Numerous neurogenic tumors can affect the musculoskeletal system, including traumatic neuroma, Morton neuroma, neural fibrolipoma, nerve sheath ganglion, neurilemoma, neurofibroma, and malignant peripheral nerve sheath tumors (PNSTs). The diagnosis of neurogenic tumors can be suggested from their imaging appearances, including lesion shape and intrinsic imaging characteristics. It is also important to establish lesion location along a typical nerve distribution (eg, plantar digital nerve in Morton neuroma, median nerve in neural fibrolipoma, large nerve trunk in benign and malignant PNSTs). Traumatic and Morton neuromas are commonly related to an amputation stump or are located in the intermetatarsal space, respectively. Neural fibrolipomas show fat interspersed between nerve fascicles and are often associated with macrodactyly. Nerve sheath ganglion has a cystic appearance and commonly occurs about the knee. Radiologic characteristics of neurilemoma, neurofibroma, and malignant PNST at computed tomography (CT), ultrasonography, and magnetic resonance imaging include fusiform shape, identification of entering and exiting nerve, low attenuation at CT, target sign, fascicular sign, split-fat sign, and associated muscle atrophy. Although differentiation of neurilemoma from neurofibroma and of benign from malignant PNST is problematic, recognition of the radiologic appearances of neurogenic tumors often allows prospective diagnosis and improves clinical management of patients.
Figure 1. Normal nerve structure. Photomicrograph (original magnification, approximately ×20; Bielschowsky silver stain) of an axial section of normal sural nerve. Nerve is surrounded by epineurium (straight arrows). Bundles of nerve fibers (∗) are surrounded by perineurium (curved arrows), creating a fascicular appearance. Adipose tissue (black arrowheads) and blood vessels (white arrowheads) are seen about the nerve.

INTRODUCTION
Benign neurogenic tumors include traumatic neuroma; Morton neuroma; neural fibrolipoma; nerve sheath ganglion; and the benign peripheral nerve sheath tumors (PNSTs), neurilemoma (schwannoma) and neurofibroma. Neurogenic neoplasms represent approximately 10%–12% of all benign soft-tissue neoplasms (1,2).

Malignant neurogenic neoplasms are called malignant PNSTs and account for 7%–8% of all malignant soft-tissue neoplasms (3,4). Neurofibroma, rarely neurilemoma, and malignant PNST may arise in association with neurofibromatosis type 1 (NF1). NF1 is a common genetic disorder representing a mesodermal dysplasia associated with multiple neurogenic neoplasms and skeletal abnormalities.

The evaluation of neurogenic neoplasms often reveals distinctive features, either lesion location, clinical history, or radiologic appearance. In this article, we review the development and histologic features of normal peripheral nerves; discuss the clinical characteristics, pathologic features, radiologic appearances, treatment, and prognosis for various musculoskeletal neurogenic tumors; and review the imaging signs of PNSTs.

DEVELOPMENT AND HISTOLOGIC CHARACTERISTICS OF NORMAL PERIPHERAL NERVES
We believe many of the imaging features of neurogenic tumors are a reflection of their similarity to the normal neurogenic tissue from which they are derived. Because of this relationship, an understanding of basic nerve anatomy and histologic characteristics is important.

Peripheral nerves are derived embryologically from neural crest tissue and migrating axons from the primitive neural tube (5). The two predominant supporting elements are the connective tissue stroma and Schwann cells, which encase all peripheral nerve axons to varying degrees. A myelinated fiber results if only one axon is encased by one Schwann cell. Unmyelinated fibers result if a Schwann cell encases many axons.

Each peripheral nerve is surrounded by a thick connective tissue sheath called the epineurium. Within the nerve, groups of axons are surrounded
Figure 2. Normal nerve appearance at MR imaging. Axial T1-weighted (repetition time msec/echo time msec = 500/20) MR image of the upper thigh shows the normal sciatic nerve (arrows) with small circular low-signal-intensity areas (arrowheads) surrounded by a background of mildly higher-signal-intensity areas representing the fascicular structure of the normal nerve.

and divided by a fibrous stroma called the perineurium, which creates multiple bundles of fibers or fascicles (Fig 1) (5). This gross appearance of a normal nerve can be recognized at ultrasonography (US) and magnetic resonance (MR) imaging, particularly in large nerve trunks such as the sciatic nerve, and has been described as a fascicular appearance (Fig 2) (6–8). Vascular supply to the peripheral nerves is relatively ample, arises from adjacent vessels, and forms longitudinally oriented channels along the nerve.

### BENIGN NEUROGENIC TUMORS

- **Traumatic Neuroma**
  Traumatic neuromas develop from a nonneoplastic proliferation of the proximal end of a severed, partially transected, or injured nerve as a result of trauma or surgery (2,9–17). Pain is the most common clinical symptom and is often reproduced with palpation or tapping on the lesion (Tinel sign). A firm soft-tissue mass at a focal pressure site may be apparent. The most common location for traumatic neuromas is the lower extremity after amputation, followed by the head and neck (frequently in the oral cavity, because more than 50% of these lesions are related to tooth extraction) (4–21). Other sites include the radial nerve and brachial plexus (22–25).

  Traumatic neuromas have been divided into two major categories based on the anatomic location of the tangled, multidirectional, regenerating axonal mass with respect to the proximal nerve end (2,18). Spindle neuromas are internal, focal, fusiform swellings secondary to chronic friction or irritation to a nondisrupted, injured but intact nerve trunk. Lateral or terminal neuromas are the result of severe trauma with partial avulsion, disruption, or total transection of a nerve (2,10,11).

  These lesions have a “bulbous-end” morphology in continuity with the normal nerve proximally, arise 1–12 months after transection or injury, and vary in size with no malignant potential (2,26). At histologic analysis, traumatic neuromas are nonneoplastic, nonencapsulated tangled masses of axons, Schwann cells, endoneurial cells, and perineurial cells in a dense collagenous matrix with surrounding fibroblasts (2,9,17). The disorganization of the neurogenic tissue (caused by multidirectional proliferation of cells in an abortive attempt to repair the injured nerve) allows this lesion to be distinguished from neurofibroma, although discrete bundles or fascicles are still recognized.

  There are only limited reports of the computed tomographic (CT) or MR imaging appearance of traumatic neuromas (25–29). Typically, a fusiform mass or focal enlargement with an entering and exiting nerve (spindle type) or only an entering nerve terminating in a bulbous shape (lateral or terminal type) is identified (Fig 3a)
Figure 3. Traumatic neuromas that developed after a below-the-knee amputation in a 33-year-old man. (a) Coronal T1-weighted (500/16) MR image shows two masses. The proximal neuroma (terminal type) has an entering tubular tibial nerve (arrowhead) ending in a bulbous expansion (*). Spindle neuroma resulting from chronic irritation of a small superficial nerve (not visible as a distinct structure) at the prosthesis attachment is seen as a nonspecific mass (arrows). (b) On an axial T2-weighted (4,300/126) image, the proximal lesion has high signal intensity with a fascicular pattern (arrow).

Lesions of small nerves may not be detected radiologically or may be seen as a nonspecific soft-tissue mass without an entering nerve (Fig 3a) (26). Lesion margins are often well defined, although some irregularity (likely related to multidirectional cell proliferation) has been seen with US. These characteristics should allow traumatic neuromas to be distinguished from other causes of amputation stump pain, including recurrent malignant tumor, osteomyelitis, abscess, bursitis, cellulitis, hematoma, heterotopic bone, foreign bodies, atrophied stump muscles, and cicatrization (9,26,27).

Traumatic neuromas typically have intermediate signal intensity (similar to that of muscle) on T1-weighted MR images and intermediate to high signal intensity on T2-weighted images (Fig 3) (9,26,29). Their signal intensity is often heterogeneous, with a ringlike pattern ("fascicular sign"), which we believe correlates with the histologic morphology of nerve fascicles and which is best seen on T2-weighted images (Fig 3b) (9). Intrinsic US and CT characteristics of these lesions are nonspecific (ie, they appear hypoechoic and with attenuation similar to that of muscle) (7,27,28).

Prevention of traumatic neuroma involves approximating the two severed nerve ends so that nerve repair and regeneration results (11, 30, 31). Multiple surgical techniques are available to remove the proximal nerve stump from the area of scar, which limits the potential both for lesion development and recurrence (11,30, 31). Initial conservative therapy, including acupuncture, cortisone injection, transcutaneous and direct nerve stimulation, and physical therapy, has been successful in up to 50% of patients (28,30,31). Surgical resection is reserved for patients in whom conservative treatment fails.

Morton Neuroma
Morton neuroma, originally described by Thomas Morton in 1876, is a nonneoplastic lesion representing perineural fibrosis of the plantar digital nerve (3). The nerve is usually affected at the level of the metatarsal head and is frequently associated with a surrounding inflammatory response. These lesions most commonly occur between the third and fourth metatarsals, and then between the second and third (32-35). Morton neuromas are uncommon between the first and second metatarsals and rare between the fourth and fifth (32,34). Because they have a marked female predilection (as high as 18:1), some suggest that these lesions are caused by nerve compression against the intermetatarsal ligament from foot position in high-heeled shoes (2,9,33–35). Although this pathogenesis intuitively seems correct, it has not been substantiated biomechanically, raising the question of other causes including ischemia (36).

Patients may experience exercise-provoked pain that may radiate into the toes or leg and is relieved by rest. Compressing the intermetatar-
Figure 4. Morton neuroma in a 45-year-old woman. (a) Short axis T1-weighted (750/15) MR image shows a 6-mm mass (*) in the interspace between the third and fourth metatarsals at the level of the metatarsal head. (b, c) Short axis fat-suppressed contrast material–enhanced T1-weighted (700/15) MR (b) and power Doppler US (c) images show marked enhancement and increased vascularity of the lesion (*). (d) Photograph of the resected specimen shows the entering plantar digital nerve (arrowheads) and the mass (arrows) distally representing perineural fibrosis.

sal space may also elicit pain (32–35). Morton neuroma is usually not palpable, although associated synovial cysts may be clinically evident. Asymptomatic lesions may be relatively common, with a prevalence of 30% reported in one series of 70 volunteers (36). These asymptomatic lesions, unlike symptomatic Morton neuromas, had no significant gender predilection and were also statistically smaller than symptomatic lesions (mean transverse diameter of 4.5 vs 5.6 mm, respectively) (36).

A Morton neuroma appears pathologically as fusiform enlargement of the plantar digital nerve at its bifurcation, with thickening of the epineural fascicles, perineural fibrosis with high collagen content (Renaut bodies), and loss of the myelinated fibers (36–38).

Radiography invariably shows normal findings and is most useful for excluding other causes of pain (39,40). US and MR imaging are superior to CT for identifying Morton neuroma (40). At US, this lesion appears as a round or ovoid, well-defined, hypoechoic mass located just proximal to the metatarsal heads in the intermetatarsal space (38,39). Small lesions (<5 mm in size) can be difficult to evaluate with US. In a series of 45 surgically treated patients, Kaminsky et al (39) reported false-negative results in two cases related to small lesion size. Power Doppler US may be a valuable adjunct for identifying these lesions and often shows increased vascularity (Fig 4c). In one study, MR imaging had an accuracy of 90%, positive predictive value of 100%, and negative predictive value of 60% in identification of Morton neuroma (37). In our experience and that of others, these lesions are most evident on coronal, small field-of-view, T1-weighted images (Fig 4) (36,37,41–44). Zanetti et al (36) suggested three MR imaging criteria for diagnosis of Morton neuroma: (a) the lesion is centered in the neurovascular bundle, within the intermetatarsal space, and on the plantar side of the transverse metatarsal ligament (Figs 4, 5);
(b) the lesion is well demarcated (excluding partial volume artifact from the adjacent joint capsule); and (c) the signal intensity of the lesion is similar to that of skeletal muscle on T1-weighted images and less than that of fat on T2-weighted images (likely reflecting high collagen content fibrosis). Erikson et al (42) reported intermetatarsal bursal fluid as an associated finding proximal to Morton neuroma in 67% of their cases. More recently, Zanetti et al (36) reported a small amount of bursal fluid in the first three intermetatarsal spaces in 67% of asymptomatic patients. A large amount of intermetatarsal bursal fluid ( 3 mm in transverse diameter) or fluid in the fourth intermetatarsal space should suggest an associated Morton neuroma (36).

Morton neuromas are markedly less conspicuous on T2-weighted MR images, making differentiation from surrounding muscle and fat difficult (Fig 5). Use of fat-suppressed T2-weighted sequences may allow better delineation. In our experience, the lesions often but not invariably enhance with intravenously administered contrast material (Fig 4b) (45,46). In a study of six patients with Morton neuromas, Terk et al (41) found fat-suppressed contrast-enhanced MR imaging to be superior for depicting lesions and used it to identify neuromas in two patients in whom other MR imaging sequences (including fat-suppressed T2 weighted) failed. However, Williams et al (44) reported that only four of 11 lesions were visible at enhanced MR imaging.

Initial treatment of Morton neuroma is directed at modifying patient footwear. When conservative management fails, other modes of therapy are used, including neurolysis, steroid injection, ultrasound therapy, and surgical release of the transverse metatarsal ligament for decompression. Surgical resection of the neuroma and involved nerve segment is the most successful treatment.

● **Neural Fibrolipoma**

Mason (47) initially described neural fibrolipoma in the English literature in 1953. Additional names for this lesion have included fibrolipomatous hamartoma of nerve, perineural lipoma, fatty infiltration of the nerve, and intraneural lipoma (47,48). Neural fibrolipoma is the preferred term, as it best describes the underlying disorder (47). The cause of this disorder is unknown, although it may be related to hypertrophy of mature fat and fibroblasts in the epineurium (48).

Patients typically present before 30 years of age, often at birth or early childhood, with a soft, slowly enlarging mass in the volar aspect of the hand, wrist, or forearm (47). Males and females are equally affected, and there is no familial predisposition (48). The upper extremity is involved in 78%-96% of cases with a marked predilection for the median nerve (85% of cases in the Silverman and Enzinger series [48] (Fig 6) (48, 49). Other sites include the lower extremity (4%-22% of cases), ulnar nerve, radial nerve, and brachial plexus (48,49). Patients present with swelling, with or without accompanying pain and neurologic symptoms including carpal tunnel syndrome (51). In 27%-67% of cases, neural fibrolipoma is associated with macrodactyly, which is referred to as macrodystrophia lipomatosa (Fig 6) (48,49).
Figure 7. Nerve sheath ganglion in a 25-year-old man with peroneal nerve distribution symptoms. (a, b) Axial T1-weighted (600/20) (a) and fat-suppressed T2-weighted (4,666/90) (b) MR images show a fluid-appearing mass (arrowheads) adjacent to the anterolateral proximal fibula and peroneal nerve (arrow). (c, d) Intraoperative photograph (c) and photograph of the sectioned gross specimen (d) show gelatinous and myxoid consistency (*), septations (straight arrows), and the fibrous wall of the ganglion (curved arrows).

This entity usually involves the second and third digits of the hand or foot, but multiple digits may be affected. Other causes of macrodactyly include angiomatosis, neurofibromatosis, Klippel-Trenaunay-Weber syndrome, and Proteus syndrome (49–57).

At gross examination, the affected nerve is diffusely enlarged (Fig 6f). The lesion appears as a tan-yellow mass within the nerve sheath, related to infiltration of the epineurium and perineurium by fibroadipose tissue (48–50). The adipose tissue surrounds and separates the usually normal-appearing nerve fascicles (Fig 6h) (48). The pathologic appearance of the nerve is identical, regardless of the presence or absence of macrodactyly. Patients with macrodystrophia lipomatosa have a diffuse, disproportionate increase in fibroadipose tissue in the affected digit (Fig 6g).

Radiographs in patients with neural fibrolipoma without macrodactyly often appear normal or may show a focal soft-tissue mass. In patients
with macrodystrophia lipomatosa, osseous and soft-tissue overgrowth are seen and often affect both the length and width of the digit (Fig 6b). The phalanges are long and broad and often splayed at their distal ends. The osseous overgrowth, usually more marked volarly and distally resulting in bowing, ceases at puberty but may lead to premature osteoarthritis. Increased radiolucent fat is often apparent in the soft tissues of the affected digit.

US of neural fibrolipoma may show alternating hyperechoic and hypoechoic bands (cablelike appearance) (Fig 6c). The MR imaging appearance is pathognomonic, consisting of longitudinally oriented cylindric foci (about 3 mm in diameter) of low signal intensity surrounded by fatty signal intensity representing nerve fascicles (Fig 6c, 6d) (50,52,53).

Treatment is difficult and controversial, depending on the extent of nerve involvement and presence of macrodactyly. Motor and sensory deficits have been reported following attempted resection (50,51).

### Nerve Sheath Ganglion

Ganglions occurring within nerve sheaths (ie, intraneural ganglions) have recently been reported and most frequently involve the large nerves about the knee (popliteal, peroneal, or tibial) at the level of fibular head (Fig 7) (58–63). The origin of the lesions is disputed, and many of them may be extensions of ganglions related to the tibiofibular joint with secondary nerve involvement, rather than primarily arising in the nerve sheath.

Patients present with a palpable mass or neurologic symptoms resulting from nerve compression. These lesions show myxoid change surrounded by a fibrous lining and often occur in the connective tissue between the nerve sheath and the nerve (Fig 7d), which often results in displacement of the adjacent nerve. These changes suggest a degenerative process as the cause.

At CT, US, and MR imaging, a nerve sheath ganglion appears as a cystic mass that may contain septations (Fig 7a, 7b) (58–63). Attenuation of the mass on CT and signal intensity on T1-weighted images may be slightly higher than expected for simple fluid and is related to its high protein content. Contrast enhancement may be seen about the rim and thin septa.

Treatment is surgical resection. In particular, if it extends from the tibiofibular joint, the lesion neck should be resected to reduce the possibility of recurrence (51,61).

### Benign PNSTs

Classically, benign PNSTs have been divided into neurilemoma (schwannoma) and neurofibroma. Although these soft-tissue neoplasms are similar and contain cellular elements closely related to normal Schwann cells, multiple clinical and pathologic features usually allow distinction (3,64).

**Neurilemoma (Schwannoma).**—Neurilemoma most frequently affects patients 20–30 years of age and constitutes approximately 5% of all benign soft-tissue neoplasms (1,3,64). Men and women are affected equally. Commonly involved sites include the spinal and sympathetic nerve roots of the head and neck, as well as nerves in the flexor surfaces of the upper and lower extremities (particularly ulnar and peroneal nerves). The posterior mediastinum and retroperitoneum may also be affected.

Neurilemomas are usually solitary, with nonaggressive features including slow growth and small size (<5 cm) (64,65). Pain and neurologic symptoms are unusual except in large tumors. Lesions are usually freely mobile to palpation except at the point of nerve attachment. In tumors of large nerves, this restricted movement is often along the long axis of the affected nerve trunks.

Although most neurilemomas are solitary and not associated with NF1, in about 5% of multiple neurilemomas, plexiform growth or association with NF1 is apparent (64). In one series, association of multiple neurilemomas with NF1 was even greater at 18% (65). Multiple neurilemomas often occur in a cutaneous distribution, and patients may have intracranial lesions (meningioma, glioma, astrocytoma) without other stigmata of NF1.

At pathologic analysis, neurilemomas are fusiform, representing the mass with the entering and exiting nerve (Figs 8–10). When large nerves
Figure 8. Peroneal nerve neurilemoma in a 49-year-old woman. 
(a–c) Coronal T1-weighted (435/40) (a) and axial T2-weighted (2,000/80) (b) MR images and longitudinal US scan (c) (photographically spliced together to show both ends of the lesion) reveal a well-defined fusiform mass (M) with entering and exiting nerve (*). Nerve appears central and within the capsule (large black arrowheads) of the mass, making distinction of neurilemoma from neurofibroma nearly impossible. MR images also reveal the surrounding fat (split-fat sign) (white arrowheads) and fascicular sign (small arrowheads in b). (d–f) Intraoperative photographs of lesion resection initially (d) reveal the fusiform mass (M) with entering and exiting peroneal nerve (*). Subsequently (e, f), incision of the epineurium (arrowheads) shows the lesion (curved arrow in e) separable from the nerve and resected with peroneal nerve fascicles left intact (straight arrows in f).
**Figure 9.** Tibial nerve neurilemoma in a 29-year-old man. (a) Lateral radiograph of the distal thigh shows a fusiform mass (*), exiting nerve (arrow), and surrounding fat (split-fat sign) (arrowheads). (b) Early arterial-phase angiogram reveals tortuous, corkscrew nutrient feeding vessels (curved arrows) at the superior aspect of the mass and the displaced superficial femoral artery (straight arrows).

**Figure 10.** Sciatic nerve neurilemoma in a 24-year-old woman with radiating leg pain. (a) Axial T1-weighted (600/15) MR image shows the mass (*) with surrounding fat (arrows) adjacent to but separable from the sciatic nerve (arrowheads), which has a fascicular appearance, findings diagnostic of a neurilemoma. (b, c) Intraoperative photographs initially (b) reveal the lesion (solid black arrow) and entering nerve (white arrow) both within the epineurium. Nodular area represents intact sciatic nerve (open arrows). Subsequently (c), the sausage-shaped neurilemoma (*) is resected from the intact sciatic nerve (arrowhead) after incision of the epineurium (arrow).
Figure 11. Neurilemoma in a 35-year-old man with a palpable soft-tissue mass. (a) Coronal T1-weighted (500/20) MR image shows an elongated, low-signal-intensity mass (arrowheads). (b) On the axial T2-weighted (2,000/90) MR image, the mass has peripheral high signal intensity (white arrow) with low signal intensity centrally (black arrow), representing the target sign. No entering or exiting nerve is seen because the affected nerve is a small gastrocnemius intramuscular branch. (c, d) Photograph of the sectioned gross specimen (c) and photomicrograph (original magnification, ×75; hematoxylin-eosin stain) (d) show corresponding more cellular Antoni A regions centrally (black *) and more myxoid Antoni B areas peripherally (white *) as well as a capsule (arrow in d).
are affected, the mass is eccentric in relationship to the involved nerve, with nerve fibers splayed about the neoplasm. Similar to neurofibromas, neurilemomas of small nerves may obliterate the nerve of origin (Fig 11). Both the neurilemoma and the affected nerve are within a true capsule, the epineurium (Figs 8, 10, 11).

The histologic hallmark of neurilemoma is identification of Antoni A and Antoni B regions (Fig 11). Lesions are also S-100 protein positive at immunohistochemical analysis (3,64,65). Antoni A areas are more organized and composed of cellular spindle cells arranged in short bundles or interlacing fascicles. Antoni B regions are hypocellular, are less organized, and contain more myxoid loosely arranged tissue with high water content. These components are intermixed within neurilemomas and occur in varying amounts. Neurilemomas in which Antoni A areas predominate are often called cellular schwannomas. They are more frequently located in the posterior mediastinum and retroperitoneum and constitute 25% of extremity lesions (3). Large neurilemomas commonly undergo degenerative changes including cyst formation, calcification, hemorrhage, and fibrosis and are often referred to as ancient schwannomas (64,65).

Treatment of neurilemoma is usually surgical excision. The affected nerve is usually separable from the neoplasm intraoperatively after incision of the epineurium, allowing the native nerve and its function to be preserved (9). Partial resection may be performed in cases that would otherwise require nerve resection for complete removal. Recurrence is unusual, even after incomplete resection, and malignant transformation is exceedingly rare.

Neurofibroma.—Neurofibroma most commonly affects patients 20–30 years of age and has no sex predilection (13,66). These lesions constitute slightly more than 5% of all benign soft-tissue tumors (1,3). Three types of neurofibromas are classically described: localized, diffuse, and plexiform (discussed with NF1). The localized variety is the most common, representing approximately 90% of these lesions, and the vast majority are solitary and not associated with NF1 (3,9). Localized neurofibromas often affect superficial cutaneous nerves, although involvement of larger nerves also occurs, causing deep-seated lesions (Figs 12, 13). Localized neurofibromas are slow-growing lesions, usually less than 5 cm in size at presentation and painless (3,9). The diffuse neurofibroma primarily affects children and young adults (Fig 14) and most frequently involves the subcutaneous tissues of the head and neck. The majority of diffuse neurofibromas (90%) are isolated lesions not associated with NF1 (3,9). Diffuse neurofibromas demonstrate a plaquelike elevation of the skin with thickening of the entire subcutis.
Figure 12. Tibial nerve neurofibroma in a 30-year-old man. (a) Axial CT scan shows a low-attenuation well-defined mass (arrow) with a center of slightly increased attenuation (white arrowheads) and incomplete fat rim (black arrowheads) (target sign). (b, c) Sagittal T1-weighted (500/17) (b) and axial T2-weighted (2,000/80) (c) MR images reveal entering nerve (open arrow in b), partial fat rim (split-fat sign), and capsule (solid arrow in b) and high-signal-intensity peripheral rim (target sign) (arrowheads in c). (d) Photograph of the axially sectioned gross specimen from debulking surgery shows the capsule (white arrows), peripheral myxoid region (black arrows), and central more solid tissue (★).
Figure 13. Spinal neurofibroma in a 31-year-old woman. (a) Coronal T1-weighted (500/15) MR image shows a paraspinal mass (*) with entering nerve in the neural foramen (arrowhead). (b) Intraoperative photograph reveals the paraspinal mass (arrow) and entering nerve (arrowhead).

Figure 14. Diffuse neurofibroma in a 31-year-old woman without neurofibromatosis. (a, b) Coronal T1-weighted (600/20) (a) and T2-weighted (2,500/80) (b) MR images show an infiltrative mass extending along connective tissue septa (arrowheads in a) involving the left buttock. On the T2-weighted image (b), the mass has prominent low signal intensity (*). (c) Photograph of the gross specimen reveals the infiltrative characteristics of the mass (*) within the subcutaneous tissue. Scale is in centimeters.
At gross examination, localized neurofibromas are fusiform, representing the mass with the entering and exiting nerve. Deep-seated lesions of large nerves (most frequently evaluated radiologically) often remain within the epineurium and, similar to neurilemomas, have a true capsule (3, 64,65). Localized neurofibromas of small nerves commonly extend beyond the epineurium, although they often remain well circumscribed. In contradistinction, diffuse neurofibroma is a poorly defined lesion in the subcutaneous fat and infiltrates along connective tissue septa. Unlike neurilemomas, neurofibromas are intimately intermixed and are inseparable from normal nerve tissue.

At histologic analysis, a localized, solitary neurofibroma is composed of interlacing fascicles of wavy, elongated cells that often contain abundant amounts of collagen. Unlike neurilemoma, neurofibromas do not contain Antoni A and B regions (3,64,65). Myxoid areas and degenerative regions are also not as prominent as they are in neurilemoma. Diffuse neurofibroma contains very uniform, prominent fibrillary collagen. Both localized and diffuse neurofibromas are positive for S-100 protein at immunohistochemical analysis, although generally not as extensively as neurilemoma (3).

Treatment of localized and diffuse neurofibromas (not associated with NF1) is often surgical resection. Unlike neurilemoma, however, neurofibromas cannot be separated from normal nerve, and complete excision of the neoplasm requires sacrifice of the nerve. Although this treatment may be acceptable in cutaneous lesions, deep-seated lesions may only be debulked or managed conservatively with observation because of the patient morbidity related to nerve damage and neurologic deficits from surgery. Local recurrence after complete excision is unusual and is more frequently associated with diffuse neurofibroma because of its infiltrative growth. Malignant transformation of these lesions, without association to NF1, is rare and not well documented in the literature.

**NEUROFIBROMATOSIS**

Several reports of this disease predate von Recklinghausen’s description in 1882. However, the first association of neural and fibrous components in this disorder is attributed to von Recklinghausen (67). NF1 and neurofibromatosis type 2 (NF2) account for 99% of cases. Musculoskeletal abnormalities predominate in the most common form, NF1, as opposed to the central nervous system manifestations (bilateral acoustic neuromas, gliomas, meningiomas) of NF2; therefore, herein the discussion is limited to NF1 (68–70).

NF1 is one of the most common genetic diseases, with an estimated frequency of one case in every 2,500–3,000 births (68–72). It is a mesodermal dysplasia, thereby affecting multiple organ systems, and is inherited as an autosomal dominant trait with a high penetrance rate. However, at least 50% of cases are believed to arise from new mutations, and its mutation rate (one per 10,000 gametes per generation) is greater than that of many other common genetic disorders (68–72). Advanced paternal age (>35 years) is a predisposing factor, producing a twofold increase in new mutations, although other factors are also important (2,70). The genetic abnormality has been localized to the pericentromeric region of chromosome 17, which is the site of a tumor suppressor gene (2,70). This genetic focus encodes the production of the protein neurofibromin that likely has some control in cell growth regulation.

**Table 1**

Criteria for Diagnosis of NF1*

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<th>Criteria for Diagnosis of NF1*</th>
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<tr>
<td>Six or more café-au-lait spots</td>
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<td>Greater than 5 mm in greatest diameter in pre-pubertal patients</td>
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<td>Greater than 15 mm in greatest diameter in postpubertal patients</td>
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<td>Two or more neurofibromas (any type) or one plexiform neurofibroma</td>
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<td>Axillary or inguinal freckling</td>
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<td>Optic glioma</td>
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<td>Two or more Lisch nodules (ie, iris hamartomas)</td>
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<td>Distinctive osseous lesions (eg, sphenoid dysplasia, pseudarthrosis)†</td>
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<td>First-degree relative with NF1, as diagnosed by above criteria</td>
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*Two or more of these criteria are required for diagnosis.
†See Table 2.
Source.—Modified, with permission, from reference 68.
Figure 15. NF1 with ribbon ribs resulting from multiple plexiform neurofibromas in a 20-year-old man. (a) Chest radiograph shows multilobulated extrapleural masses (arrowheads) and scalloping of all ribs with a ribbonlike appearance. (b) Photograph of the autopsy gross specimen reveals that the rib abnormalities resulted from multiple neurofibromas of intercostal nerves (*) arising from the spinal cord (arrows).

Table 2

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<th>Osseous Abnormalities Associated with NF1</th>
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<tr>
<td>Scoliosis (short or long segment)</td>
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<td>Kyphosis (often predominant deformity)</td>
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<td>Facial or orbital dysplasia</td>
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<td>Lambdoid suture defects (left sided)</td>
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<td>Pseudarthrosis (particularly of the tibia and congenital)</td>
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<td>Periosteal abnormalities (reaction, cysts)</td>
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<td>Multiple nonossifying fibromas or fibroxanthomas</td>
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<td>Rib deformity (eg, ribbon ribs)</td>
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<tr>
<td>Posterior vertebral body scalloping (dural ectasia)</td>
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</table>

The clinical criteria for the diagnosis of NF1 are listed in Table 1, and the classic triad consists of cutaneous lesions, skeletal deformity, and mental deficiency. Café-au-lait spots are identified in approximately 90% of patients, usually within the first several years of life (2,68–72). Although café-au-lait spots are not pathognomonic of NF1 (since they are also seen in tuberous sclerosis and fibrous dysplasia), their size, distribution, and shape in NF1 aid in differentiating this condition from other diagnoses (70–72). They are caused by increased melanin pigment in the basal epidermal layer and represent another manifestations of the underlying neural crest abnormality. The axilla is a frequent location of café-au-lait spots (2,9). The extent of café-au-lait spots often parallels disease severity. Another pigmentation abnormality seen in more than 90% of patients with NF1 (and not associated with NF2 or seen in the normal population) is the Lisch nodule, which is an asymptomatic pigmented hamartoma of the iris (68–70).

Skeletal abnormalities are common in NF1 (Fig 15), occurring in approximately 25%–40% of cases, again reflecting the multigorgan effects of mesodermal dysplasia (9,70). Although an extensive discussion is beyond the scope of this article, these osseous manifestations are listed in Table 2. The most frequent skeletal abnormality is scoliosis.
Figure 16. Plexiform neurofibromas about the elbow and distal thigh in a 21-year-old woman with NF1. (a) CT scan of the mid-thigh level shows multiple low-attenuation plexiform neurofibromas (arrowheads), several of which show a central area of higher attenuation (arrows), representing the target sign. (b, c) Sagittal T1-weighted (800/20) (b) MR image of the elbow and axial T2-weighted (2,000/90) (c) MR image of the lower thigh reveal convoluted multinodular masses and thickening (arrowheads) from plexiform neurofibromas and numerous areas of target sign on the T2-weighted image (arrows in c). (d, e) Intraoperative photographs of the distal thigh initially (d) show the bag-of-worm (arrows) appearance of serpentine plexiform neurofibromas. Subsequent incision (e) of the distal sciatic nerve epineurium (arrowhead) reveals markedly thickened nerve branches (*).
Figure 17. Elephantiasis neuromatosa of the upper extremity in a 29-year-old woman with NF1. (a, b) Forearm radiograph (a) and photograph of the amputation specimen (b) show massive enlargement of the upper extremity with dysplastic changes of the radius and ulna, including dislocation (arrowhead). (c) Intraoperative photograph of the axillary dissection shows extensive plexiform neurofibromas with bag-of-worms appearance caused by multinodular thickening (*) of all nerves and their branches.

The hallmark of NF1 is the neurofibroma. Neurofibromas usually occur initially in childhood or adolescence, subsequent to detection of café-au-lait spots. These lesions can occur in any location of the body including soft tissues (superficial or deep) and viscera and in some reports more commonly affect males (2). Growth of neurofibromas is usually slow; however, more rapid episodes of growth can be associated with pregnancy, puberty, or malignant transformation.

All three types of neurofibromas (localized, diffuse, and plexiform) can be associated with NF1. Localized neurofibroma is the most common type seen with NF1. However, histologically, both localized and diffuse neurofibromas are not characteristic of NF1 because most of these lesions occur in an isolated pattern not associated with this underlying condition. In contradistinction to localized neurofibromas in patients without any underlying disease, those associated with NF1 more frequently involve large deep nerves (particularly the sciatic nerve and brachial plexus), are large in size, and are invariably multiple in number. Localized neurofibromas in NF1 often affect the dermis and subcutaneous tissue and are referred to as fibroma molluscum when pedunculated (2, 9, 70).

Plexiform neurofibromas are essentially pathognomonic of NF1, and development of these lesions usually occurs in early childhood and precedes cutaneous neurofibromas (68–72). Pathologically, a plexiform neurofibroma represents diffuse involvement of a long nerve segment and its branches with tortuous expansion, and its gross appearance has been described as a “bag of worms” (Fig 16). Because of their large size, these lesions commonly extend beyond the epineurium into the surrounding tissue. Plexiform neurofibromas may be associated with massive and disfiguring enlargement of an extremity called elephantiasis neuromatosa (Fig 17) (73–76). This condition may be accompanied by osseous hypertrophy related to chronic hyperemia.
Figure 19. Malignant PNST in a 42-year-old man with NF1 and rapid enlargement of a mid-thigh neurofibroma resulting from malignant transformation. (a, b) Coronal T1-weighted (634/18) (a) and inversion recovery (3,000/60; inversion time, 160 msec) (b) MR images show a thickened sciatic nerve entering and exiting (straight solid arrows in a) a focal heterogeneous mass with a rim of fat (split-fat sign) (curved arrow). A central area of necrosis (•) has high signal intensity on the inversion recovery image, as does the tumor extension along the entering nerve proximally and exiting nerve distally (arrowheads in b) and a second subcutaneous neurofibroma (open arrow in b). (c) Axial fat-suppressed contrast-enhanced T1-weighted MR image shows the mass with ill-defined margins (white arrows), resulting from invasion of surrounding tissues, and nodular peripheral enhancement (black arrows) with lack of contrast (•) in a necrotic center. (d) Photograph of the gross specimen shows multinodular thickening of a plexiform neurofibroma of both the sciatic nerve and its branches (solid arrows) and a necrotic center in the malignant PNST (open arrow).
Figure 18. Bilateral spinal neurogenic neoplasms in a 21-year-old man with NF1. CT scan shows bilateral paraspinal masses (*) with nerves entering from the neural foramina (arrowheads). The larger low-attenuation mass on the left is a malignant PNST, whereas the smaller right-sided lesion is a neurofibroma.

Figure 20. Malignant PNST in the thigh of a 22-year-old man with NF1. Gallium-67 scintiscan obtained 5 days after injection shows intense uptake of radionuclide in the malignant PNST (*) but no accumulation in multiple other neurofibromas that were clinically evident.

Treatment of patients with NF1 is complicated by the multiplicity of lesions and is often nonsurgical. Attempts at surgical resection are usually reserved for markedly symptomatic lesions that substantially compromise function. Because of the large size of many of these lesions, surgical resection is often incomplete, leading to frequent recurrences. Malignant transformation to malignant PNST is the most feared complication of NF1 (Figs 18, 19). The estimated prevalence of malignant transformation varies from 2% to 29%, with an average of approximately 5% (2,9).

MALIGNANT PNSTS

The World Health Organization Committee for the Classification of Soft-tissue Tumors has standardized terminology, and malignant PNST is now the accepted nomenclature for a spindle cell sarcoma arising from nerve or neurofibroma or demonstrating nerve tissue differentiation (Figs 18–21) (4). Malignant PNSTs account for
Figure 21. Malignant PNST of the sciatic nerve in a 12-year-old girl. (a) Axial T2-weighted (2,000/90) MR image shows a mass (black arrowheads) posterior to the acetabulum with the fascicular sign (white arrowheads) and decreased size of gluteal muscles from atrophy (arrows). (b) Photograph of the sectioned gross specimen reveals fascicular morphology (*) of the malignant PNST, corresponding to the MR imaging appearance.

5%–10% of all soft-tissue sarcomas and usually affect adult patients 20–50 years of age with an approximately equal sex distribution (3,4). It is estimated that these lesions are associated with NF1 in 25%–70% of cases and that in these patients, malignant PNSTs occur a decade earlier and have a male predilection: 80% of patients with malignant PNSTs and NF1 are male (Figs 18–21) (4,9).

Malignant PNSTs most commonly involve major nerve trunks including the sciatic nerve, brachial plexus, and sacral plexus (77). Patients present with pain and neurologic symptoms of motor weakness and sensory deficits more frequently than do patients with benign PNSTs. In patients with NF1, sudden increase in size of a previously stable neurofibroma should be viewed with great suspicion of malignant transformation and lead to immediate biopsy (Fig 19). Malignant PNST can also be a secondary neoplasm related to previous radiation therapy. Such tumors develop after a long latent period (10–20 years) following irradiation and account for 11% of malignant PNSTs (4,78).

Malignant PNSTs are fusiform, a shape caused by the entering and exiting nerve, which is clearly evident at gross pathologic examination (Fig 19) (4,9). The tumor frequently spreads along the entering and exiting nerve, with the epineurium and perineurium becoming thickened proximally and distally to the mass. The tumor cells are arranged in fascicles, resembling fibrosarcoma, and areas of hemorrhage and necrosis are frequent. Additional heterotopic regions are seen histologically in 10%–15% of tumors and include foci of mature cartilage and bone, rhabdomyosarcoma elements (malignant Triton tumor), and glandular or epithelioid components (4,9). Most malignant PNSTs are considered high-grade sarcomas.

Treatment of malignant PNST is complete surgical excision with wide resection margins. Adjuvant chemotherapy and radiation therapy are also often used. Despite this aggressive treatment, local recurrence and distant metastases are common, seen in 40% and 60% of patients, respectively (4,77). Wanebo et al (78) reported a 5-year survival rate of only 43.7%. Worsened prognosis is associated with older patient age, larger tumor size, more central location of the tumor, and positive margins after resection. Although some researchers believe patients with NF1 have a significantly poorer prognosis, this contention is now somewhat controversial because several recent reports have shown that all patients with malignant PNSTs have a similar prognosis regardless of the presence of underlying NF1 (78,79). Metastases most frequently affect the lung, bone, pleura, and retroperitoneum, with only regional lymph nodes involved in only 9% of cases (4,77–79).

- Imaging of PNSTs
  The most common findings of PNSTs (including benign PNST, NF1, and malignant PNST) seen at radiography are either normal or only a nonspecific soft-tissue mass. In rare cases, a fusiform
mass with surrounding fat may be seen (Fig 9a). Occasionally, soft-tissue and osseous overgrowth associated with elephantiasis neuromatosa and other skeletal manifestations of NF1 may be recognized at radiography (Fig 17) (70,80). A primary bone location for PNSTs is exceedingly rare, and bone involvement by either extrinsic erosion or invasion is unusual. Calcification (osteoid, chondroid, or amorphous) is uncommon and mild in extent when present (70,80). Both bone involvement and mineralization are more common in larger lesions and malignant PNSTs and reflect the heterogeneity of these lesions seen pathologically.

Angiography of deep PNSTs demonstrates displacement of major vascular structures owing to the site of origin of the lesion within the neurovascular bundle. The degree of increased vascularity is variable and more prominent in malignant PNSTs (81–85). A characteristic at angiography that should suggest a neurogenic neoplasm is the identification of corkscrew-type vessels at the upper or lower poles of the tumor, which represent hypertrophy of nutrient nerve vasculature (Fig 9b) (81,82).

Bone scintigraphic findings of PNSTs are nonspecific and reflect the vascularity, bone involvement, or mineralization within the tumor. Typically, only mild uptake of radionuclide is seen at all phases of imaging unless calcification or bone involvement is extensive. In two reports, however, gallium-67 citrate imaging was described as very helpful for differentiating benign from malignant PNST (Fig 20) (83,86). Although only small numbers of patients were involved, significant uptake of Ga-67 citrate was seen in malignant PNSTs compared with minimal or no accumulation in benign PNSTs (83,86,87).

As with other soft-tissue neoplasms, these lesions are more easily characterized with advanced imaging techniques (CT, US, MR) (88–90). In our opinion and experience, the most important imaging feature that should always suggest the diagnosis of neurogenic neoplasm is recognition of a fusiform mass, which represents the tubular entering and exiting nerve in a typical nerve distribution. This relationship is usually easy to detect in lesions affecting large, deep nerves that are frequently imaged because the clinical presentation is that of a nonspecific soft-tissue mass (Figs 8, 10, 12, 19). In contradistinction, in superficial PNSTs, it is often difficult or impossible to identify this appearance and imaging findings are nonspecific (Fig 11). However, these superficial lesions, as with other cutaneous or subcutaneous lesions, often are not imaged because of the “ease of clinical assessment.”

In our experience, MR imaging is superior to CT and US for demonstrating the virtually pathognomonic, fusiform appearance of PNST because of its large field of view and multiplanar capabilities. Cerofolini et al (91) reported this finding in 94% of their 17 cases. PNSTs of the paraspinal region often have a dumbbell shape with extension into an enlarged neural foramen (Figs 13, 18). This neural foraminal component is analogous to the entering nerve seen in peripheral lesions (92–97). Spinal PNSTs must be differentiated from meningoceles (70%–80% of the latter lesions occur in patients with NF1 and are often multiple) because of differences in treatment (70). Meningoceles characteristically are cystic, fill with contrast material after myelography (with or without CT), and have a posterior mediastinal location without calcification. Spinal neurofibromas in patients with NF1 are often bilateral, and a prominent disparity in size should be viewed with suspicion that the larger lesion harbors malignant PNST (Fig 18) (92–97).

Theoretically, differentiation of neurofibroma from neurilemoma should be possible because of their differences in location relative to the normal nerve. In neurilemoma, the mass is eccentric and separable from normal nerve, but in neurofibroma, the two structures are intimately related, intermixed, and indistinguishable. Indeed, Cerofolini et al (91) believed they could discern this relationship in 65% of 17 cases. In our experience, however, this distinction is fraught with difficulty because both lesions are often in deep locations within the epineurium and have similar intrinsic imaging characteristics relative to normal nerve. This similarity often precludes radiologic discrimination between these lesions except in large nerves such as the sciatic nerve (Figs 8, 10, 12).

Plexiform neurofibromas invariably show a pathognomonic imaging appearance identical to their gross pathologic features of diffuse nerve thickening (Figs 15–17) (98–101). There is often nodularity and involvement of nerve branches, which creates the appearance of a serpentine “bag of worms.” Diffuse neurofibromas show a reticulated, linear branching pattern within the subcutaneous tissue, replacing the fat and creating a honeycomb appearance (Fig 14) (9). Several imaging characteristics of neurogenic neoplasms are frequent and are listed in Table 3. On unenhanced CT scans, PNSTs frequently have low attenuation (often as low as 5–25 HU) (Figs 12a, 16a, 18). This appearance has been
Table 3
Imaging Signs of Neurogenic Neoplasms

<table>
<thead>
<tr>
<th>Sign</th>
<th>Modality Depicting the Sign</th>
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<tbody>
<tr>
<td>Fusiform</td>
<td>MR (less well seen with CT, US)</td>
</tr>
<tr>
<td>Entering and exiting nerve</td>
<td>MR (less well seen with CT, US)</td>
</tr>
<tr>
<td>Low attenuation</td>
<td>Unenhanced CT</td>
</tr>
<tr>
<td>Target sign</td>
<td>T2-weighted MR (less well seen with CT)</td>
</tr>
<tr>
<td>Fascicular sign</td>
<td>T2- and proton density–weighted MR</td>
</tr>
<tr>
<td>Split-fat sign</td>
<td>T1-weighted MR (less well seen with CT)</td>
</tr>
<tr>
<td>Associated muscle atrophy</td>
<td>T1-weighted MR</td>
</tr>
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attributed to several factors including high lipid content of myelin from Schwann cells, presence or entrapment of fat, endoneurial myxoid tissue with high water content (Antoni B areas in neurilemomas), and cystic areas (hemorrhage or necrosis in neurofibroma) (102-107). Heterogeneity and higher attenuation may be seen in neurogenic neoplasms and is a more common feature of malignant PNST (84, 85).

On MR images, the signal intensity of neurogenic neoplasms is relatively nonspecific and is similar to that of muscle on T1-weighted images and higher than that of fat on T2-weighted MR images. Diffuse neurofibromas often show predominant low signal intensity on T2-weighted MR images, a finding we presume is related to the high collagen content of these lesions (Fig 14b). Heterogeneity in PNSTs is variable, although it is more prominent in malignant PNSTs (Figs 18, 19), including, in uncommon cases, fluid-fluid levels from hemorrhage. Mann et al (108) attempted to quantify this heterogeneity in distinguishing benign from malignant PNST by using fuzzy cluster analysis.

The target sign has been described as being nearly pathognomonic of neurofibroma on T2-weighted MR images and consists of low-to-intermediate signal intensity centrally with a ring of high signal intensity peripherally (Figs 11b, 16c) (94-97). This MR imaging finding corresponds pathologically to fibrous tissue (with high collagen content) centrally and more myxoid tissue peripherally (Figs 11c, 11d, 12d). Suh et al (94) described this finding in 70% of 10 cases of neurofibromas. In our experience, however, this prevalence is an overestimate of the frequency of this finding. We strongly agree that the MR imaging target sign should always suggest a neurogenic neoplasm, although it can be seen in neurilemoma and malignant PNST, as well as neurofibroma (Fig 11b). It is most common, in our experience, in plexiform neurofibroma and less frequent in malignant PNST (Fig 16c).

CT can also demonstrate the target sign (peripheral low attenuation with central higher attenuation), although not as well as MR imaging, which reflects the superior contrast resolution of the latter modality (Figs 12a, 16a) (105-107).

In our experience, another intrinsic MR imaging characteristic that should suggest neurogenic neoplasm is the fascicular sign (9). This sign manifests as multiple small ringlike structures (with peripheral higher signal intensity) on either T2- or proton density–weighted MR images (Figs 8b, 21a). We believe this sign corresponds to the fascicular bundles seen pathologically in neurogenic neoplasms, particularly in more differentiated benign PNSTs (Fig 8b). This appearance recapitulates that seen in normal nerves, as has been demonstrated with both MR imaging and US (Figs 2, 10a) (7, 8). The fascicular sign, as expected, is more frequent in benign PNSTs than in malignant PNSTs (which are more anaplastic lesions), for which it may be present only in small foci of the lesion.

The margins of benign PNSTs are usually well defined at US, CT, and MR imaging (109-119). In fact, a capsule that represents the epineurium (higher-attenuation and low-signal-intensity rim on CT and all MR images, respectively) may be apparent (Figs 8, 10–12). Unlike Beggs (29), we have not found this finding to be particularly helpful in distinguishing deep-seated neurofibroma from neurilemoma. The finding reflects the underlying pathologic features of both of these lesions because they are usually contained within the epineurium (29). On the other hand, indistinct margins are far more frequent in malignant PNSTs as a result of their more infiltrative growth (Fig 19). Plexiform neurofibromas may also show ill-defined margins, and diffuse neurofibromas always appear indistinct and infiltrative owing to their subcutaneous spread along connective tissue septa (9, 98).

A rim of fat (the split-fat sign) is often present about neurogenic neoplasms and has been described previously on CT scans, although it is much easier to appreciate on T1-weighted MR images (Figs 8a, 10a, 12a, 12b) (103). Because
the neurovascular bundle is normally surrounded by fat, masses arising in this site maintain a rim of fat about them as they slowly enlarge. Although not a specific sign for PNST, this finding suggests a tumor origin in the intermuscular space about the neurovascular bundle and neurogenic neoplasms are the most frequent cause. The split-fat sign is more common in benign PNSTs and lesions of large nerves. A malignant PNST less frequently demonstrates a complete fat rim, reflecting its more infiltrative growth pattern (Fig 19a).

Muscle atrophy with striated, increased fat content or decreased size has been associated with PNSTs and was reported by Stull et al (109) in 23% of their cases (Fig 21a). Muscle atrophy is not commonly seen with other soft-tissue masses. This finding can be quite subtle in muscle supplied by the affected nerve, may require comparison with the normal side, and is best seen on T1-weighted MR images.

Contrast enhancement at CT or MR imaging, similar to angiographic appearances, is variable in both benign and malignant PNSTs. Generally, more contrast enhancement is apparent in malignant PNSTs (Fig 19b) (9,120). The pattern of enhancement is also variable and is commonly either heterogeneous and diffuse or peripheral. However, lesions demonstrating the target sign typically enhance more prominently centrally. Irregular nodular peripheral enhancement with central necrosis is typical of malignant PNST (Fig 19a–19c), although central necrosis can also be seen in ancient schwannomas.

The evaluation of neurogenic neoplasms with US has not been extensively reported. In our experience, although the tumor margin and fusiform shape with entering and exiting nerve can be demonstrated by US, MR imaging is superior in this assessment (Fig 8c) (6,7,121,122). To our knowledge, the target sign, fascicular sign, split-fat sign, associated muscle atrophy, or other intrinsic characteristics suggesting neurogenic neoplasm or helping distinguish benign from malignant PNST have not been reported with US.

**CONCLUSIONS**

In summary, in the vast majority of neurogenic tumors, the diagnosis can be suggested from their imaging appearances. It is important to establish lesion location along a typical nerve distribution such as in Morton neuroma (plantar digital nerve), neural fibrolipoma (median nerve), or benign and malignant PNSTs (large nerve trunk). Lesion shape and intrinsic imaging characteristics (Table 3) also provide clues to the diagnosis. One or more of these characteristics is commonly present in these lesions. Associated osseous abnormalities are frequently recognized in NF1 and neural fibrolipoma. The differentiation of neurilemoma from neurofibroma is often problematic (except in lesions of large nerves) owing to the difficulty in identifying the eccentric location of the nerve within the mass in the former lesion. Differentiation of benign from malignant PNST is also often very difficult. Imaging features suggestive of malignancy include large size (>5 cm), prominent vascularity or enhancement, infiltrative margins, marked heterogeneity with central necrosis, rapid growth, and, perhaps the most definitive, increased uptake of Ga-67 citrate. Recognition of these imaging features is important for prospective diagnosis and to help guide therapy in the clinical management of these patients.

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