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● *Technical Note*

# LONGITUDINAL DESIGN FOR SONOGRAPHIC MEASUREMENT OF MEDIAN NERVE SWELLING WITH CONTROLLED EXPOSURE TO PHYSICAL WORK USING AN ANIMAL MODEL

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**Abstract—In the study described here, we examined the feasibility of a longitudinal design to measure sonographically swelling of the median nerve caused by controlled exposure to a work task and to evaluate the relationship of changes in morphology to diagnostic standards. Fifteen macaques, *Macaca fascicularis,* pinched a lever in various wrist positions at a self-regulated pace (8 h/d, 5 d/wk, 18–20 wk). Nerve conduction velocity (NCV) and cross-sectional area (CSA) were measured every 2 wk from baseline through working and a 6-wk recovery. Trending across all subjects revealed that NCV slowed and CSA at the carpal tunnel increased in the working arm, whereas no changes were observed in CSA either at the forearm or for any measure in the non-working arm. There was a small negative correlation between NCV and CSA in the working arm. This study provides validation that swelling can be observed using a longitudinal design. Longitudinal human studies are needed to describe the trajectory of nerve swelling for early identification of median nerve pathology. (E-mail: sroll@usc.edu) © 2013 World Federation for Ultrasound in Medicine & Biology.**

***Key Words:*** **Median mononeuropathy, Sonography, Carpal tunnel syndrome.**

## INTRODUCTION

Sonography is becoming widely used in the diagnosis of carpal tunnel syndrome (CTS). In chronic stages of the disorder, measuring cross-sectional area (CSA) of the median nerve with sonography is up to 93% sensitive and 100% specific (Roll et al. 2011a). In addition to a diagnostic threshold of 10 $mm^2$, additional parameters have been proposed to distinguish among various severities of the disorder, such as mild, moderate and severe (Roll et al. 2011b; Wong et al. 2004). Research is also evaluating morphologic changes after surgical releases of the carpal tunnel, indicating various potential trajectories of continued median nerve swelling and possible eventual remediation (Kim et al. 2012; Pimentel et al. 2013; Vogelin et al. 2010).

Taken together, the research supporting and advancing the use of sonography for diagnosis of CTS in chronic and medical states is abundant; however, there is a significant gap in understanding the acute morphologic progression of median nerve pathology. Research related to the acute onset of the disorder is primarily mechanistic, focusing on contributory factors such as repetitive movement, vibration, awkward positions and anthropometry (Barr et al. 2004; Bongers et al. 2006; Kamolz et al. 2004; Lim et al. 2008). A few imaging studies have attempted to evaluate tissue morphology as a physiologic mechanism in the development of CTS, focusing primarily on the movement of tendons and lumbrical muscles (Cobb et al. 1994; Ham et al. 1996; van Doesburg et al. 2012; Yoshii et al. 2009). However, as with other literature, these imaging studies are primarily mechanistic and only attempt to identify relationships between anthropometry and chronic pathology, with little focus on the acute morphologic changes of the median nerve.

We have previously reported that it is feasible to use a longitudinal study design to collect sonographic images in workers to evaluate changes in morphology over time (Evans et al. 2010). There are significant challenges to successful identification of acute changes in median nerve morphology and to establishment of a link between exposure and morphologic changes in a human model.

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The primary challenge is that exposure is difficult to control unless the task being completed is routine and highly repetitive, such as assembly line work. Additionally, there are a variety of confounding factors that may include other personal, environmental and physiologic variables (Feuerstein et al. 2004; Roll et al. 2013), which would require significantly large sample sizes. Therefore, even given the availability of a highly standardized exposure pattern in a targeted workforce, no large-scale studies have been completed to investigate acute morphologic changes in the median nerve. Without this research, no evidence exists to provide clear parameters regarding the frequency and duration of the exposureor the sonographic monitoring necessary to indicate appreciable change in morphology in the acute progression of median nerve pathology.

To begin evaluating the link between physical task exposure and acute changes in morphology over time, we used an animal model. Although rat and rabbit models have been used to study etiologic mechanisms of carpal tunnel syndrome (Clark et al. 2003; Diao et al. 2005), only one case study report using sonographic imaging to diagnose carpal tunnel in an animal (*e.g.,* cow) was identified in current literature (Lippold et al. 2007). Therefore, we set out to evaluate the novel combination of an animal model and sonographic imaging in assessment of longitudinal changes in median nerve morphology in the acute stages of median nerve pathology. The objectives of this study were (i) to examine the feasibility of sonographically measuring, over time, acute changes in the median nerve caused by controlled exposure to a work task, and (ii) to determine the relationship of changes in morphology to diagnostic standards using electromyography.

## METHODS

A prospective, longitudinal animal cohort study was approved by the Institutional Animal Care and Use Committee at The Ohio State University. Fifteen macaques, *Macaca fascicularis,* were trained to reach through a tube and pinch a lever with varied wrist positions to receive a treat (Sommerich et al. 2007). Once trained, the macaques were allowed to work at a self-regulated pace for up to 8 h/d, 5 d/wk. Macaques were allowed to use only the left hand to complete the pinching task, and the non-working environment was controlled to ensure that the working hand had no significant additional physical exposure. The working phase lasted 18–20 wk and was followed by a recovery phase of 6 wk, during which the macaques participated only in enrichment activities. One subject sustained a finger injury unrelated to the pinching task and was removed from working earlier than the other subjects. This subject received similar non-work enrichment activities, and data collection was continued as scheduled. Because the objectives of this study were to evaluate global trends, the data for this subject were included in the analysis.

Baseline data were collected during initial training and every 2 wk thereafter throughout the working and recovery phases. During data collection, the macaques were sedated and wrapped in warm towels to maintain body temperature. Vital signs were monitored throughout data collection, and skin temperature was maintained between 35°C and 37°C. At each time point, sensory nerve conduction velocity (NCV) was collected followed by sonographic evaluation of the median nerve. A full description of the data collection protocol for electrodiagnostic testing has been previously reported (Sommerich et al. 2007), and the sonography protocol follows.

Sonographic evaluation was completed with a Logiq i hand-carried unit with a 12-MHz linear transducer (GE Healthcare Ultrasound, Milwaukee, WI, USA). Equipment quality control for maximum penetration, axial resolution and lateral resolution was completed weekly using a general-purpose urethane tissue-mimicking phantom (CIRS, Norfolk, VA, USA). The median nerve was evaluated in cross section, beginning at the mid-forearm and progressing distally to the carpal tunnel. Transverse images were collected at a point approximately half-way between the elbow and wrist, at the entrance to the carpal tunnel identified by the distal end of the radius, and in the proximal carpal tunnel at the level of the pisiform bone (Roll and Evans 2009). Sagittal images of the median nerve were obtained as the nerve passed over the carpal bones into and through the carpal tunnel.

Compared with human studies of the median nerve, the structures within the animals were significantly smaller (Fig. 1). During collection of baseline data on the first three subjects, cine clips were obtained in the transverse plane, moving proximal to distal from the mid-forearm to the carpal tunnel. To ensure accurate identification of structures and validate image acquisition and analysis, still frames from these cine clips were matched to magnetic resonance images of these subjects' arms that had been collected on the same date for another portion of the study. The locations and boundaries of the median nerve were successfully identified in all sonographic images by the research team. This validated image acquisition protocol and the following image analysis protocol were then completed across all time points in each of the 15 subjects.

Image analysis primarily included measurement of the CSA of the median nerve *via* a direct trace around the inner hyper-echoic border on each image, as has been well described and reported in previous literature (Roll et al. 2011b). To minimize measurement error, measures for each image were completed five times, the