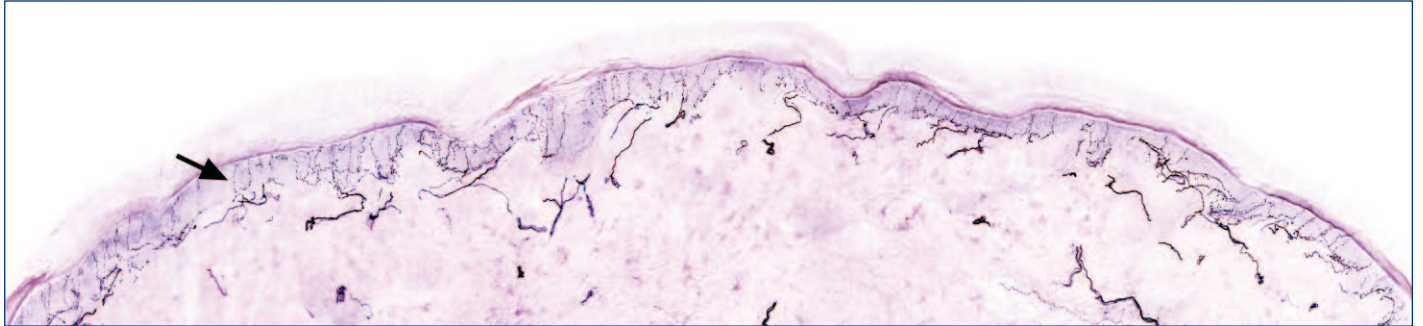


Epidermal Nerve Fiber Density (ENFD)



Intraepidermal nerve fibers in skin biopsy

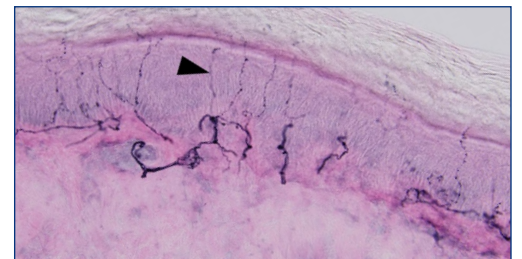
Full width view of a 3 mm punch biopsy from the thigh with intraepidermal nerve fibers (arrow) visualized by immunohistochemical labeling for PGP9.5 (above).

The Epidermal Nerve Fiber Density (ENFD) test is the most sensitive and reliable test for small fiber neuropathy (Lauria et al, 2010; Hays et al, 2010). Skin specimens are routinely obtained using a 3 mm punch biopsy at Therapath's standard sites including the foot, distal leg (calf), and proximal thigh. The small nerve fibers are visualized by immunohistochemistry, using an antibody to an axonal protein, PGP9.5, and the number and structural integrity of the small fibers is evaluated by a pathologist. Patients with small fiber neuropathy exhibit a reduction in the ENFD, or structural abnormalities such as axonal swellings, that are indicative of neuropathy.

The sensitivity of skin biopsy in diagnosing small fiber neuropathy has been reported to be 88.4%, in comparison to 54% for the clinical examination, and 49% for quantitative sensory testing (QST). The specificity of the test is 95% to 97% (Lauria and Devigli, 2007; Devigli et al, 2008), and the test is normal in non-peripheral neuropathic causes for pain such as multiple sclerosis (Hermann et al, 2010).

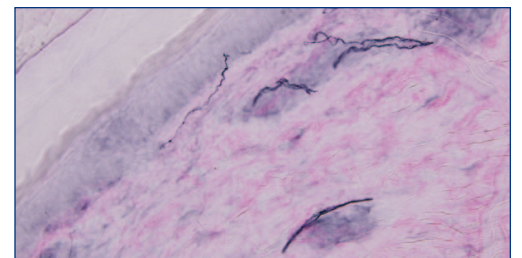
In length dependent neuropathies, the ENFD is more severely reduced distally at the foot or calf, but in sensory neuronopathies, it may be preferentially reduced proximally at the thigh (Gorson et al, 2008). In mono-neuropathy or multifocal neuropathy, a reduction in the ENFD may be seen in the distribution of the affected nerves in comparison to the unaffected side (Schuning et al, 2009).

**More information on ENFD, including a complete list of references can be found on our website.*



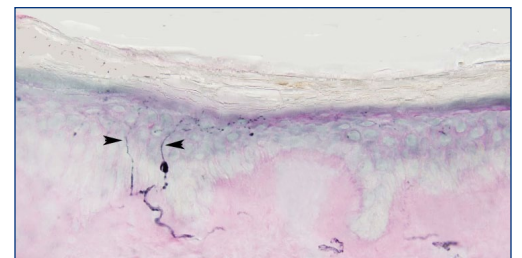
Normal IENFD

Representative sample from a biopsy with normal epidermal nerve fiber density. Arrow points to a small nerve fiber.



Abnormal IENFD

Skin with abnormally low intraepidermal nerve fiber density, consistent with small fiber neuropathy.



Axonal Bulbing

This image demonstrates skin with significantly reduced epidermal nerve fiber density, consistent with small fiber neuropathy. The small arrowhead points to the epidermal nerve fiber and just below is an axonal swelling.