young patients given the risk of secondary malignancy.[4,30] The utility of cryoablation is limited to small and moderately sized tumors in extra-abdominal locations.[4]

Clinical Trials

Enrollment in a clinical trial may be considered an option for appropriate patients[1]

Surgery is associated with local recurrence rates ranging from 24% to 77%[8,9]*

*Based on observational data, factors associated with local recurrence postsurgery include tumor location, age of the participant, and tumor size.[27]

Patient Resources

Because desmoid tumors are rare, a diagnosis can raise more questions for patients than answers. SpringWorks Therapeutics is committed to helping you provide resources and information for your patients with desmoid tumors.

Discussion Guide

Frequently asked questions that can inform and empower your patient toward a more meaningful conversation about their condition

Access the guide

Advocacy Groups

The following advocacy organizations can provide additional information for your patients:

The Desmoid Tumor Research Foundation

National Organization for Rare Disorders

Rein in Sarcoma

Sarcoma Alliance for Research through Collaboration

The organizations listed are independent of SpringWorks Therapeutics. SpringWorks is providing these links to help patients find more information about desmoid tumors, but inclusion on this list does not represent an endorsement or a recommendation from SpringWorks for any group or organization. Logos are used with permission. Additional organizations are listed on **DesmoidTumors.com/HCP**.

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