Tenosynovial Giant Cell Tumor (TGCT)

Overview and Pathogenesis

For additional resources, please visit our HCP Medical website / Oncology page https://medical.emdserono.com/en_US/medinfo/therapeutic-areas/oncology/disease-awareness.html

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Summary of contents

What is TGCT?

TGCT is a rare, soft-tissue tumor that can have significant impact on patients' lives[1–3]

- TGCT originates in the synovial lining of joints, bursae, and tendon sheaths, causing them to thicken and overgrow[1,2,4]
- As tumors grow, they can cause damage to the surrounding tissue and structures of the affected limb, leading to severe disability if left untreated[1,4]
- TGCT is benign and non-life threatening, but tumors are locally aggressive and may recur[5,6]
- TGCT can potentially become a chronic disease[1,7]

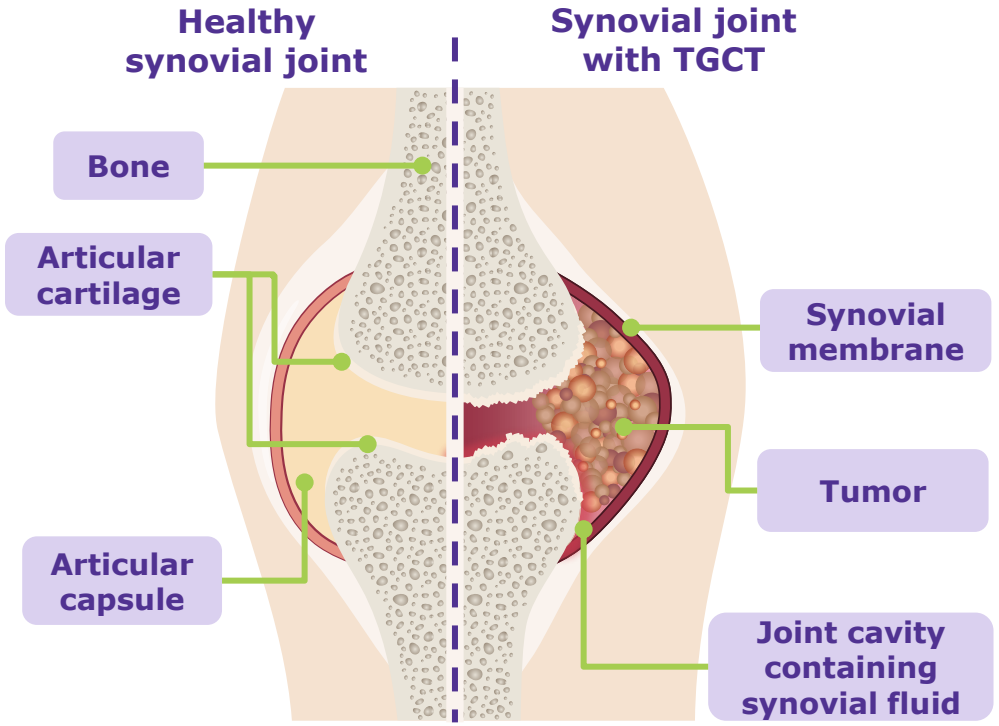
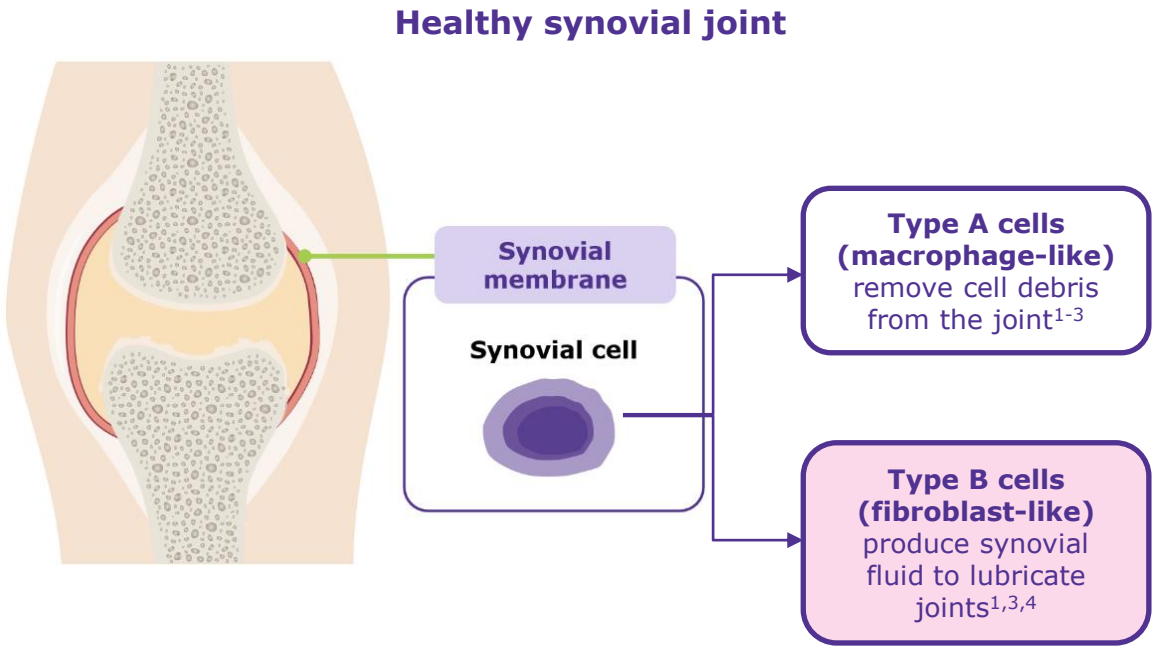


Figure adapted from OpenStax. https://openstax.org/books/anatomy-and-physiology/pages/9-4-synovial-joints. https://creativecommons.org/licenses/by/4.0

TGCT, tenosynovial giant cell tumor

1. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 2. Mastboom MJ et al. Interact J Med Res 2018;7:e4; 3. Ehrenstein V et al. J Rheumatol 2017;44:1476–83; 4. de Saint Aubain Somerhausen N, van de Rijn M. Tenosynovial giant cell tumour. In: Soft Tissue and Bone Tumours. WHO Classification of Tumours. 5th Edn, Vol 3, 2020; 5. Robert M et al. Front Immunol 2022;13:820046; 6. Spierenburg G et al. Expert Opin Ther Targets 2022;26:333–45; 7. National Organization for Rare Disorders. https://rarediseases.org/rare-diseases/tenosynovial-giant-cell-tumor/ [Accessed May 6, 2025]

What type of cells are involved in TGCT?



Together, both types of synovial cells regulate the composition and turnover of synovial fluid[2]

While both type A and type B synovial cells are involved in TGCT, type B cells are responsible for the overproduction of a specific growth factor called CSF-1 and driving tumor growth[3]

What is CSF-1?

In healthy cells, CSF-1 is a cytokine that regulates

- survival
- proliferation
- differentiation
- function

of inflammatory white blood cells, such as macrophages and their precursors[5,6]

Figure adapted from OpenStax. https://openstax.org/books/anatomy-and-physiology/pages/9-4-synovial-joints. https://creativecommons.org/licenses/by/4.0

CSF-1, colony-stimulating factor-1; TGCT, tenosynovial giant cell tumor

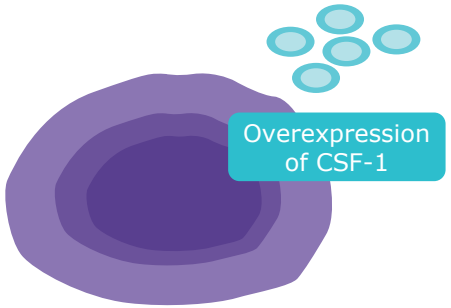
1. Smith MD. Open Rheumatol J 2011;5:100–6; 2. Knab K et al. Front Med (Lausanne) 2022;9:862161; 3. Chandler AC et al. J Orthop Res. 2022; 40:1918–25; 4. de Sousa EB et al. Stem Cell Res Ther 2014;5:112; 5. van der Heijden L et al. J Surg Oncol 2023;128;478–88; 6. Spierenburg G et al. Expert Opin Ther Targets 2022;26:333–45

Why do some TGCT neoplastic cells markedly overproduce CSF-1?[1,2]

CSF-1 in TGCT

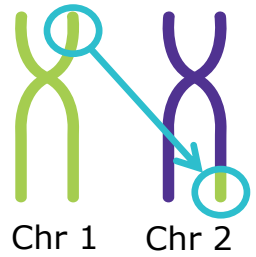
Genetic abnormalities lead to overexpression of CSF-1 in a small number of cells[1,2]

Neoplastic synovial cell[1]



Key example of genetic abnormality[a]

A chromosome abnormality that leads to a translocation of a portion of chromosome 1 to chromosome 2[2]



Translocation resulting in TGCT:
t(1;2) (p13;q37) causing (*COL6A3::CSF1*) fusion[b,2,3]

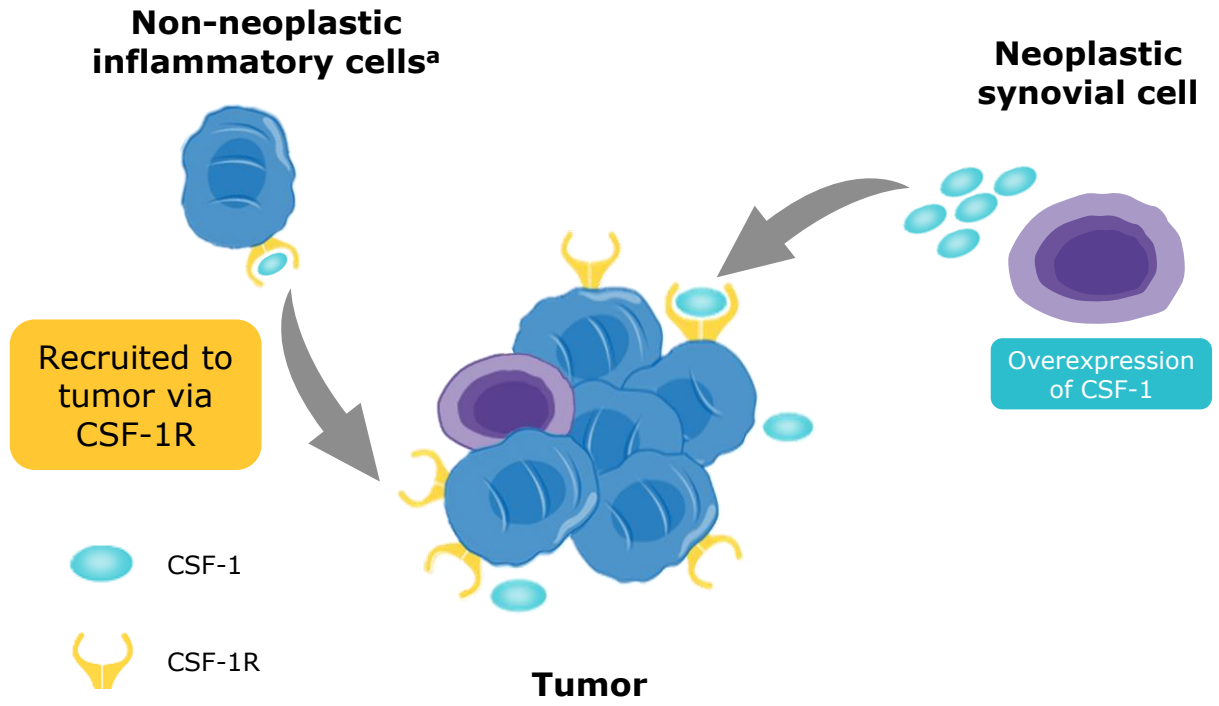
[a]Other abnormalities include truncation of the *CSF-1* gene and trisomy 5 and 7; [b]Fusion of *CSF-1* gene to COL6A3 promotor driving CSF-1 overexpression[3]
Chr, chromosome; COL6A3, collagen alpha-3(VI); CSF-1, colony-stimulating factor-1; TGCT, tenosynovial giant cell tumor

1. van der Heijden L et al. J Surg Oncol 2023;128;478–88; 2. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 3. Lin CC. J Immunother Precis Oncol 2021;4:105–14

CSF-1 overproduction promotes tumor growth by inducing local recruitment and accumulation of inflammatory macrophages[1,2]

- High levels of CSF-1 bind to CSF-1R found on non-neoplastic inflammatory cells, such as macrophages[1]
- CSF-1–dependent activation of these inflammatory cells leads to the recruitment of these cells into the joint[1]
- These non-neoplastic inflammatory cells comprise the majority of the tumor[1–3]

Overview of TGCT disease mechanism[1–4]



[a]TGCT cell composition includes mononuclear cells and various types of macrophages[1,3]

CSF-1, colony-stimulating factor-1; CSF-1R, colony-stimulating factor-1 receptor; TGCT, tenosynovial giant cell tumor

1. Spierenburg G et al. Expert Opin Ther Targets 2022;26:333–45; 2. Robert M et al. Front Immunol 2022;13:820046; 3. de Saint Aubain Somerhausen N, van de Rijn M. Tenosynovial giant cell tumour. In: Soft Tissue and Bone Tumours. WHO Classification of Tumours. 5th Edn, Vol 3, 2020; 4. van IJzendoorn DGP et al. Clin Cancer Res 2022;28:4934–46

Several different names have previously been used to refer to TGCT[1–3]

Previous names included:

Giant cell tumor of the tendon sheath (GCT-TS)

&

Pigmented villonodular synovitis (PVNS)

As of 2013, the World Health Organization classified

TGCT

as a unified disease name for these historical terms

There are two subtypes:

Localized, also known as nodular (L-TGCT)

Presents as a growth or mass of nodules connected to a specific, usually smaller, joint[2,3]

Diffuse (D-TGCT)

Often affects a large joint; infiltrative and locally aggressive and can progress to cause damage to the joint, cartilage, and bone[2,3]

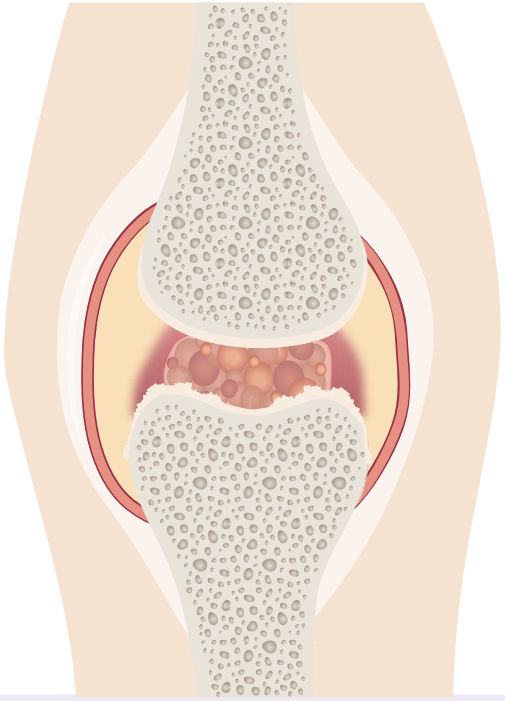
TGCT, tenosynovial giant cell tumor

1. de Saint Aubain Somerhausen N, van de Rijn M. Tenosynovial giant cell tumour. In: Soft Tissue and Bone Tumours. WHO Classification of Tumours. 5th Edn, Vol 3, 2020; 2. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 3. National Organization for Rare Disorders. https://rarediseases.org/rare-diseases/tenosynovial-giant-cell-tumor/ [Accessed May 6, 2025]

TGCT may occur either inside or outside the joint[1–3]

Intra-articular

Tumor grows within the joint



Extra-articular

Tumor extends outside the joint

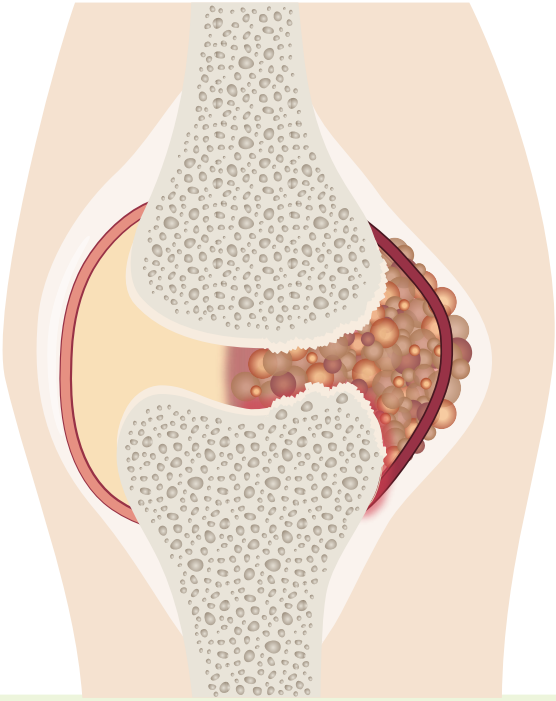


Figure adapted from OpenStax. https://openstax.org/books/anatomy-and-physiology/pages/9-4-synovial-joints. https://creativecommons.org/licenses/by/4.0

TGCT, tenosynovial giant cell tumor

1. Dhanda S et al. Malays J Med Sci 2014;21:4–19; 2. Lui TH, Leung YT. Arthrosc Tech 2022;11:e2039–47; 3. Spierenburg G et al. Eur J Surg Oncol 2024;50:107953

D-TGCT is typically more aggressive, destructive, and difficult to treat than L-TGCT[1,2]

L-TGCT

- Approximately 80–90% of cases[2,3]
- Predominantly affects digits and wrist (85%)[2,4,5]
- Single, well-defined tumor, generally encapsulated[6,7]
- Slow growing[7]
- Tumor size: 0.5–4 cm[8]
- Higher predominance of extra-articular form (approximately 90%)[9]

D-TGCT

- Approximately 10–20% of cases[2,3]
- Affects larger joints (e.g., knee); can occur in other locations (e.g., ankle and hip joints)[2,9]
- Multiple nodules without distinct boundaries, sponge-like[3,6–8]
- Typically more destructive and locally aggressive[2]
- Tumor size: >5 cm[8]
- Most cases of the extra-articular form are believed to be an extension of primary intra-articular disease[10]

Click to see distribution rates in D-TGCT

D-TGCT, diffuse-tenosynovial giant cell tumor; L-TGCT, localized-tenosynovial giant cell tumor; TGCT, tenosynovial giant cell tumor

1. Spierenburg G et al. Exp Opin Ther Targets 2022;26:333–45; 2. Mastboom MJL et al. Acta Orthop 2017;88:688–94; 3. Ehrenstein V et al. J Rheumatol 2017;44:1476–83; 4. Gouin F, Noailles T. Orthop Traumatol Surg Res 2017;103(1S):S91–7; 5. Ushijima M et al. Cancer 1986;57:875–84; 6. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 7. National Organization of Rare Disorders. https://rarediseases.org/rare-diseases/tenosynovial-giant-cell-tumor [Accessed May 6, 2025]; 8. de Saint Aubain Somerhausen N, van de Rijn M. Tenosynovial giant cell tumour. In: Soft Tissue and Bone Tumours. WHO Classification of Tumours. 5th Edn, Vol 3, 2020; 9. Spierenburg G et al. Insights Imaging 2023;14:22; 10. Choi WS et al. Cancers 2024;16:402

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- Approxim…
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…ses[2,3]
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D-TGCT cases by joint[1]

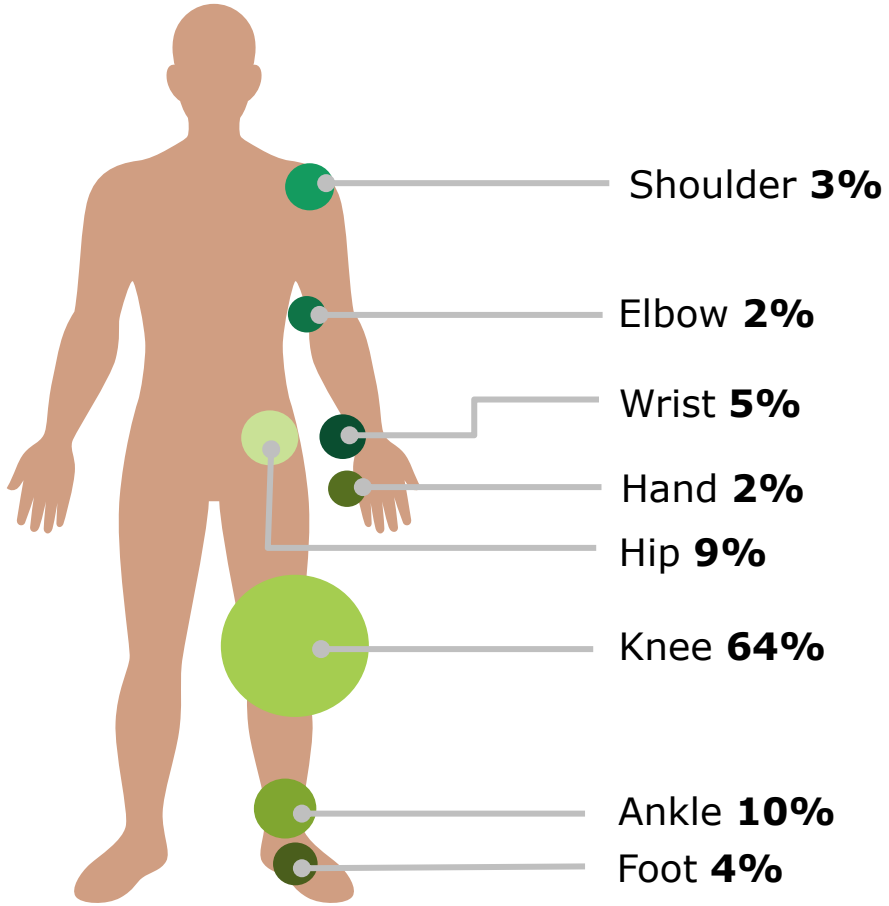


Figure adapted from Mastboom MJL et al. Acta Orthop 2017;88:688–94
D-TGCT, diffuse tenosynovial giant cell tumor
1. Mastboom MJL et al. Acta Orthop 2017;88:688–94

D-TGCT, diffuse-ten…
1. Spierenburg G et… 2017;44:1476–83;
4. Gouin F, Noailles… 2023;112:102491; 7…
Aubain Somerhausen N… Spierenburg G et al. Insights Imaging 2023;14:22; 10. Choi WS et al. Cancers 2024;16:402

…de Saint …0; 9.

Epidemiology

Due to the low incidence of TGCT, epidemiological data are scarce and heterogeneous[1,2]

Approximate worldwide incidence

43
new cases per 1 million people per year[a,2]

Prevalence

L-TGCT
44.3
cases per 100,000[b,3]

D-TGCT
11.5
cases per 100,000[b,3]

[a]based on a study done in the Netherlands (2009-2013); [b]registry-based cohort study in Denmark (2012)

D-TGCT, diffuse-tenosynovial giant cell tumor; L-TGCT, localized-tenosynovial giant cell tumor; TGCT, tenosynovial giant cell tumor

1. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 2. Mastboom MJL et al. Acta Orthop 2017;88:688–94; 3. Ehrenstein V et al. J Rheumatol 2017;44:1476–83

Patients with D-TGCT may have a higher risk of disease recurrence than patients with L-TGCT[1,2]

Epidemiological data for TGCT are scarce and heterogeneous, with data from the two currently available studies presented below[1,2]

Lifetime rate of recurrence[a,1]

Patients who experienced recurrence:

L-TGCT	D-TGCT
Up to 15%*	Up to 55%

[a]Systematic review of studies published between 1968 and 2011, including papers on pigmented villonodular synovitis[2]; *Recurrence after complete resection

Rate of recurrence in patients with prior surgery[b,2]

Patients who experienced at least 1 recurrence:

L-TGCT	D-TGCT
Up to 34%	Up to 72%

[b]Cross-sectional analysis of the TGCT Support international registry, including 497 patients with TGCT who answered an electronic questionnaire[3]

Time to recurrence[3]

L-TGCT	D-TGCT
Mean time to recurrence:	Mean time to recurrence:
4.6 years	2.8 years

D-TGCT, diffuse-tenosynovial giant cell tumor; L-TGCT, localized-tenosynovial giant cell tumor; TGCT, tenosynovial giant cell tumor

1. Verspoor FGM et al. Futur Oncol 2013;9:1515–31; 2. Stern S et al. Future Oncol 2025;21:1501–10; 3. Siegel M et al. PLoS One 2021;16:e0260795

TGCT primarily occurs in a younger, working-age adult population and can be life-limiting[1,2]

Age

Can occur at any age, but most common in people aged 25–50 years[1,3]

Median age of 33 years[2]

Etiology

The etiology of TGCT is not well understood[4]

Gender

61%

L-TGCT is slightly more predominant in women, but D-TGCT is relatively equal across men and women[1]

51%

D-TGCT, diffuse-tenosynovial giant cell tumor; L-TGCT, localized-tenosynovial giant cell tumor; TGCT, tenosynovial giant cell tumor

1. Ehrenstein V et al. J Rheumatol 2017;44:1476–83; 2. Mastboom MJ et al. Interact J Med Res 2018;7:e4; 3. Spierenburg G et al. Exp Opin Ther Targets 2022;26:333–45; 4. de Saint Aubain Somerhausen N, van de Rijn M. Tenosynovial giant cell tumour. In: Soft Tissue and Bone Tumours. WHO Classification of Tumours. 5th Edn, Vol 3, 2020

Signs and symptoms

Signs and symptoms vary from patient to patient and overlap with other disorders, impeding accurate diagnosis and optimal treatment[1,2]

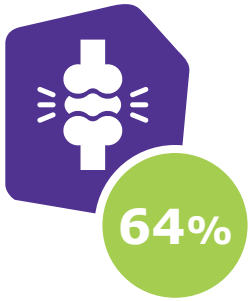
Most common symptoms: Estimated frequency based on patient reports[2]

Swelling

Pain

Stiffness

Limited range of motion



Joint instability

Sound during movement

TGCT, tenosynovial giant cell tumor

1. Bernthal NM et al. Orphanet J Rare Dis 2021;16:191; 2. Gelhorn HL et al. Clin Ther 2016;38:778–93

Pain in patients with TGCT[1]

Impact of pain

- "Pain" is the most common word that patients associate with TGCT[1]
- Pain is a significant factor for emotional and psychological burden, even after surgery[1]
- Many patients cannot sleep through the night without muscle relaxants and/or sleeping pills on a regular basis[1]

Recommendations from a consensus of TGCT experts[2]:

Patients should be referred to pain specialists depending on disease and symptom burden[2]

There are no data for pain management in TGCT; existing guidelines for chronic pain treatment should be used[2]

Approaches to address chronic pain may include[2,3]:

- Lifestyle changes
- Physical therapy
- Complimentary therapies e.g., meditation, acupuncture, etc.
- Surgery
- NSAIDs, steroids, and opioids

Chronic pain is pain that lasts for over 3 months[3]

NSAID, nonsteroidal anti-inflammatory drug; TGCT, tenosynovial giant cell tumor

1. Cook NS et al. Adv Ther 2020;37:2813–28; 2. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 3. American Society of Anesthesiologists. https://madeforthismoment.asahq.org/pain-management/types-of-pain/ [Accessed April 30, 2025]

Diagnosis

Diagnosis

Accurate diagnosis is still a challenge in patients with TGCT[1,2]

Patients are often referred to orthopedic surgeon by their PCP for diagnosis[a,1,3]

- X-ray is used to detect changes in bones to confirm/exclude differential diagnoses[4–6]
- MRI is the recommended method to determine TGCT diagnosis and subtype due to its ability to visualize soft tissue[4]

A biopsy is conducted to confirm diagnosis[4]

Diagostic challenges

- X-ray is typically the first imaging used for patients and may show the presence of cortical erosion of the bone; however, true bone invasion is not typical for TGCT tumors and suggests an aggressive neoplasm. Therefore, X-rays can only rule-out underlying bone involvement, but cannot provide a confirmatory diagnosis of TGCT[6]
- Variable MRI results and lack of awareness of TGCT may lead to further delays in diagnosis[2,7]

[a]Medical oncologists, rheumatologists, and sport medicine specialists may also be involved in clinical evaluation and diagnosis[1,4]

MRI, magnetic resonance imaging; PCP, primary care physician; TGCT, tenosynovial giant cell tumor

1. Bernthal NM et al. Orphanet J Rare Dis 2021;16:191; 2. Riedel RF et al. Cancer*Care*®. 2021, New York, NY; 3. Stern S et al. Future Oncol 2025;21:1501–10;
4. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 5. Bhimani MA et al. Clin Orthop Relat Res 2001;386:197–202;
6. Dania V et al. Medicina 2024;60:1675; 7. Spierenburg G et al. Insights Imaging 2023;14:22

Magnetic Resonance Imaging (MRI)

- MRI is used to show disease extent, presence of joint effusion, and secondary degenerative changes[1,2]

MRI can detect differences between L-TGCT and D-TGCT[3]:

L-TGCT on MRI

- Usually seen near tendon sheath; less frequently near bursae or joint
- Often presents as a discrete and encapsulated mass[2]
- Joint effusion typically absent
- Tissue usually shows moderate/marked heterogeneous enhancement on MRI with areas of hyperintense or hypointense signal intensity[4]

D-TGCT on MRI

- Extensive joint involvement
- Irregular margins and blooming artifacts[a]
- More frequent joint effusions and subchondral cysts[b]

MRI results can be variable due to heterogeneous histologic composition and growth patterns[5]

D-TGCT, diffuse-tenosynovial giant cell tumor; L-TGCT, localized-tenosynovial giant cell tumor; MRI, magnetic resonance imaging; TGCT, tenosynovial giant cell tumor

[a]In TGCT, hemosiderin buildup causes blooming artifacts on MRI, making the tumor appear larger or darker[3]; [b]Subchondral cysts are fluid filled sacs found in bone beneath cartilage

1. Spierenburg G et al. Expert Opin Ther Targets 2022;26;333–45; 2. Choi WS et al. Cancers (Basel) 2024;16:402; 3. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 4. Huang G-S et al. AJR Am J Roentgenol 2003;181:539–43; 5. Spierenburg G et al. Insights Imaging 2023;14:22

Diagnosis

Time from symptom onset to diagnosis is highly variable and can range from months to years[1,2]

Time from onset of symptoms to diagnosis[2]

>24 months

(About one third of patients with TGCT were diagnosed >24 months after onset of symptoms)

Approximately 25% of patients had at least five medical visits related to their symptoms before an accurate diagnosis[1]

Diagnostic delays can lead to[1,3,4]:

- reduced QoL
- missed treatment opportunities
- irreversible damage, including bone and cartilage erosion, and joint degeneration

Based on a recently published whitepaper, patients have reported that TGCT can be a lonely diagnosis[4]

QoL, quality of life; TGCT, tenosynovial giant cell tumor

1. Bernthal NM et al. Orphanet J Rare Dis 2021;16:191; 2. Stern S et al. Future Oncol 2025;21:1501–10; 3. van der Heijden L et al. J Surg Oncol 2023;128;478–88;
4. Riedel RF et al. Cancer*Care*®. 2021, New York, NY

Patients want HCPs to change their perspective on the disease and consider the patient experience[1,2]

Why?

- The understanding of healthcare professionals (HCPs) about the impact of disease and treatment on patients' lives may be limited[3]
- Patients feel their experience is minimized by the perception of the disease being "benign"[4]

How?

Clinical outcome assessments (COAs) measure how patients feel and function[5]. COAs can include[5–7]:

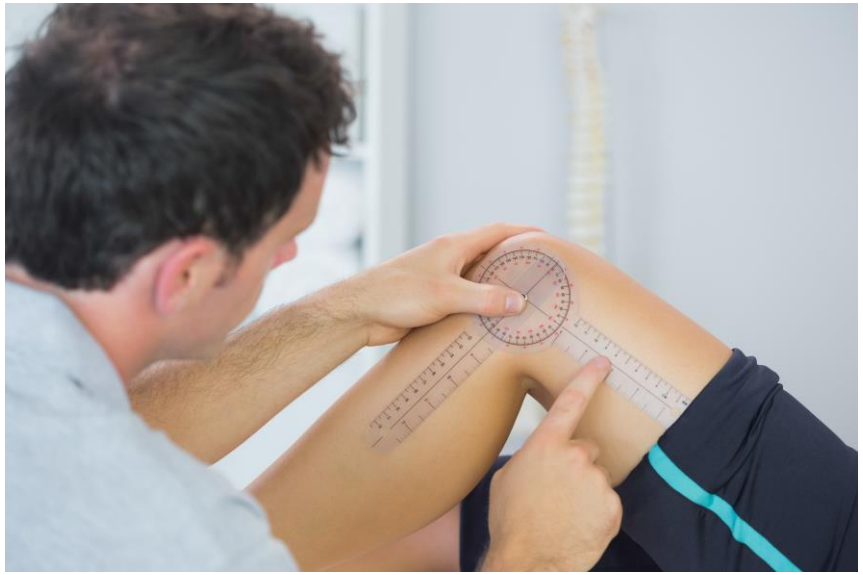
- Objective measures e.g., range of motion (ROM)
- Patient-reported outcomes (PROs) assessments that evaluate the patient experience including impact of therapy on QoL, symptom improvement, and daily function

COAs can be used to capture the patient's experience with the disease and its treatment[5,6]

QoL, quality of life; TGCT, tenosynovial giant cell tumor

1. TGCT Support. Sarcoma Patient Advocacy Global Network meeting. https://www.sarcoma-patients.org/wp-content/uploads/CTOS_advocacy-lounge-tgct-poster-FINAL-10292024_A2.pdf [Accessed April 30, 2025]; 2. Riedel RF et al. Cancer*Care*® 2021, New York, NY; 3. Nelson EC et al. BMJ 2015;350:g7818; 4. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 5. Kim Y et al. Cancer Med 2023;12:16945–57; 6. Niu X et al. Future Oncol 2024;1–8; 7. Speck RM et al. J Patient Rep Outcomes 2020;4:61

ROM is an objective clinical measure of physical functioning that can be used alongside PROs[1–4]



Goniometer being used to measure ROM

ROM

- Measures the patient's ability to move the affected joint[5]
- Measured by a HCP using a device called a goniometer[2,3,5,6]
  - Measures angle of motion in degrees
  - Smaller than normal angle means a limited range of motion or reduced joint mobility
- Important measure of the impact of disease that can directly affect the patient's well-being and QoL[4,6]

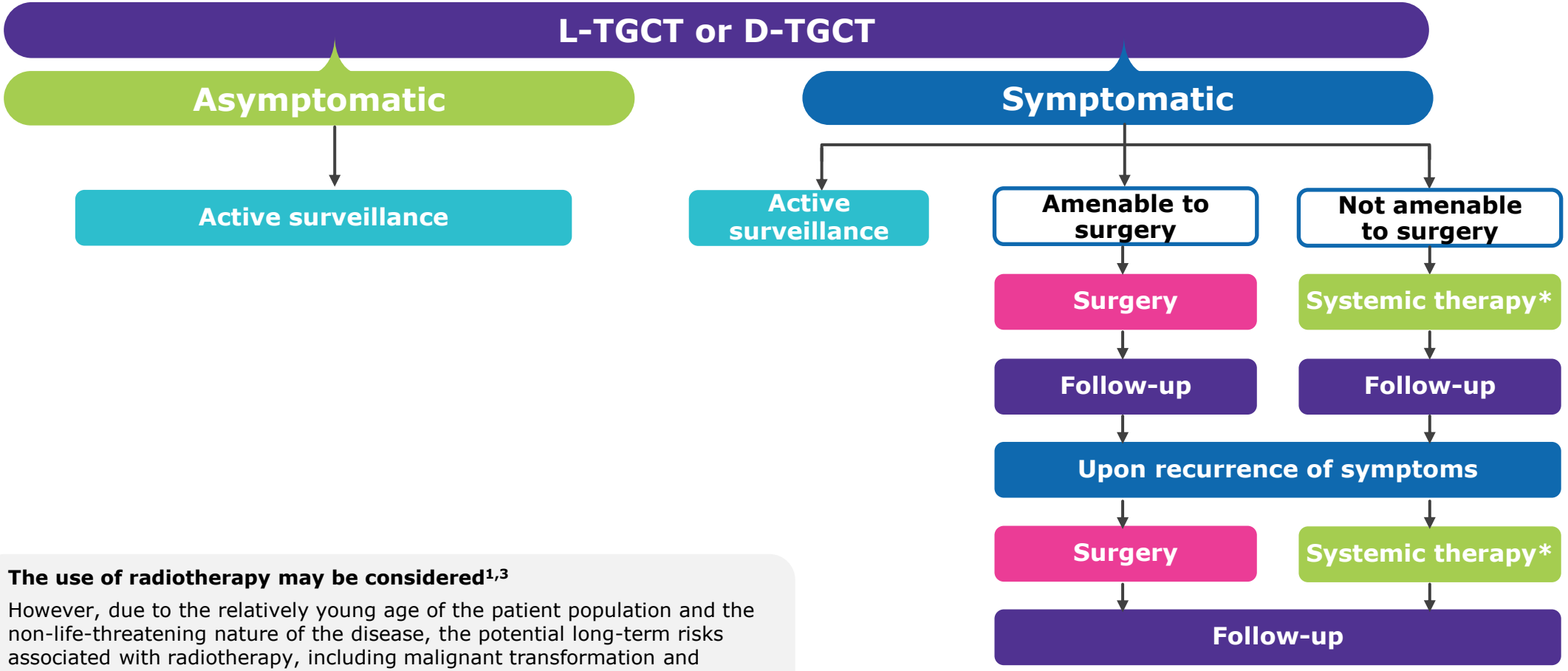
ROM can be used to objectively monitor disease progression or recovery by tracking changes in joint mobility over time[1-4]

HCP, healthcare professional; PRO, patient-reported outcome; QoL, quality of life; ROM, range of motion; TGCT, tenosynovial giant cell tumor

1. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT05804045?tab=table [Accessed April 7, 2025]; 2. ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT02371369 [Accessed April 7, 2025]; 3. Speck RM et al. J Patient Rep Outcomes 2020;4:61; 4. Niu X et al. Future Oncol 2024:1–8; 5. Verywell Health. https://www.verywellhealth.com/overview-range-of-motion-2696650 [Accessed April 7, 2025]; 6. Verywell Health. https://www.verywellhealth.com/what-is-a-goniometer-2696128 [Accessed April 7, 2025]

Treatment

Treatment strategy mainly relies on a patient's symptoms and their eligibility for surgery[1,2]



*Aiming to regulate the colony-stimulating factor (CSF-1) pathway

The use of radiotherapy may be considered[1,3]

However, due to the relatively young age of the patient population and the non-life-threatening nature of the disease, the potential long-term risks associated with radiotherapy, including malignant transformation and fibrosis, joint stiffness, or other sequelae are significant concerns[1]

D-TGCT, diffuse-tenosynovial giant cell tumor; L-TGCT, localized-tenosynovial giant cell tumor; TGCT, tenosynovial giant cell tumor

1. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 2. Spierenburg G et al. Eur J Surg Oncol 2024;50:107953; 3. van der Heijden L et al. J Surg Oncol 2023;128;478–88

Active surveillance is considered as the first treatment option for patients who are asymptomatic or have manageable symptoms[1]

Active surveillance:

Physical therapy and **pain medications** (e.g., NSAIDs) may be used to manage symptoms[2]

MRI to monitor disease and evaluate symptoms[3]

Considered for symptomatic patients if there is a risk of major morbidity from surgery or treatment and if symptoms are manageable with alternative options (e.g., pain medications)[1,2]

The decision should be shared with the patient after a thorough discussion of the benefit/risk ratio within the multi-disciplinary team[1]

Frequency of follow-up should be individualized, based on symptoms, tumor growth pattern, and anatomic location[1]

Patients with symptom progression are evaluated and may undergo treatment, including surgery or systemic therapy[1,2]

MRI, magnetic resonance imaging; NSAID, non-steroidal anti-inflammatory drug; TGCT, tenosynovial giant cell tumor

1. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 2. Spierenburg G et al. Eur J Surg Oncol 2024;50:107953; 3. National Organization for Rare Disorders. https://rarediseases.org/rare-diseases/tenosynovial-giant-cell-tumor/ [Accessed February 26, 2025]

Surgery

Surgery is the primary treatment for symptomatic patients who are amenable to surgery and for whom surgery can be accomplished without significant morbidity[1]

First treatment, including surgery, usually occurs within 3 months of diagnosis[2]

Orthopedic surgeon or orthopedic oncologist removes the tumor[3]

Recovery may be quicker for arthroscopic surgery than for open surgery (open synovectomy)[3]

Follow-up and monitoring post-surgery are recommended[4]

Challenges of surgery

- Surgery may have varying outcomes depending on the skill of the surgeon and challenging excision caused by tumor location or poorly demarcated, irregular boundaries[3,5]
- Limited treatment options exist for patients with unresectable or complex disease presentations[5]

Up to 52% of patients with D-TGCT experience recurrence within 2 years, while up to 5% of patients with L-TGCT experience recurrence within 3 years;[4] these recurrences may require repeat surgery[1,4]

D-TGCT, diffuse-tenosynovial giant cell tumor; L-TGCT, localized-tenosynovial giant cell tumor; TGCT, tenosynovial giant cell tumor

1. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 2. Stern S et al. Future Oncol 2025;21:1501–10; 3. Riedel RF et al. Cancer*Care*®. 2021, New York, NY; 4. Siegel M et al. PLoS One 2021;16:e0260795; 5. van der Heijden L et al. J Surg Oncol 2023;128;478–88

Surgical options for TGCT[1,2]

L-TGCT[1,3,4]

Preferred surgical method: Arthroscopy

- Minimally invasive surgery to examine and repair joints
- Can be done as an outpatient procedure
- Can only access disease inside the joint
- Usually curative

D-TGCT[1–3,5]

Preferred surgical method: Open synovectomy

- Open surgery to remove the synovium
- High recurrence rate due to infiltrative disease and challenges in achieving complete resection
- Increased patient morbidity and risk of post-operative complications
- Long rehabilitation

- Recurrent TGCT may lead to irreversible secondary osteoarthritis[3]
- Arthroplasty (any surgical procedure aimed at restoring joint function, including joint replacement, resurfacing a joint or using a prosthesis) is used to treat TGCT after recurrences or to repair the extensive damage to the bone caused by osteoarthritis[3]
- Total arthroplasty is associated with a low rate of local recurrence and improvement in function[3]
- An observational registry of 497 patients from 32 countries found that 2 patients (0.4%) had to undergo amputation as part of their TGCT treatment journey[6]

The decision on surgical management should include patients' needs and preferences[2]

D-TGCT, diffuse-tenosynovial giant cell tumor; L-TGCT, localized-tenosynovial giant cell tumor; TGCT, tenosynovial giant cell tumor

1. National Organization for Rare Disorders. https://rarediseases.org/rare-diseases/tenosynovial-giant-cell-tumor/ [Accessed February 26, 2025]; 2. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 3. Robert M et al. Front Immunol 2022;13:820046; 4. OrthoInfo. https://orthoinfo.aaos.org/en/treatment/arthroscopy/ [Accessed March 17, 2025]; 5. van der Heijden L et al. J Surg Oncol 2023;128;478–88; 6. Stern S et al. Future Oncol 2025;21:1501–10

Systemic treatment

Patients with difficult to manage symptomatic disease (e.g., recurrence) or when surgery is not an option due to significant morbidity (moderate/severe functional impairment) may be candidates for systemic treatment and be referred to medical oncologists[1-3]

The aims of systemic therapy include[1,4]:

- Reducing the burden of the disease
- Decreasing surgical morbidity
- Reducing the risk of recurrence
- Improving QoL

Systemic therapies that are currently available or under development primarily aim to regulate the CSF-1 pathway[5,6]

CSF-1, colony-stimulating factor; QoL, quality of life; TGCT, tenosynovial giant cell tumor

1. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 2. Spierenburg G et al. Expert Opin Ther Targets 2022;26:333–45;
3. Riedel RF et al. Cancer*Care*®. 2021, New York, NY; 4. Palmerini, E et al. Curr Oncol Rep 2025. doi: 10.1007/s11912-025-01679-x 5. Lin C-C. J Immunother Precis Oncol 2021;4:105–14; 6. Stern S et al. Future Oncol 2025;21:1501–10

Monitoring disease/treatment outcomes

Validated[a] PRO instruments are used for assessing the impact of disease and guiding treatment decisions[1-3]

PROs are standard, qualitative measures, including self-administered questionnaires validated for use in TGCT[1–3]. PROs can:

Evaluate the impact of therapeutic interventions on health status[1,2,4,5]

- Symptom improvement
- QoL enhancement
- Restoration of daily functions

Assess risks/benefits of therapeutic interventions[5–7]

- Show how treatment adverse events may impact patients
- Provide information for informed risk/benefit discussions between patients and HCPs

Integrate with clinical measures for optimal disease management[1,2,4–6]

- Inform development of personalized treatment plans
- Influence treatment decision-making

PRO assessments have been reported not to be routinely used in clinical practice[8–11]. Clinical teams report that time limitations pose a barrier for patient-centered measures[9]

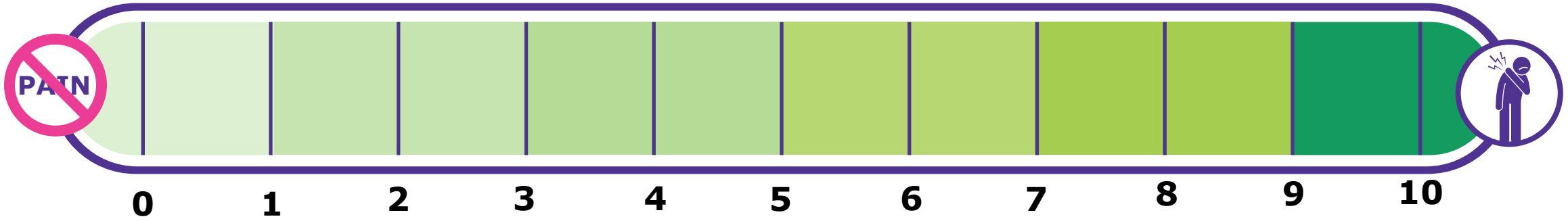
[a]Evidence based tool

HCP, healthcare professional; PRO, patient-reported outcome; QoL, quality of life; TGCT, tenosynovial giant cell tumor

1. Palmerini E et al. Oncologist 2023;28:e425–35; 2. Gelhorn HL et al. Clin Ther 2016;38:778–93; 3. Speck RM et al. J Patient Rep Outcomes 2020;4:61; 4. Niu X et al. Future Oncol 2024:1–8; 5. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 6. Bernthal NM et al. Orphanet J Rare Dis 2021;16:191; 7. Riedel RF et al. Cancer*Care*® 2021, New York, NY; 8. Cure Today. https://www.curetoday.com/view/nurse-tells-patients-with-tgct-to-speak-out-about-pain [Accessed April 24, 2025]; 9. Tap WD et al. J Clin Oncol 2022;40(28_Suppl):056; 10. Higginson IJ et al. BMJ 2001;322:1297–300; 11. Nguyen H et al. J Med Radiat Sci 2021;68:186–195

Numeric rating scale (NRS) is used to measure stiffness and pain[1]

- Single item, self-evaluated questionnaire[1]
- Single question each for pain and stiffness to assess "worst" pain or stiffness in the last 24 hours[1]
- Generally used in combination with other PROs to provide a more comprehensive assessment[1,2]



Rated on a scale from 0 (no pain/stiffness) to 10 (pain/stiffness as bad as you can imagine)[1]

Stiffness and pain NRS can capture the intensity of symptoms and track efficacy of treatment over time[1,2]

PRO, patient-reported outcome; TGCT, tenosynovial giant cell tumor

1. Speck RM et al. J Patient Rep Outcomes 2020;4:61; 2. Niu X et al. Future Oncol 2024:1–8

Brief Pain Inventory (BPI) rapidly assesses the severity of pain and its impact on daily function[1,2]

BPI[1,2]

Self-evaluated questionnaire measuring severity of pain, impact of pain on daily function, location of pain, pain medications, pain relief in the past 24 hours

Provides 2 main scores:

Pain severity[1,2]

- Includes 4 items:
  - Worst pain in the last 24 hours
  - Least pain in the last 24 hours
  - Pain on average
  - Pain right now
- Rated from 0 (no pain) to 10 (pain as bad as you can imagine)

Pain Interference[1,2]

- Includes 7 items:
  - General activity
  - Mood
  - Walking ability
  - Sleep
  - Enjoyment of life
  - Normal work (including housework)
  - Relationship with other people
- Rated from 0 (pain does not interfere with activity) to 10 (pain completely interferes with activity)

BPI is a multi-dimensional assessment which can be used to monitor changes in the intensity of pain and its impact on daily activity[1,2]

TGCT, tenosynovial giant cell tumor

1. Palmerini E et al. Oncologist 2023;28:e425–35; 2. MD Anderson Cancer Center. https://www.mdanderson.org/research/departments-labs-institutes/departments-divisions/symptom-research/symptom-assessment-tools/brief-pain-inventory.html [Accessed April 24, 2025]

Patient-Reported Outcomes Measurement Information System-Physical Function (PROMIS-PF) is used to measure functional outcomes[1–4]

PROMIS-PF[1-3]

- Self-evaluated questionnaire
- Questions can be customized to focus on specific functional domains, i.e. the affected joint in the upper or lower extremities
  - A 13-item scale and an 11-item scale were previously customized for patients with tumors in the lower and upper extremities; 9 items were found in both scales
- Rated on a scale from 1 (unable to do an activity) to 5 (able to do activity without any difficulty)[a]
- Scores are expressed as T-scores, a standardized score with a mean of 50 and standard deviation (SD) of 10
  - Lower PROMIS-PF T-scores represent higher impact on the ability to carry out daily living activities. For example, a person with a T-score of 40 is one SD worse than the average

PROMIS-PF measures the impact of disease on the patient's ability to perform daily activities. Higher scores represent better functional outcomes[1,2]

[a]**Example of PROMIS-PF questions:** Does your health now limit you in lifting or carrying groceries?; Are you able to go up and down stairs at a normal pace?; Are you able to go for a walk of at least 15 minutes?

TGCT, tenosynovial giant cell tumor

1. Palmerini E et al. Oncologist 2023;28:e425–35; 2. Gelhorn HL et al. Clin Ther 2016;38:778–93; 3. Speck RM et al. J Patient Rep Outcomes 2020;4:61; 4. Gelhorn HL et al. J Patient Rep Outcomes 2019;3:6

EQ-5D-5L is a validated PRO tool used to measure generic health status[1,2]

EQ-5D-5L consists of 2 parts: 1) descriptive questionnaire and 2) visual analogue scale[1,2]

EQ-5D-5L Part 1

- Self-evaluated questionnaire[2]
- Includes 5 domains (one question each)[1,2]
  - Mobility
  - Self-care
  - Usual activities
  - Pain or discomfort
  - Anxiety or depression
- Each domain has 5 levels ranging from 'no problems' to 'extreme problems' or 'unable to perform,' with sum utility score ranging from 0 to 1[1,2]

EQ-5D-5L Part 2: EQ-VAS

- Self-rated measure of an individual's overall perception of current health and health related QoL[1–3]
- Participants are asked to rate their health state according to how they feel on the day of the test[2]
- Rated on a scale of 0 to 100[1–3]
  - 0: worst health you can imagine
  - 100: best health you can imagine

Click for more info about other relevant PROs

EQ-5D-5L Part 1 provides a profile of a respondent's health state[1,2]. Lower scores on the EQ-VAS indicate a lower perceived overall health by the patients[1-3]

EQ-5D-5L, EuroQol 5-Dimension 5-Level; EQ-VAS, EuroQol Visual Analogue Scale; PRO, patient-reported outcome; TGCT, tenosynovial giant cell tumor

1. Palmerini E et al. Oncologist 2023;28:e425–35; 2. EQ-5D https://euroqol.org/wp-content/uploads/2023/11/EQ-5D-5LUserguide-23-07.pdf [Accessed April 24, 2025];
3. Speck RM et al. J Patient Rep Outcomes 2020;4:61

COAs are important to demonstrate the clinical relevance of novel therapies in nonmalignant diseases, such as TGCT[1,2]

Tumor shrinkage may not correlate with improvement in patient's symptoms[1,2]

- Reduction in tumor size is not a sufficient outcome if patient symptoms do not improve
- Some patients may benefit from treatment without significant tumor shrinkage

COAs are valuable in determining whether the benefits of treatment outweigh the adverse events[1–4]

COA, clinical outcome assessments; TGCT, tenosynovial giant cell tumor

1. Gelhorn HL et al. Clin Ther 2016;38:778–93; 2. Palmerini E et al. Oncologist 2023;28:e425–35; 3. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 4. Cure Today. https://www.curetoday.com/view/tgct-quality-of-life-impact-can-be-quite-similar-to-cancer [Accessed April 24, 2025]

Summary

The burden of TGCT and its management can negatively impact QoL[1–4]

Because TGCT is locally aggressive, some patients may continue to experience a decline in QoL even after recommended treatment[2,5,6]

QoL, quality of life; TGCT, tenosynovial giant cell tumor

1. Cook NS et al. Adv Ther 2020;37:2813–28; 2. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 3. Gelhorn HL et al. Clin Ther 2016;38:778–93; 4. Lopez-Bastida J et al. Orphanet J Rare Dis 2021;16:294; 5. Gelhorn HL et al. J Patient Rep Outcomes 2019;3:6; 6. Mastboom MJ et al. Interact J Med Res 2018;7:e4

TGCT can result in a substantial physical, emotional, and financial burden for patients[1–4]

The often recurrent and potentially debilitating nature affects physical, emotional, and social well-being[1–3]

>70% of patients felt an impact on their ability to concentrate[5]

Functional impairment and disability may hinder daily activities and societal participation[2,4]

>80% of patients reported pain interfered with their day-to-day activities and enjoyment of life over the past 7 days[5]

Lost income, and ambulatory expenses strain mental and financial QoL[1–4]

Almost 25% of patients changed occupation or retired early due to TGCT[5]

QoL, quality of life; TGCT, tenosynovial giant cell tumor

1. Bernthal NM et al. Orphanet J Rare Dis 2021;16:191; 2. Lin F et al. J Occup Environ Med 2021;63:e197–202; 3. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 4. Mastboom MJ et al. Interact J Med Res 2018;7:e4; 5. Stern S et al. Future Oncol 2025;21:1501–10

Summary

TGCT is a rare, non-life threatening, soft-tissue tumor that originates in the synovial lining of joints, bursae, and tendon sheaths, causing them to thicken and overgrow[1–4]

TGCT growth is caused by overproduction of a protein called CSF-1 by neoplastic synovial tumor cells. CSF-1 binds to its receptor found on non-neoplastic inflammatory cells, such as macrophages, leading to the recruitment of these cells into the joint, where they comprise the majority of the tumor[1,2,5,6,7]

There are two types of TGCT, localized (also known as nodular) and diffuse, which affect patients differently and have an estimated prevalence of 44.3 per 100,000 and 11.5 per 100,000 respectively[3,5,8]

TGCT primarily occurs in a younger, working-age population; the etiology of TGCT is not well understood.[2–4] It can have a major impact on patients' daily living and QoL, with common signs and symptoms including pain, swelling, stiffness, and limited range of motion[4,5,9]

Treatment strategy mainly relies on a patient's symptoms, and whether they are amenable to surgery.[1,10] Patients with difficult to manage symptomatic disease or when surgery is not an option due to significant morbidity may be candidates for systemic treatment[1,5,11]

CSF-1, colony-stimulating factor-1; QoL, quality of life; TGCT, tenosynovial giant cell tumor

1. Stacchiotti S et al. Cancer Treat Rev 2023;112:102491; 2. de Saint Aubain Somerhausen N, van de Rijn M. Tenosynovial giant cell tumour. In: Soft Tissue and Bone Tumours. WHO Classification of Tumours. 5th Edn, Vol 3, 2020; 3. Ehrenstein V et al. J Rheumatol 2017;44:1476–83; 4. Mastboom MJ et al. Interact J Med Res 2018;7:e4; 5. Spierenburg G et al. Expert Opin Ther Targets 2022;26:333–45; 6. van der Heijden L et al. J Surg Oncol 2023;128;478–88; 7. Robert M et al. Front Immunol 2022;13:820046 8. Mastboom MJ et al. Acta Orthop 2017;88:688–94; 9. Gelhorn HL et al. Clin Ther 2016;38:778–93; 10. Spierenburg G et al. Eur J Surg Oncol 2024;50:107953;; 11. Riedel RF et al. Cancer*Care*®. 2021, New York, NY