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What's New with Intraneural Ganglion Cysts?

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■ BACKGROUND: **Intraneural ganglion cysts (IGCs) are rare, mucin-filled lesions that develop within peripheral nerves, most commonly the common peroneal nerve arising from the superior tibiofibular joint. Their pathogenesis has been explained by the unified articular theory. Over the past two decades, new anatomic, imaging, and surgical insights have refined this theory and its clinical application and have been supported by historic perspectives.**

■ METHODS: **Recent case series, illustrative reports, and systematic reviews from our group and others were analyzed to highlight emerging concepts in the pathoanatomy, imaging, and management of IGCs. Emphasis was placed on common and atypical and rare sites and presentations, advanced imaging techniques, and evolving surgical strategies.**

■ RESULTS: **Novel findings include crossover patterns and the identification of extreme subparaneurial cysts explaining extensive propagation, recognition of nearly invisible cysts and joint connections on high-resolution magnetic resonance imaging more so than ultrasound, and validation of a phasic mechanism of cyst evolution. Surgical advances include the layered U approach for peroneal IGCs, a joint-only strategy for IGCs, and fluorescein-assisted intraoperative localization. Analysis of the world literature demonstrates a progressive rise in articular branch identification and treatment (5% in the 1990s to 58% in 2021), correlating with a reduced intraneural recurrence rate when the joint connection is addressed.**

■ CONCLUSIONS: **Current evidence supports the unified articular theory as the definitive explanation for all IGCs. Successful management requires articular branch disconnection and/or treatment of the joint source. Future work should focus on advanced imaging, standardized outcomes, and minimally invasive articular approaches.**

INTRODUCTION

Intraneural ganglion cysts (IGC) are benign, mucin-filled lesions that develop within peripheral nerves, often causing mononeuropathy due to nerve compression.[1] The most commonly affected nerves are the common peroneal nerve (CPN) at the superior tibiofibular joint (STFJ), followed by the ulnar nerve at the elbow and the tibial nerve at the ankle and knee regions.[2] Their origin has long been debated, with various treatment approaches suggested; however, outcomes have generally been unsatisfactory, with frequent and often underreported recurrences. Once thought to be rare, IGCs are becoming more commonly recognized. The prevalence of IGCs is not well described, but a recent study reported the prevalence of CPN IGC in the setting of peroneal mononeuropathy is 18%.[3] With the widespread availability of high-resolution magnetic resonance imaging (MRI) and ultrasound (US), IGCs are being observed more often.

The unified articular theory was introduced in 2003 for the formation of CPN IGCs at the fibular neck/head region based on the consistent finding of a cystic articular branch connection to the anterior aspect of the STFJ.[4] The propagation of the cyst would explain the typical involvement of the deep peroneal distribution musculature. The following three key principles have emerged: 1) these cysts originate from a defect in the capsule of a nearby joint, allowing joint fluid to escape and move below the epineurium of an articular nerve branch, consistent with Hilton's law which states that nerve trunks supplying the muscles that move a joint also provide sensory innervation to the skin overlying the insertions of those muscles, and to the joint itself[5];2) the fluid travels along the path of least resistance; and 3) pressure dynamics contribute to the formation and propagation of the cyst in a phasic manner.

Although the articular theory has reshaped management of IGCs, recent literature has introduced additional refinements in pathoanatomic understanding, imaging interpretation, and surgical anatomy that have not been
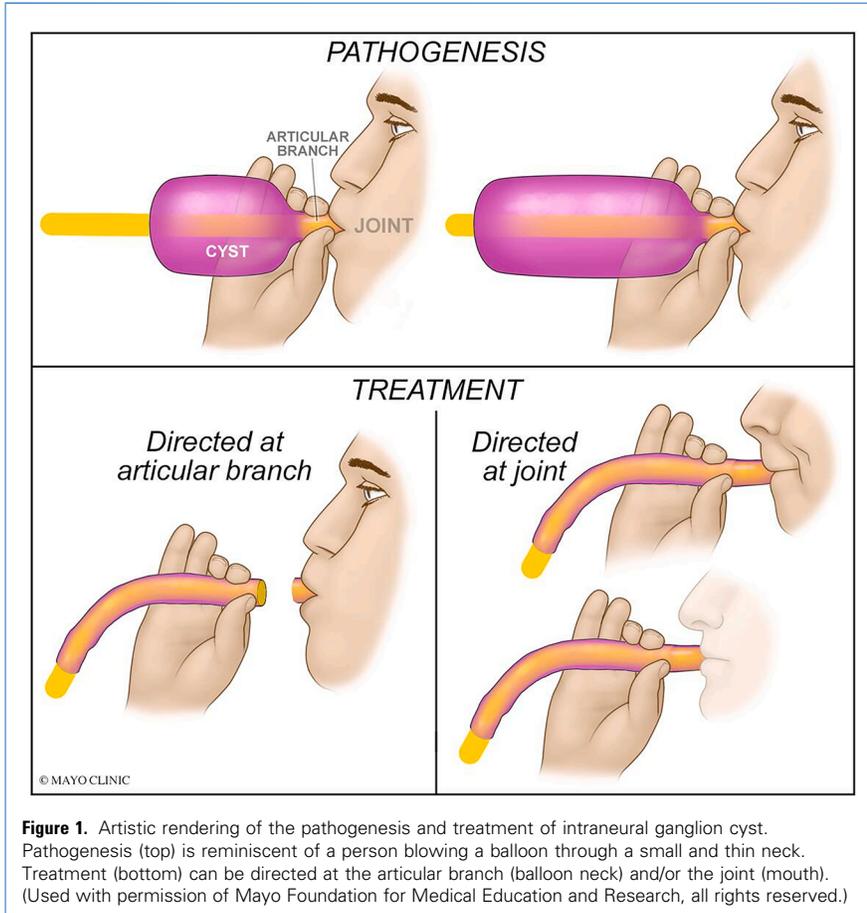
Figure 1. Artistic rendering of the pathogenesis and treatment of intraneural ganglion cyst. Pathogenesis (top) is reminiscent of a person blowing a balloon through a small and thin neck. Treatment (bottom) can be directed at the articular branch (balloon neck) and/or the joint (mouth). (Used with permission of Mayo Foundation for Medical Education and Research, all rights reserved.)

comprehensively synthesized. This review consolidates these novel observations across the CPN and other IGCs and evaluates how they have informed contemporary surgical strategies and recurrence prevention.

LESSONS LEARNED FROM COMMON CASES: CPN PROTOTYPE AT THE STFJ

Pathoanatomy

CPN IGCs at the STFJ constitute 60.6% of all IGC cases in the literature.[2] However, only one half of these have been found to have articular connections in the literature. In our experience with more than 100 peroneal IGCs, we have identified the involved articular branch in all cases.[1,6] We have previously also reinterpreted imaging and found previously missed STFJ articular branch connections with the CPN ganglion.[2,7] Moreover, even in peroneal neuropathy cases of reportedly negative MRI, Wilson

et al.[8] found that 64% of cases had evidence of a CPN ganglion cyst, signifying that this might be a more common problem than once believed.

The principles of the synovial theory are simple and intuitive, just like blowing up a balloon through a thin neck (**Figure 1**). The first principle of the articular theory describes a joint connection and capsular defect—a joint problem. In fact, Malghem et al.[9] reported these connections on arthrography in 1998. CPN IGCs at the STFJ are commonly associated with degenerative joint changes. A subset of patients without arthritic changes might have a positive history of trauma. Desy et al.[2] showed that 13% of patients with IGCs had a history of trauma. It is quite rare for IGCs to develop in a normal appearing joint without history of trauma. We hypothesize that in pediatric patients, joint laxity might be the primary issue. Once the capsular rent happens, fluid

travels according to the path of least resistance—the second principle—through the articular branch. Cyst propagation occurs in stages with increasing pressures, spanning from the STFJ (stage 0), the articular branch (stage 1), the deep peroneal fascicular group (stage 2), the CPN (stage 3), and the sciatic nerve (stage 4) (**Figure 2**). However, IGCs undergo a roller coaster phenomenon where they can regress/deflate and inflate at different times according to the third principle of the articular theory—the pressure dynamics. Extraneural rupture can occur according to the path of least resistance.[10]

Nearly Invisible Cysts. Several studies have provided robust pathologic evidence in support of the articular theory with articular branches affected by synovial fluid that then propagates proximal, as seen in the CPN prototype during stage 0 and 1.[1,4] A newer part of the spectrum of IGCs that we described are the nearly invisible cysts.[11] According to the third key principle of the articular theory, the formation of IGCs is dynamic or phasic. Serial imaging has demonstrated that these cysts can undergo significant fluctuations in size and morphology, sometimes becoming nearly undetectable. This variability, evident in both progressive and regressive phases, supports the existence of nearly invisible or occult cysts.[11] Such cysts may remain confined to the articular branch, as illustrated in a recent case involving the lateral plantar nerve during surgery for presumed tarsal tunnel syndrome.[12] Although previous reports have suggested the possibility of spontaneous regression, these newer findings provide stronger evidence of near-complete resolution of cysts without rupture, just as part of the roller coaster phenomenon.[11]

Nearly Invisible Joint Connections. If you cannot see the cyst, you might also not see the joint connection. We have recently reported a case of a nearly invisible joint connection—a phenomenon that challenges even advocates of the articular theory.[13] The fundamental principle of the articular theory is the identification of an often very small articular branch which ideally needs to be seen on preoperative MRI. Desy et al.[2,14] have previously
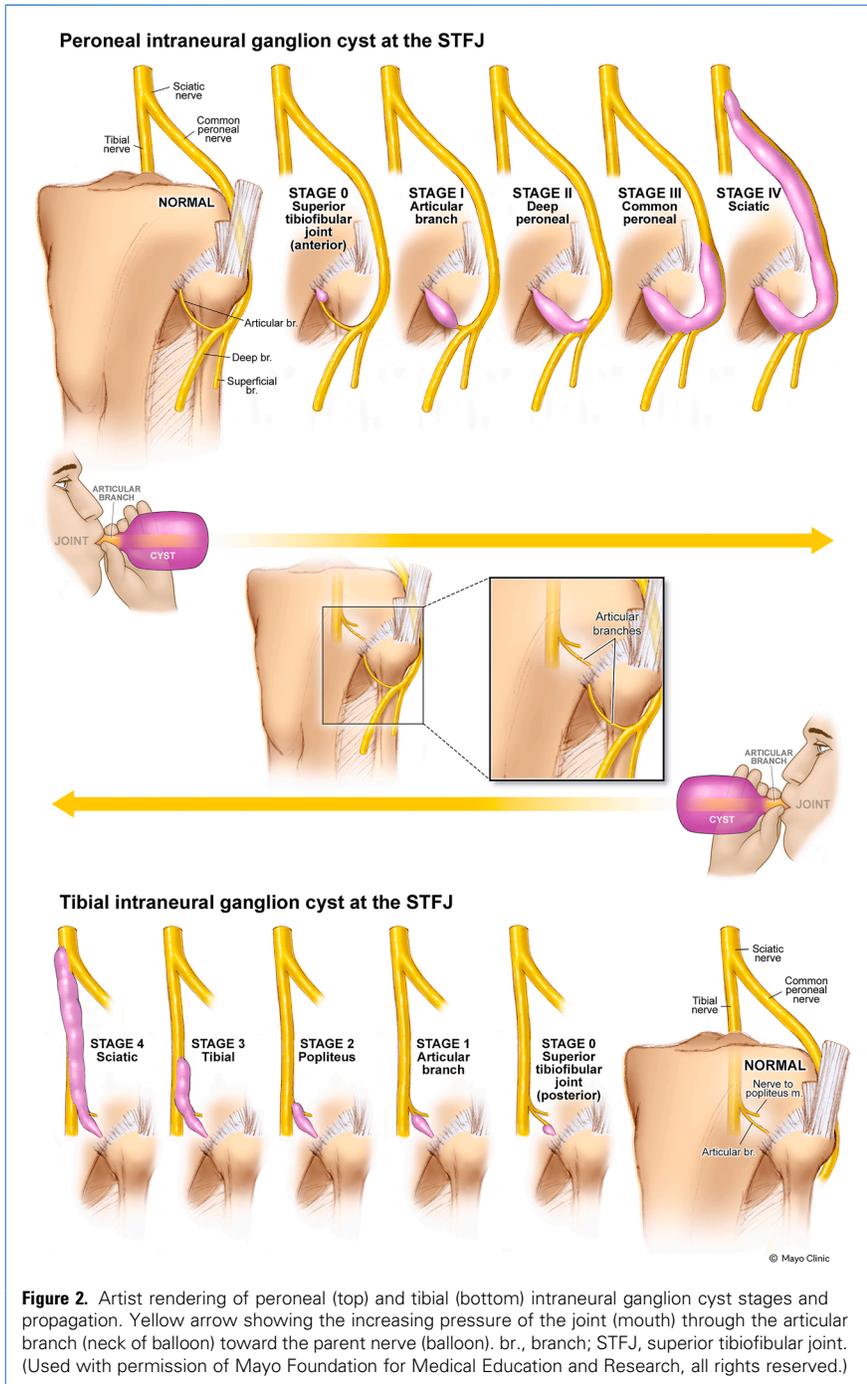
Figure 2. Artist rendering of peroneal (top) and tibial (bottom) intraneural ganglion cyst stages and propagation. Yellow arrow showing the increasing pressure of the joint (mouth) through the articular branch (neck of balloon) toward the parent nerve (balloon). br., branch; STFJ, superior tibiofibular joint. (Used with permission of Mayo Foundation for Medical Education and Research, all rights reserved.)

Extreme Subparaneurial Cysts. Understanding the distinct nerve layers—specifically the epineurium and the surrounding paraneurial layers—is essential for elucidating the mechanism of IGC development and propagation, which originate within the subepineurial compartment—consisting of dense fascicles—and may subsequently extend into the subparaneurial compartment—consisting of a loose space.[10,15] The ASCENT phase (phase I) represents the initial passage of articular cyst fluid from the STFJ through the articular branch into the CPN beneath the epineurium.[16] In phase II (CROSSOVER), the IGC reaches the sciatic bifurcation, where it transfers through an opening in the epineurium to enter the subparaneurial space. The subepineurial cyst acts like a subterranean geyser channel; once the internal pressure surpasses a critical threshold, the cyst erupts and transitions from the subepineurial to the subparaneurial compartment, a potential space capable of significant expansion. As the cyst enlarges, fluid redistribution occurs within and between these compartments according to the path of least resistance. Phase III (SUBPARANEURIAL ASCENT/DESCENT) ensues when the elevated intraneural pressure in combination with the low compliance of the paraneurial layer and gravitational forces drives cystic fluid upward or downward within the subparaneurial space. The extension may be significant, both proximally and distally, resulting in extreme subparaneurial cysts.[16] Extraneural rupture of the cyst can also occur with resultant cystic fluid in the soft tissues and muscle.

Consequently, a large IGC originating from the STFJ may propagate along the tibial or peroneal nerve into the sciatic nerve at the thigh or buttock or down to the sural nerve, explaining atypical clinical presentations.[10,17,18] An extreme subparaneurial cyst thus denotes both the remarkable longitudinal nerve involvement and the specific compartment affected—the subparaneurial space—which becomes involved during the crossover phase.

Sequential or Metachronous IGCs. The articular theory has held true with all the IGC cases in our experience. Important

identified joint connections in many cases where original authors did not, based solely on reinterpretation of available imaging. Only a very experienced radiologist at our institution was able to pinpoint the joint connection on MRI and that was on single images in the sagittal, coronal, and axial planes. That case highlights the spectrum of the imaging characteristics of the articular branch in the setting of IGCs. An occult joint connection poses a significant diagnostic dilemma, especially for skeptics of the unified articular theory. When the joint connection is not seen, look again.

lessons were learned by delving into the atypical cases and presentations. The potential pathoanatomic and pathophysiological explanations when multiple nerves are affected by ganglion cyst were discussed in the previous section. The common explanation is one articular branch (i.e., anterior STFJ) affecting the peroneal nerve and subsequently the tibial nerve and after the sciatic crossover phase and terminal branch descent.[19] Our prior published case of a sequential tibial and peroneal cyst arising from the same joint highlights the shared pathogenesis of this joint-related problem.[20] In that case, articular branches of the peroneal (anterior STFJ) and tibial (posterior STFJ) were separately identified providing an alternative and uncommon explanation when these two nerves are affected. In this case of coexistent peroneal and tibial IGCs, the former cyst and articular branch were not identified during prospective or retrospective review of the MRI scans, illustrating the principle of satisfaction of search.[21] The telltale sign in these situations might be in the affected nerve compartments. Subepineurial cysts in both the peroneal and tibial nerve (i.e., signet ring sign) should point to two separate joint connections, whereas a signet ring or tail sign in one with evidence of subparaneurial cyst (i.e., wedding ring, owl-eye, tram track) in the other would point to a typical ganglion cyst during terminal branch descent after crossover.[19,22] The example of sequential or metachronous IGCs bespeak joint origin and shows an articular approach is required.

Coexisting Intraneural and Extraneural Ganglion Cysts. Based on the unified articular theory, IGCs extend from joints along the articular branch. Similarly, other synovial joint cysts can be found in extraneural locations, including within bone, and soft tissues such as muscle—findings which bespeak a shared pathogenesis.[23,24] Sometimes the capsular vessels can be involved, in which case the cystic fluid extends along the adventitia of an artery or vein through a capsular rent.[24] These combinations of cysts can be seen before or after intervention synchronously or metachronously.

Imaging

MRI and US. All the novel observations that occurred during the workup of atypical case presentations shared a common factor: high-resolution MRI or expert radiologist and neurosurgeon or both. The value of expert treating physicians cannot be understated. High-resolution MRI and often the use of 7-T MRI has enhanced our pathoanatomic understanding by identifying occult cysts and articular branches and subparaneurial propagation patterns as previously discussed.[11,25,26] An alternative to MRI is high-resolution US.[27] Some investigators have favored US as their primary imaging modality.[28,29] US is the primary imaging modality when an MRI cannot be performed or when artifact due to prosthesis/hardware limits visualization of the cyst and nerves. Although US can identify cystic lesions and suggest the presence of a ganglion cyst, its diagnostic accuracy is operator-dependent, and visualization of the articular branch is frequently difficult.[30] In a recent study by Lenartowicz et al.,[31] MRI was found to be significantly more effective than US in detecting a joint connection, identifying it in 62% of cases compared with only 16% with US ($P < 0.01$). High-resolution MRI also remains the gold standard for distinguishing IGCs from other cystic lesions, particularly extraneural ganglia (including paralabral cysts),[32,33] cystic schwannomas,[34] and nerve abscesses.[35] Alternatively, the application of three-dimensional rendering and advanced reconstruction can enhance visualization of IGCs and point to the articular branch.[36] Even though high-resolution imaging can definitely help, low resolution can be adequate if one knows where to look for the articular connections.

MRI Signs. A multitude of pathognomonic MRI signs have been described over the past 20 years. They are all based on the pathoanatomic and pathophysiological principles of IGC development. In our recent comprehensive review of MRI findings in IGCs, we introduced the concept of phase-based MRI signs, integrating the temporal evolution of cyst formation into imaging interpretation.[37] The common radiologic signs,[10,16,22,24,38-40] described for peroneal and tibial IGCs at the STFJ

during phase I (ASCENT), phase II (CROSSOVER), and phase III (SUBPARANEURIAL ASCENT/DESCENT), are presented in Table 1.

These signs are thought to be highly specific. In addition to those, evidence of STFJ degeneration and anterior leg compartment denervation changes (not very specific) are also commonly seen in the peroneal prototype IGC cases.[8] Some of these signs aim to establish the joint connection and promote targeted surgical disconnection.

Surgical Anatomy and Technique

Layered U Approach. Understanding the anatomy of the peroneal nerve along with its articular trunk and branch is critical to perform a safe and durable procedure. We have described a consistent U shape of the articular branch around the fibular head and its involvement with cysts in peroneal IGCs.[41] We prefer the use of a tourniquet. The layered U approach involves a U-type skin incision around the fibular head, U-type division of the fascia, and peroneus longus fascia and dissection across the fibular neck. This is followed by superomedial dissection of the U-type configuration of the articular branch toward the anterior portion of the STFJ. The benefit of this approach is that it minimizes the risk of injury to the superficial and deep peroneal branches (which need not be separately identified). Closer to the STFJ, care should be taken to identify and protect the tibialis anterior and patellar branches off of the articular trunk to avoid inadvertent ligation of those instead of the terminal articular branch (Figure 4). The anatomy of the U-shaped articular branch to the STFJ is constant, and this is important because the external appearance may not be significantly enlarged or cystic in some cases. The articular branch should be ligated or disconnected, and a portion can be submitted for pathology. Disconnection of the articular branch in cases of IGC is akin to disconnecting the neck of a (water) balloon (Figure 1). Even though the cyst will likely resolve without cyst decompression, we typically make a small epineurial opening directly over an area of obvious or prominent cyst,

Table 1. Common MRI Signs Described for Peroneal and Tibial Intraneural Ganglion Cysts at the Superior Tibiofibular Joint During Phase I (ASCENT), Phase II (CROSSOVER), and Phase III (SUBPARANEURIAL ASCENT/DESCENT)

MRI Sign	Phase	Description
Tail sign[22]	I	Represents the pathoanatomic joint connection through the articular branch, marking the route by which synovial fluid first enters the nerve to initiate cyst formation (**Figure 3**).
Transverse limb sign[22]	I	Reflects cyst propagation along the transverse limb of the articular branch, confirming intraneural rather than extraneural extension (**Figure 3**).
Signet ring sign[22]	I	Highlights displacement of nerve fascicles by an epineurial cyst, illustrating how cyst pressure expands within the nerve sheath while preserving fascicular integrity.
U or J sign[22]	I	Shows the characteristic configuration of the articular branch involved by the cyst, demonstrating its proximal tracking from the joint along the descending and ascending limbs.
Clock face sign[38]	I	Highlights the consistent anatomic relationship between the cyst and the fibula. It confirms localization of the articular branch with the signet ring usually seen between the 4 and 5 o'clock position, whereas the tail sign presents at the 11 to 12 o'clock position on axial slices on the left side. It also distinguishes intraneural from extraneural cysts.
Balloon sign[39,40]	I	Represents pressurized cyst expansion through a narrow articular neck into the nerve, indicating unidirectional fluid propagation from the joint connection. This was originally described in tibiotalar origin cysts affecting the tibial nerve at the ankle.
Wishbone sign[24]	I	Demonstrates a shared origin between intraneural and adventitial (vascular) cysts at the neurovascular bundle, supporting a common articular—synovial pathogenesis.
Wedding ring sign[10,16]	II/III	Indicates cyst crossover at the sciatic bifurcation, where subepineurial fluid breaches into the subparaneurial space and partially or fully surrounds the nerve.
Ring-within-ring sign[10,16]	II/III	Depicts simultaneous subepineurial and subparaneurial cysts, where subparaneurial cyst surrounds a signet ring sign.
Owl-eye sign[10,16]	II/III	Represents more complete circumferential subparaneurial cyst expansion around the epineurium, reflecting a more prominent wedding ring sign.
Tram track sign[10,16]	II/III	Illustrates extreme longitudinal subparaneurial extension of cyst fluid along the nerve's course, corresponding to late-phase, high-pressure propagation. These can become extensive, involving the proximal sciatic down to the sural nerve.

MRI, magnetic resonance imaging.

and decompress the contents of the cyst by milking the lower extremity proximal and distal to the STFJ (**Figure 4**). This may, in theory, facilitate symptomatic recovery. Resection of the cyst wall should be avoided because it carries unnecessary neurologic injury risk. Unfortunately, a significant number of patients undergo risky/unnecessary cyst resections without articular branch disconnection. This simple and predictable layered U technique has allowed us to safely perform this operation in scarred or altered surgical fields in cases of recurrence/persistence or multilobulated, large cysts.

The last step of the procedure involves STFJ disarticulation with complete synovectomy and cartilage resection, which is shown to reduce risk of intraneural and extraneural recurrence.[6] This bony procedure has not been widely adopted because neurosurgeons are not familiar with this anatomy or technique. However, it can be done in conjunction with orthopedic surgeons; risks of the bony procedure are minimal (no ligamentous laxity or joint instability). We prefer joint resection rather than fusion of the STFJ because it is easier to perform and faster to rehabilitate. A notable exception to STFJ resection is in the skeletally immature pediatric population. It is our preference that joint resection is not undertaken in pediatric patients because it might pose risk to skeletal growth and limb development.[42]

Fluorescein as an Intraoperative Adjunct. Another newer addition to the surgical technique armamentarium for IGCs is the utilization of intravenous fluorescein.[43] This adjunct has a favorable side effect profile and is widely used in cranial neurosurgery. Availability of an operative microscope with a dedicated yellow 560-nm filter is required. We have previously used 1 mg/kg of 10% fluorescein after intubation but before tourniquet insufflation to allow for its circulation in a case of a 49-year-old man with a peroneal IGC at the STFJ. The fluorophore selectively enhanced the abnormal cystic deep peroneal side of the nerve and the articular branch.[43] Using fluorescein in atypical cases, cases with an occult cyst or joint connection, or when the surgeon is not very familiar with the anatomy, may facilitate identification and confirmation of the articular branch.

Surgical Outcomes

An analysis of surgical outcomes of peroneal IGCs at the STFJ confirmed the predictability of outcomes in these cases.[1] In their report of 24 patients who underwent articular branch disconnection and cyst decompression (without STFJ resection), they did not find any intraneural recurrences. Three patients however suffered extraneural recurrences. Two of these patients were symptomatic and were subsequently treated with STFJ resection, whereas the one asymptomatic patient was followed clinically. As shown in **Figure 2**, an increasing number of surgeries are now treating the joint connection which is shown to minimize intraneural recurrences. Percutaneous cyst aspirations have been performed and even though they may help temporarily due to reduction of mass effect, they cannot cure the disease and are plagued
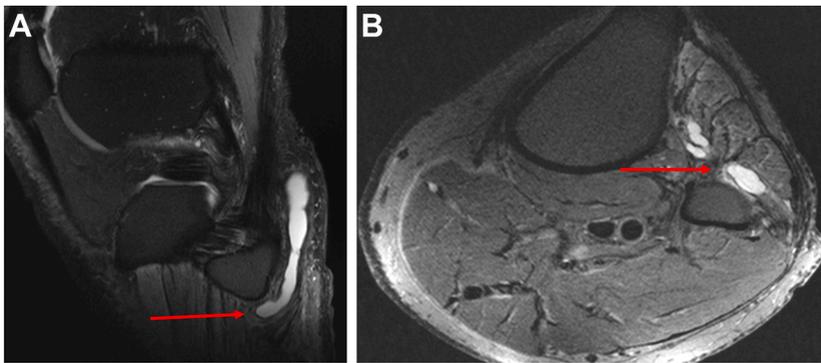
Figure 3. Magnetic resonance imaging T2 fat suppressed (**A**) sagittal sequences showing the tail sign (*red arrow*) right around the fibular neck heading toward the superior tibiofibular joint and (**B**) axial sequences showing the transverse limb sign (*red arrow*).

by intraneural recurrence (odds ratio [OR], 12.6; 95% CI, 2.4−93.8; P = 0.0035).[2]

In a more recent study by Wilson et al.,[6] 65 patients undergoing resection of the STFJ with articular branch ligation and cyst decompression for CPN IGCs showed no intraneural recurrences. The rate of extraneural recurrence in that cohort was 9% (symptomatic in 6%). The authors also reported the average volume of resection for patients with recurrence was 1349 versus 3018 mm³ in control patients that did not have a recurrence (P = 0.018). They concluded that more aggressive STFJ resection is required to minimize the risk of extraneural recurrence and also found that this did not induce joint instability.

A case series and systematic review of outcomes after surgery for CPN IGC came

to similar conclusions.[44] In the case series part, all five patients demonstrated improvement in pain and motor function without any evidence of cyst recurrence. In the systematic review part, which included a total of 128 patients, they reported consistent improvement in motor function; however, pain and sensation outcomes were not commonly reported. Wilson et al.[45] reported significant improvement in 65 patients with peroneal IGC from median preoperative dorsiflexion of 2 of 5 grade to 5 of 5 over an average follow-up of 14 months. Gonzalez et al.,[46] in a study of CPN ganglion cysts at the STFJ, reported that predictors of incomplete symptomatic recovery included intraneural involvement (compared with extraneural; OR, 3.93), cyst recurrence (OR, 6.04), and participation in contact

sports (OR, 9.85). Ligation of the articular branch of the peroneal nerve served as a protective factor (OR, 0.29). The strongest predictor of cyst recurrence was a prior history of knee arthritis (OR, 20.01), whereas STFJ arthrodesis significantly reduced this risk (OR, 0.04).

MOVING BEYOND THE CPN AT THE STFJ

Tibial Nerve at the STFJ

The CPN from the anterior part of the STFJ allowed principles of Hilton's law to show the findings of the tibial nerve at the posterior aspect of the STFJ. The tibial nerve provides innervation to the posterior part of the STFJ through articular branches.[17] Accordingly, we have previously identified and surgically treated tibial IGCs at the STFJ using the same surgical principles of cyst decompression and articular branch disconnection.[17] However, this approach has several challenges, and in an attempt to overcome these, we introduced the concept of joint-only procedures.

Novel Joint-Only Focused Approach. Tibial IGCs arising from the posterior aspect of the STFJ are more challenging to treat. The posterior approach through the popliteal fossa can directly address the posterior STFJ articular branch (but is close to neighboring vessels); however, to resect the STFJ, an anterior approach is necessary in our experience. In 2023, we presented a novel strategy for these cysts which involved resecting the synovial surface of the STFJ from an anterior approach only without disconnecting the (posterior) articular branch to the joint or decompressing the cyst.[47] This study reported a consecutive series of seven patients (mean age, 43 years; 57% male) who presented with tibial neuropathy. Postoperatively, all patients had significant improvement in their preoperative pain, three patients (43%) regained partial motor function, and four patients (57%) continued to experience sensory deficits. Follow-up MRI scans demonstrated complete cyst regression in five patients and partial regression in one patient. Complete regression occurred in 2−8 months. The patient with partial regression had the
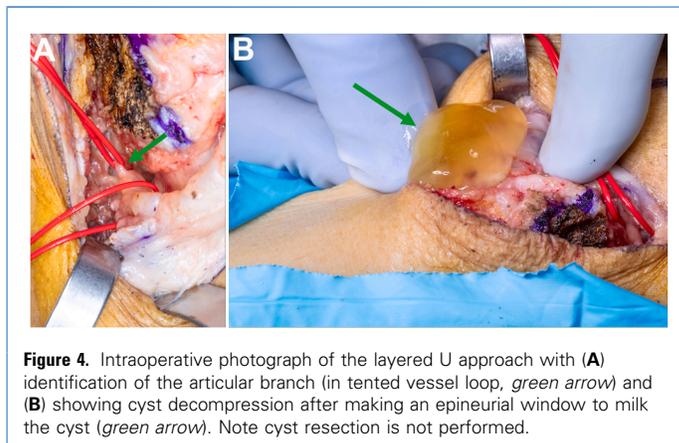

Figure 4. Intraoperative photograph of the layered U approach with (**A**) identification of the articular branch (in tented vessel loop, *green arrow*) and (**B**) showing cyst decompression after making an epineurial window to milk the cyst (*green arrow*). Note cyst resection is not performed.

largest cyst preoperatively measuring 15 cm, which reduced to 2 cm over 2 years. One patient did not have available post-operative imaging (due to insurance limitations). The study highlights that addressing the primary joint source alone can induce cyst regression, serving as a proof of concept. The surgical approach was similar to the layered U approach except only STFJ disarticulation and cartilage removal were performed once the peroneal nerve was identified and protected. The posterior STFJ articular branches of the tibial nerve could not be addressed with this approach. We think that a combination approach including articular branch disconnection, cyst decompression, and/or joint resection is likely required to achieve faster and more complete recovery. This technique how-ever could be preferred for patients with smaller tibial cysts at the STFJ with normal neurologic examination. Although this joint-only procedure could be applied to peroneal IGCs from the STFJs, we have used a belt-suspender approach to eliminate intraneural recurrence of the IGC: disconnecting the articular branch and resecting the STFJ because the anterior-based surgical approach allows direct visualization of the articular branch and the joint.

CPN and Tibial Nerve at the Knee (Tibiofemoral) Joint. The same principles of Hilton's law allowed the definition at other less common sites such as the CPN and tibial IGCs from the tibiofemoral joint. The knee joint has articular branches from multiple nerves including, the tibial, peroneal, femoral, and obturator nerves.[48] The peroneal nerve provides articular connections to the anterolateral and posterolateral part of the knee.[49,50] The tibial nerve provides mostly innervation to the posterior part of the knee.[51]

Smith et al.[50] discussed 4 cases of peroneal IGCs with an articular connection to the posterolateral knee joint. The patient who underwent surgery by their group underwent articular branch disconnection after it was clearly seen on preoperative MRI and confirmed during surgery. During follow-up, there was no cyst recurrence and the patient had a full recovery. Lenartowicz et al.[51] reported 2 illustrative cases of tibial IGCs arising from the

tibiofemoral joint and discussed 14 cases that were identified in the literature. The rich innervation of the tibial nerve to the knee joint can result in more complex development of ganglia than those arising from the STFJ. The branching patterns of the tibial articular connections to the posterior tibiofemoral joint can be lateral, central, and medial. However, by applying the same surgical principles, they found comparable outcomes after surgery for tibial cysts with STFJ versus tibiofemoral origin, when the articular branch is disconnected.[51] Following the same principles and adapting the surgery has proven to successfully treat cysts at the knee joint regardless of origin.

LESSONS LEARNED FROM OTHER COMMON AND RARE SITES

Historical Perspective
We have come a long way since the first reported ganglion cyst by Beauchêne in 1810, which was a serous cyst of the ulnar nerve at the elbow.[52] Its pathogenesis was unknown at the time. After an exhaustive investigation by the senior author (R.J.S.), they located the specimen and concluded that the origin of the cyst was from the elbow joint, dissected through a capsular rent, and followed the path of the articular branch into the ulnar nerve.[52] Also, in that index case, the affected and enlarged articular branch was found.[52] The first description of a joint-related IGC that was recognized by the original authors dates to 1884. This case was described by T. Swinford Edwards and

refers to a specimen of an ulnar nerve with a connection to a carpal joint.[53] Joint connections have been found more consistently in the past two decades (Figure 2). Using our database of the world's literature in IGCs, we have estimated the rate of surgeries that are treating the joint connection is increasing over the years (Table 2). A historical perspective not only highlights the evolution of our understanding of IGCs but also reinforces the validity of the unified articular theory by tracing how persistent clinical patterns, once dismissed or misinterpreted, now align with modern anatomic and imaging evidence.

Any Nerve with an Articular Branch can be Affected
With the broader approval of the unified articular theory, rare sites and nerves with IGCs are being reported along with their affected articular branches. As proof of concept, we tested the superficial radial nerve as a site because it had never been identified with a joint connection.[2] We challenged the notion that this nerve follows different principles for IGC formation. On imaging reinterpretation, we demonstrated wrist connections at the trapeziotrapezoid, the radioscaphoid joints.[54] These connections can be subtle and are frequently missed, as our group has shown.[54] Naam et al.[55] reported their experience with 15 IGCs at the hand. They stated that articular branches were not seen on imaging or intraoperatively before the introduction of the articular theory and subsequently

Table 2. Percentage of Surgeries That Have Treated the Joint Connection Over the Years (1992—2021)

Year	Total	Treated Joint Connection	% Surgeries that Treated Joint Connection
1992—1996	38	2	5
1997—2001	93	5	5
2002—2006	129	20	16
2007—2011	115	38	33
2012—2016	143	53	37
2017—2021	192	111	58

Numbers and analyses are from the prospectively maintained database of the world's cases of intraneural ganglion cysts, maintained by the senior author.

highlighted that after its introduction, the articular branch connection was identified in all eight patients. Hung et al.[56] identified the first posterior interosseous nerve IGC from the scapholunate joint in 2018 during a routine cadaveric dissection.

Other new nerves (and joint connections) are being identified; the inferior alveolar nerve cyst involving the trigeminal nerve,[57,58] palmar cutaneous branch of the median, and ulnar superficial branch have been affected by IGCs.[2] For all these cases, operations are not even defined; however, the principles should remain the same, including ligation of the articular branch, cyst decompression (not resection), and removal of joint cartilage/repair of the capsular rent if feasible. However, adapting the surgical approach is required according to the regional anatomy.

Larger joints including the shoulder and hip have given rise to IGCs as well. Axillary and suprascapular nerve cysts arising from the glenohumeral joint have been reported.[59] A sciatic IGC connected to the hip joint has had a cyst ascending up to L5 spinal nerve into the extraforaminal space. The patient underwent decompression and ligation of the articular branch and had no recurrence at six-month follow-up.[60] Femoral, obturator, and superior gluteal nerve cysts have been found connected to the hip joint as well.[2,61] The cases illustrated the complex nature of joint innervation, explained IGCs, and cyst propagation in other locations, and have helped teach anatomy through pathology.

Challenging Known Anatomy

Although Hilton's law underscores the fundamental relationship between joint innervation and nerve supply, a more comprehensive perspective requires integrating the lesser-known anatomy of articular branches as characterized by anatomists such as Gardner.[62-65] Knowledge of the articular anatomy and its innervation is fundamental in the realm of denervation procedures. Lessons learned from smaller joints such as the STFJ can be applied to larger joints such as the hip and the shoulder. These joints, as previously described, have more articular branches involved.[5] Joint denervation for

pain—either through conventional techniques or radiofrequency ablation—has become popular in the treatment of multiple pain syndromes emanating from the zygapophyseal joints of the spine, tibiofemoral, first carpometacarpal joint, and others.[66-68]

A reason for not identifying a joint connection, exemplified by Wilson et al.,[69] is that not all articular branches are known or well described. In two cases of superficial ulnar intraneural ganglia, the authors failed to identify a joint connection. However, as the aphorism reminds us, the eyes see what the mind knows! In contrast to widely available anatomic sources, Murakami[70] described an articular branch to the fifth metacarpophalangeal joint and/or other carpal joints coming from the superficial ulnar nerve. Subsequent cadaveric dissections by the authors confirmed this articular branch and what challenged the unified articular theory now provided further support for it.[69] We have yet to identify nerves without articular branches that have been affected by IGCs—and we think we will not—as consistent with Hilton's law.

Adapting the Surgical Approach: A Focus on the Joint

Rare sites provide a unique opportunity to advance the field of IGCs through novel approaches. A quintessential example is a case series of 13 patients with sciatic neuropathy secondary to IGCs arising from the hip joint. An articular connection was identified in all patients on preoperative MRI. The authors performed arthroscopic hip surgery during which they enlarged the periarticular connection and eliminated the one-way valve effect of the articular branch through the joint.[71] They reported that IGCs resolved on postoperative MRI in nine patients (69%). All 12 patients with preoperative abnormalities showed improvement on postoperative electrodiagnostic studies. The single patient (8%) who suffered symptomatic recurrence underwent revision arthroscopic decompression successfully.

Prasad et al.[72] reported the successful treatment of suprascapular IGC through an arthroscopic approach in two cases. The first patient underwent a shoulder

magnetic resonance arthrography that showed intraarticular contrast extending from a labral tear as a narrow neck into a suprascapular IGC. During arthroscopy, a small amount of cyst fluid was noted to enter the joint through the labral tear which was subsequently repaired, without articular branch disconnection. At one-year follow-up, complete resolution of the cyst was seen on MRI and the patient had fully recovered. The second patient was initially thought to have an extraneural ganglion cyst and underwent a hybrid arthroscopic (for the labral tear) and open (for cyst resection) approach. Reevaluation of preoperative imaging and three-dimensional reconstructions confirmed an IGC of the suprascapular nerve with crossover in the upper trunk and descent at the division level. The authors think that suprascapular IGCs are always associated with labral tears. The classic approach would be open surgery to resect with IGC, and if the labral tear is not identified, articular branch disconnection is imperative.[33,73,74] However, with adapting the surgical technique to the regional anatomy, the most important parts of the surgical treatment are repair of the labral tear, followed by resection of the articular branch and decompression of the cyst. A joint-focused approach for suprascapular cysts with labral tear repair might provide a durable treatment for suprascapular cysts without articular branch disconnection. The description of the articular branch anatomy of small and big joints is reshaping the management of IGCs. A focus on the joint by means of labral/capsule repair versus capsulotomy is already underway.

Historical Trends

Over the years, and since the introduction of the unifying articular theory, there has been a trend of articular branch localization on preoperative imaging and intraoperatively. Desy et al.,[2] in a systematic review and reinterpretation of the world's literature, analyzed 645 patients with IGCs at various locations. Joint connections were identified in 48% of this cohort.[2] They showed a statistically significant association between failure to ligate the articular branch or address the joint and rate of cyst recurrence.

Recurrence Rates

Using our database of the world's literature on IGCs, we found an overall recurrence rate (intraneural and extraneural) of 12% for all sites. This is similar to the rate reported in the previous systematic review of the literature.[2] Recurrences occur after all types of intervention as shown in Table 3. However, the rates of recurrence were the least when the articular branch was ligated. Table 4 presents the demographics of patients who had a recurrence. An important limitation worth discussing is that the validity of description of articular branch resection is questionable. Our practice is to submit the articular branch for pathologic analysis to prove the presence

Table 4. Demographics of Patients with Recurrence (n = 110)

Patient Characteristic	Total
Age (years)	37 (8–67)*
Men/women/not reported	69/26/15
Right/left/not reported	30/38/42
Symptom duration (months)	13 (0.2–96)
Trauma	20 (18)

Numbers and analyses are from the prospectively maintained database of the world's cases of intraneural ganglion cysts, maintained by the senior author. Values are mean (range), number of patients, or number of patients (%).
*Four cases did not report patient age.

Table 3. Rates of Intraneural and Extraneural Cyst Recurrence Stratified by Type of Surgery

Type of Surgery	Count	Total	Recurrence Rate (%)
Resection	44	376	12
Incision and evacuation	25	112	22
Not specified	9	52	17
Decompression	8	23	35
Incision and evacuation and ligation of articular branch	8	100	8
Percutaneous aspiration	7	9	78
Partial resection	3	27	11
Percutaneous aspiration and steroid injection	3	10	30
Ligation of articular branch	1	7	14
Resection and ligation of articular branch	1	63	2
Arthroscopic incision and evacuation	1	3	33
Total	110	943	12

Numbers and analyses are from the prospectively maintained database of the world's cases of intraneural ganglion cysts, maintained by the senior author.

of nerve tissue along with the cyst, which is only rarely reported by surgeons performing resection of the offending articular branch.

Moving Beyond a Theory

It has been more than 20 years after the initial report of the unified articular theory. We think that the joint connection is present in 100% of cases, and the cases that fail to identify it, do so because of poor imaging resolution and inattention, among other reasons. Importantly, in every case that we have had the opportunity to reinterpret, original imaging studies in which the authors did not identify a joint connection preoperatively or intraoperatively, we have been able to demonstrate an unrecognized joint connection; we have reported many examples.[75] The concepts of the articular theory explain IGCs in any nerve, anywhere in the body.[33,76,77] The articular origin has gained significant traction in the literature with articular connections being recognized more frequently (Table 2). Currently, evidence is limited by lack of standardized imaging protocols, insufficient follow-up, and variable imaging interpretation and surgical experience across the various centers.

Future Perspective

We think that our recent finding for the potential of ganglion cyst to crossover into the subparaneurial compartment opens doors for future research on IGCs. Understanding the anatomy of peripheral

nerves thereby is very important, especially the paraneurium. Physiological mechanisms, that we have compared with the eruption of a geyser, can explain extreme circumferential distribution patterns. More research is needed to elucidate whether the same mechanism can occur at sites other than the CPN at the STFJ. Future studies should also focus on patient-reported outcomes, quality of life measures, and return to function in addition to recurrence rates and motor recovery.

CONCLUSIONS

In this study, we have discussed the work that our group and others have reported over the past two decades. Since 2003, with the first report of the unifying articular theory for an IGC,[4] we have witnessed several advances in the field. What started as a theory—the controversial concept of an articular connection always being involved in an IGC—is now more broadly accepted by surgeons dealing with this disease. Over the years, we have shown that more articular branches are found on preoperative MRI and intraoperatively. We have reinterpreted several cases of previously negative MRI, and have identified the articular connection on imaging. Similarly, we have reoperated on a significant number of recurrent IGCs after the articular connection was not identified during the first or second surgeries.

The short follow-up and limited preoperative and postoperative MRI is a factor that hinders growth and understanding of IGCs. Without preoperative MRI, the surgeon's ability to identify an articular branch is limited. Without postoperative MRI, data on intraneural and extraneural recurrence are limited. Even when MRI is performed, it is commonly not reviewed by radiologists or surgeons with expertise and deep understanding of this pathology. We suggest better and more frequent imaging in these patients. Future studies should include data on recurrences, and clinical outcomes and longer follow-up. Despite extensive investigation over the last two decades, the field remains largely divided between those who endorse the unified articular theory and those who challenge

it. With a few exceptions,[78] most published case reports or series fall into one of two categories: those that identify articular connections and those that do not. The study by Naam et al.[55]—which compares cases before and after the introduction of the articular theory—represents a welcome example of thoughtful analysis across both eras.

The unifying articular theory promotes unifying concepts. The principle for all IGCs is the same regardless of site or age. It explains all cases and has anatomic principles. We have learned important pathoanatomic lessons by focusing on recognition of nearly invisible cysts and joint connections on high-resolution MRI and on extreme subparaneurial cysts and crossover patterns explaining extensive propagation. Novel MRI signs have been described during the various phases of CPN IGCs. For CPN IGCs at the STFJ, the lowest rate of intraneural recurrence occurs after articular branch disconnection and/or joint-related surgery. The favorable recovery of footdrop after the layered U approach that is performed through a small incision has proven to be predictable. We have translated the basic principles of this disease from the common cases to the rare ones and have applied the anatomy from the cadaver to the patients. Because the surgical field is moving toward less invasive surgery, we anticipate the development of novel techniques for IGC management, with a focus on the joint. Many questions have been answered over the past several years, but many remain.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Pavlos Texakalidis: Conceptualization, Investigation, Methodology, Visualization, Writing — original draft, Writing — review & editing. **Godard C.W. de Ruiter:** Conceptualization, Investigation, Methodology, Writing — original draft, Writing — review & editing. **Kimberly K. Amrami:** Conceptualization, Investigation, Methodology, Project administration, Writing — original draft, Writing — review & editing. **Robert J. Spinner:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Validation, Writing — original draft, Writing — review & editing.

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