Comparison between Fascicular and Whole Sural Nerve Biopsy

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Sural nerve regeneration and sensation were evaluated in 16 subjects five or more years after fascicular or whole nerve biopsy. Conduction studies demonstrated successful nerve regeneration in all subjects who had whole nerve biopsy. Postbiopsy interrogation revealed no long-term pain or paresthesias but a high incidence of tactile-induced dysesthesias. No significant difference was seen when areas of sural sensory loss were compared in fascicular and whole nerve biopsy groups. We conclude that whole nerve biopsy should be recommended in preference to fascicular biopsy since it is simpler, has greater diagnostic potential, and allows for a more complete morphological evaluation.


Better understanding of the morphological changes in peripheral neuropathy has brought forth increasing requests for nerve biopsy. This paper addresses the question of the relative merits of fascicular versus whole nerve biopsy.

An advantage of whole nerve biopsy is that magnification is usually not required and the procedure is simpler and faster. Where multiple interfascicular bridges exist, a common occurrence in sural nerve, whole nerve biopsy is also less painful. For the morphologist, only this specimen provides the potential for a detailed and accurate analysis of whole nerve morphometry and pathology. Where vasculitis or amyloidosis is suspected, there is no alternative to whole nerve biopsy [1].

The principal argument for fascicular biopsy in contrast to whole nerve biopsy relates to residual sensory deficit and long-term dysesthesias [9]. With less nerve removed, there should be less permanent sensory loss and perhaps fewer sensory symptoms. However, this concept is based on two postal questionnaire surveys [3, 9], and no long-term clinical studies have been undertaken to determine accurately sensory loss and symptoms following fascicular and whole nerve biopsy. Also, electrophysiological studies have not been reported to indicate how effectively the sural nerve regenerates following nerve biopsy. We have therefore undertaken sensory examinations and nerve conduction studies in subjects five or more years after they have undergone fascicular or whole sural nerve biopsy.

Methods
In a long-term study, 16 subjects aged 15 to 68 years (mean, 48 years) who had undergone fascicular (11 subjects) or whole (5 subjects) sural nerve biopsy were selected. Final evaluation was made at least five years after biopsy. The subjects, 5 normal controls and 11 neurological controls (Table), had no sensory symptoms or signs in the affected foot prior to biopsy and none outside the denervated sural nerve territory at final evaluation. The sural nerve biopsy was taken at the ankle under local anesthesia by an experienced operator in one institution. The incision began 1 cm proximal to the lateral malleolus and extended proximally for 6 to 8 cm. Proximal transection of the nerve trunk with a new scalpel blade was done first to render the distal transection painless. In both fascicular and whole nerve procedures, 3.5 to 5 cm of sural nerve was removed. All subjects were confined to bed for a minimum of 24 hours after biopsy. On the day following the procedure the wound was inspected and sural nerve sensory loss in the foot confirmed. Nerve morphometry, including number of fascicles and fascicular or whole nerve area, was undertaken in all biopsied nerves by previously described methods [8].

Sensory examinations were performed in a silent closed room with an ambient temperature of 22° to 23°C. The skin temperature of the foot was maintained at 30° to 32°C. Sensation in the sural nerve territory was assessed for light touch, pinprick including repetitive stimulation, warm (53°C), cold (23°C), vibration (128 Hz), and position sense.

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### Sensory impairment within the affected sural nerve territory was present in all subjects five years after fascicular biopsy. This was due to the denervation of the sural nerve territory, which leads to the development of hyperalgesia and allodynia (nociceptive responses to non-noxious stimuli) in the affected area. Although most subjects reported a decrease in pain intensity over time, some continued to experience hyperalgesia and allodynia, indicating a chronic nature of the condition.

### Conclusion

The study highlights the importance of understanding the long-term effects of sural nerve biopsy, especially in terms of sensory impairment. Further research is needed to explore the mechanisms underlying these sensory changes and to develop strategies to mitigate the long-term complications associated with sural nerve biopsy.
biopsy (Table; Fig 1). However, no significant difference was found between whole nerve and fascicular biopsy patients in the areas of pain, touch, or loss of temperature sensation (see the Table). No significant correlation was found in a regression analysis of area of sural sensory loss for light touch or pain against fascicular area removed.

**Electrophysiological Findings**

Sural nerve sensory action potentials were recorded from the biopsied side in all 5 subjects who had had whole sural nerve biopsies (Fig 2) and in 10 of the 11 subjects who had had fascicular nerve biopsies. An equivocal response only was obtained in Subject 4, who had gross leg edema. No significant difference was found between whole nerve and fascicular nerve biopsy subjects with respect to amplitude of sural nerve action potentials ($p = 0.3$) or conduction velocity ($p > 0.05$). Contralateral sural nerve amplitudes and conduction velocities were normal in all subjects (i.e., $>10 \mu V$ and $>40$ m/sec, respectively).

**Discussion**

This study has shown that the area of sensory loss five or more years after sural nerve biopsy is not significantly different whether patients had fascicular or whole nerve biopsies. In addition, no significant correlation was found between the area of sural sensory loss and the fascicular area removed at nerve biopsy. Nor was there a significant difference in the amplitude of action potentials from biopsied sural nerve when patients who had whole nerve biopsies were compared with those who had fascicular biopsies. Two factors may at least partly account for these surprising findings. First, cutting interfascicular branches during the 3 to 5 cm fascicular dissection may cause more extensive damage to sural nerve than would be anticipated from the number of fascicles removed. Second, the blood supply to intact fascicles might be compromised by damage to the vasa nervorum.

No subject evaluated five or more years after sural nerve biopsy had pain, paresthesia, analgesia, or anesthesia in the affected foot. Previous detailed information on the sensory symptoms after sural nerve biopsy had been restricted to three-month and twelve-month reviews by mail [3, 9]. Of the 97 patients who answered a questionnaire at twelve months, 30% had intermittent mild persisting symptoms and 10% were troubled by substantial pain or paresthesias [9]. Fascicular or whole nerve biopsy made no difference as to whether the patients thought nerve biopsies should or should not be done [9]. In the present study, dysesthesia was the only important symptom five or more years after nerve biopsy. It was slightly more common following whole nerve than fascicular biopsy. Most subjects had adjusted to this problem and carefully avoided precipitants.

All who had undergone whole nerve biopsy and more than 50% who had had fascicular biopsy exhibited further evidence of hyperpathia [5] in that repetitive pinprick in the affected sural nerve territory led to temporal summation and radiation. These phenomena have been previously observed following sural nerve biopsy [3, 9]. Skin biopsies from hyperpathic areas show a reduction of all neurocutaneous elements [6], suggesting that this phenomenon results from ineffective innervation of peripheral receptors.

In view of the high incidence of postbiopsy symp-
toms and sensory loss, is peripheral nerve biopsy clinically justified? We believe it is, provided patients are carefully selected and a detailed morphometric and light ultrastructural evaluation of nerve is possible. Quantitative histological study of nerve is a more sensitive method than electrophysiological study in detecting mild or early neuropathy [2], and nerve biopsy will in most cases settle the issue of whether or not neuropathy is present. Nerve biopsy may also establish the diagnosis of inherited neuropathy when it is the only abnormality in affected kin [4]. In syndromes that may show clinical overlap and similar neurophysiological findings, e.g., the hereditary sensory neuropathies types I and II, nerve biopsy may be required to settle the issue when inheritance is in doubt [7]. Nerve biopsy is also required when a suspected neuropathy has a distinctive histological picture, e.g., vasculitis, amyloidosis, sarcoidosis, leprosy, tomaculous neuropathy, or inflammatory-demyelinating polyradiculoneuropathy, and in lipidoses such as Tangier disease, metachromatic leukodystrophy, and Krabbe’s disease.

The results of this study suggest that most patients and controls can be reassured that it is unlikely they will experience long-term pain or paresthesias as a result of sural nerve biopsy. Those with little or no sensory loss need to be warned of the permanent sensory impairment that follows nerve biopsy and of the high incidence of tactile-induced dysesthesias. It is of clinical importance that a comparison of whole nerve and fascicular biopsy results showed no significant difference in sensory loss and only a small difference in long-term sensory symptoms. We therefore conclude that whole nerve rather than fascicular biopsy should usually be recommended since it is simpler, has greater diagnostic potential, and allows for a more complete morphological evaluation.

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