



## Short communication

## The use of real-time ultrasound in microneurography

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## ABSTRACT

The use of microneurography to measure muscle sympathetic nerve activity has provided important insights in human physiology. However, placing microelectrodes into nerves can be challenging, particularly in certain patient populations. In this paper, we describe the use of real-time ultrasound guidance to assist with microneurography, including advantages, disadvantages, and proper training.

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## 1. Introduction

Microneurography is a technique used in humans to measure post-ganglionic sympathetic neural activity directed towards muscle and skin. It is commonly performed by introducing a microelectrode percutaneously into the nerve to be studied and then adjusting the electrode until a satisfactory signal is recorded that represents the targeted neural output and has adequate signal-to-noise ratio for analysis and quantification. This technique relies on the placement of the electrode primarily based on the sounds heard via an amplifier system (usually 80,000- to 100,000-fold amplification) and requires an extensive amount of training, knowledge of anatomy, recognition of the subtle and characteristic sounds associated with the target signal, and experience. Variable success rates are reported (ranging from ~60–85%) and the success rate in certain subject populations (e.g., subjects who are obese) may be lower. We report here the first use of real-time ultrasound-guided percutaneous microneurography. We also discuss important considerations of the use of ultrasound in microneurography, including advantages and disadvantages as well as suggestions for introducing ultrasound into practice.

## 2. History of Microneurography

The use of microneurography for the direct measurement of sympathetic neural activity (SNA) in human subjects was first developed in Uppsala, Sweden in the late 1960s (Vallbo et al., 2004). This group of clinical neurophysiologists came across SNA by

chance during studies designed to record activity from large muscle spindle afferents.

Post-ganglionic sympathetic nerves directed to the skeletal muscle vasculature are noradrenergic vasoconstrictor nerves, which exhibit tonic resting activity that occurs in a so-called “bursting” pattern. This muscle sympathetic neural activity (MSNA) is the most commonly measured using microneurography. Each burst of sympathetic nerve activity represents a collection of action potentials from individual neurons. Because of the strong influence of the arterial baroreflex on efferent MSNA, the bursts exhibit a regular relationship with the cardiac cycle. However, non-baroreflex influences also affect the gating of efferent activity, such that (normally) not every cardiac cycle is associated with a sympathetic burst.

Currently, the most common way to search for the MSNA signal is to start with external (transcutaneous) electrical stimulation of the nerve to identify candidate sites for the nerve search. Subsequently, the microelectrode is introduced across the skin and manipulated with small, slow movements while the investigators listen for signals from an amplifier system. Usually, the placement of the electrode into the nerve bundle results in a “discharge” of activity. Further micro-adjustment of the electrode is necessary to locate, isolate and optimize the MSNA signal. In addition to the relationship with the cardiac cycle, other characteristics helpful in identifying a good MSNA signal include an afferent response when the muscle spindle is stretched but not when the skin is stroked (which would indicate a skin SNA signal), an increase in activity during voluntary end-expiratory apnea, no change in activity in response to a sudden startle stimulus (such as a loud noise), and an increase in activity during decreases in blood pressure or orthostasis (Vallbo et al., 2004).

In some populations, including individuals who are overweight or obese, longer microelectrodes may be necessary to be able to reach the nerve. Both the increased distance from the skin to the nerve and

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the difficulty controlling longer microelectrodes add to the difficulty of microneurography in these populations.

We have been using ultrasound for several years for invasive procedures such as the placement of arterial and central venous catheters and nerve blocks for pain and anesthesia. The advantages of the use of ultrasound for this purpose are now widely accepted and the use of live ultrasound guidance is policy in our institution for most central venous catheterizations. These experiences have resulted in a high level of familiarity with the use of ultrasound and we reasoned that it could be used to guide the placement of microelectrodes for measurement of MSNA. Based on our subsequent experience, we believe individuals who are trained in the use of ultrasound can utilize it successfully to locate peripheral nerves and to guide the placement of microelectrodes into the nerve. It may be especially beneficial in those populations where locating nerves using conventional non-image guided microneurography is more difficult (e.g., subjects with peripheral obesity).

### 3. Advances in Ultrasound

In the last two decades, relatively inexpensive, user-friendly, portable ultrasound machines capable of generating high-resolution images in real-time have been developed. In particular, higher frequency ultrasound probes (transceivers) and better post-processing has made the identification of small anatomical objects such as peripheral nerves easier. Consequently ultrasound is now widely used in research and clinical applications, including guiding needle-based procedures under live visualization. These advances also make ultrasound attractive for use in microneurography. However, it is important that the advantages and limitations of ultrasonography are understood before it is used for any diagnostic or interventional procedure, including microneurography. Additionally, development of expertise in both microneurography and interventional ultrasound procedures is essential before the use of ultrasound in microneurography is considered.

### 4. Technique

We have used ultrasound to image the peroneal nerve along the lateral aspect of the lower leg at the fibular head as well as at the popliteal fossa posteriorly. We have also imaged the three major nerves of the upper extremity (radial, ulnar, and median) at various locations along the arm. In all cases, the nerves were clearly distinguishable from surrounding tissues. We have performed ultrasound-guided microneurography of the radial nerve but the majority of our studies involve measurement of MSNA at the peroneal nerve near the fibular head. As this is also the most commonly used site in the literature, we will focus on this site in our description of the technique.

Microneurography is an invasive procedure and therefore aseptic technique is used. The skin and ultrasound probe are cleaned with a chlorhexidine and/or alcohol solution and sterile microelectrodes and ultrasound gel are used. A linear, high-frequency (12–15 MHz) probe is used to image the nerve and microelectrode during placement. The depth of the image required is dependent on the nerve to be imaged and the body habitus of the subject, but the machine display is typically set at 2–3 cm. The probe is placed posterior to the tibial tuberosity at the lateral aspect of the leg with minimal pressure using adequate ultrasound gel to ensure probe contact (Fig. 1). The peroneal nerve can be identified in a cross-sectional view by its oval or round shape and its bright, speckled appearance due to the reflective nature of the nerve fascicles and the connective tissue (Fig. 2).

The microelectrode is inserted in an in-plane approach percutaneously 1–2 cm posterior to the probe. This allows the microelectrode to stay as close to 90° to the ultrasound beam for best wave reflection and image production. This cross-sectional, in-plane technique



**Fig. 1.** Photo showing the placement of probe at the lateral aspect of the lower leg to image the peroneal nerve in cross-section at the fibular head (black dot on skin represents caudal border of the fibular head). It is important that attention be paid to ergonomics, including placement of the ultrasound screen, and that an assistant be available to help with adjustments of the ultrasound machine.

requires that the lower leg of the subject be elevated to allow space for the microelectrode and guiding hand. This may require that a longer microelectrode (40–50 mm) be utilized due to the increased distance this approach creates from the microelectrode insertion site to the nerve. The microelectrode is visualized as it is advanced anteriorly and medially to the external border of the nerve and then into the nerve. Ultrasound-guided microneurography at other sites, such as the peroneal nerve at the popliteal fossa (Fig. 3) and nerves of the upper extremity (radial and median nerves) (Figs. 4 and 5), can be performed using similar techniques. In-plane imaging of the needle being advanced into a cross-sectional image of the nerve allows for the most accurate placement of microelectrode. Out of plane techniques can be used, but it is difficult to know if the very tip of the microelectrode is in the field of view of the ultrasound beam and therefore the operator must rely on movement of the surrounding tissues to determine the approximate location of the microelectrode. We have occasionally placed microelectrodes while imaging the nerve longitudinally as well, but it is more difficult to maintain a proper longitudinal image of the nerve while keeping the full length of the microelectrode in view.

We have found that with ultrasound the time required to place the microelectrode into the nerve can be reduced to just a few minutes. In many cases, the characteristic discharge of nerves is heard immediately and the subject experiences sensations that are associated with intraneuronal placement. This is reproducible enough that we will alert subjects just prior to entry of the microelectrode into the nerve that they may start to feel transient paresthesias or cramping sensations. In some cases, immediate bursts of MSNA can be observed, but usually further small adjustments of the electrode are needed in order to be able to obtain a satisfactory signal using the criteria described above. If an adequate signal cannot be obtained, the use of ultrasound facilitates

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