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Ultra-high-definition (22 MHz) ultrasound of the ulnar nerve: additional value and normative data

Mike Ruettermann[1,2], Dieuwke C. Broekstra[1], Gerbrand J. Groen[3] and Jan Willem Elting[4]

Abstract

We studied 30 healthy volunteers (60 arms), categorized into three age groups with equal numbers to verify if a 22 MHz compared with a 15 MHz ultrasound transducer has additional value for studying the intraneural architecture of the ulnar nerve throughout its course. At six sites, there were no differences in cross-sectional area measurements between the two transducers. With both, the cross-sectional area was significantly larger at the medial epicondyle compared with the other sites and smaller at the mid-forearm and Guyon's canal compared with the mid-upper arm. With higher age the cross-sectional area significantly increased. Significantly more fascicles were visible distal to the medial epicondyle compared with more proximal sites, as well as in men compared with women. Finally, higher body weight was related to a significantly smaller number of fascicles being seen. A 22 MHz transducer depicts more details of the intraneural architecture than a 15 MHz transducer. Our data can be used as normative data or reference values in analysing ulnar nerve pathology.

Level of evidence: II

Keywords

High-definition ultrasound, ulnar nerve, intraneural architecture, fascicles, normative data

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Introduction

In recent years, high-resolution ultrasound has become more accepted as an additional means of diagnosing ulnar nerve entrapment (UNE) at the elbow, which is the most common neuropathy after carpal tunnel syndrome (Beekman et al., 2004a; Campbell, 2000). Ulnar nerve ultrasound examination can also be used in the early diagnosis of polyneuropathy in diabetes mellitus patients (Chen et al., 2017). In cases of incomplete recovery after surgery, where clinical and electrodiagnostic tests do not lead to a precise diagnosis, detailed information on the intraneural ultrastructure of the nerve through ultrasound could provide valuable additional information (Beekman et al., 2004b).

However, since technical developments continue and new transducers with higher resolutions are developed, the possibilities and limitations of ultra-high ultrasound frequencies have not yet been validated for clinical use. Additionally, using these

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[1] Department of Plastic Surgery, University Medical Centre Groningen, University of Groningen, The Netherlands
[2] Institute for Hand and Plastic Surgery Oldenburg, Oldenburg, Germany
[3] Paincentre Department of Anesthesiology, University Medical Centre Groningen, University of Groningen, The Netherlands
[4] Clinical Neurophysiology, Department of Neurology, University Medical Centre Groningen, University of Groningen, The Netherlands

Corresponding Author:
Mike Ruettermann, Department of Plastic Surgery, University Medical Centre Groningen, PO Box 30.001, 9700 RB Groningen, The Netherlands.
Email: mikeruettermann@yahoo.com

frequencies makes it possible to gain normative data on intraneural architecture. This study aimed to determine whether a 22 MHz ultrasound transducer (Esaote MyLabOne® by Esaote Europe B.V., Maastricht, The Netherlands) is suitable for diagnostic use in the ulnar nerve, to gather normative data for this frequency and establish possible additional value by looking at the intraneural anatomical architecture with the ultra-high-resolution transducer compared with a standard 15 MHz transducer on the same machine.

Methods

The study protocol was approved by the institutional review board (METC2012.235). We recruited 30 healthy volunteers, who all gave written informed consent. They consisted of three age groups: young adults 18–30 years, adults 31–50 years and seniors 51–65 years, which was done because previous reports on normative data used non-heterogeneous study groups. For the same reason an equal number of volunteers was included in each group. Volunteers with any symptoms of entrapment neuropathy of their ulnar nerve, a history of generalized neuropathy, a history of elbow injury/surgery, elbow abnormalities or systemic diseases of the nervous system (e.g. diabetic polyneuropathy) were excluded.

Age, sex, height, weight and handedness were recorded, and the cross-sectional area (CSA) of the ulnar nerve was measured at six sites in 60 arms with a 15 MHz and a 22 MHz transducer, both on an Esaote MyLabOne® (Esaote Europe B.V., Maastricht, The Netherlands) scanner using fixed settings for all measurements (Figure 1). Ultrasonic measurements were taken, with the patient supine and their arm abducted 90° from the body and flexed 90° at the elbow, by technicians with more than 8 years' experience of peripheral nerve ultrasound. We measured six sites along the course of the ulnar nerve.

1. Mid-humerus.
2. 2 cm proximal to the medial epicondyle.
3. At the medial epicondyle.
4. 2 cm distal to the medial epicondyle.
5. At the mid-forearm (halfway between 3. and 6.).
6. At Guyon's canal.

These sites were chosen for two reasons: to make the data gathered comparable with the existing publications (Cartwright et al., 2007; Ozturk et al., 2008), as well as to take important surgical landmarks for nerve entrapment into account (Assmus et al., 2011). The CSA was measured by tracing just inside the hyperechogenic rim of the ulnar nerve with the transducer perpendicular to the nerve in order to get the smallest, most precise measurement using the continuous trace function with a pencil directly on the monitor. Furthermore, the whole course of the ulnar nerve (axilla to wrist) on both sides was scanned to rule out anatomical variants.

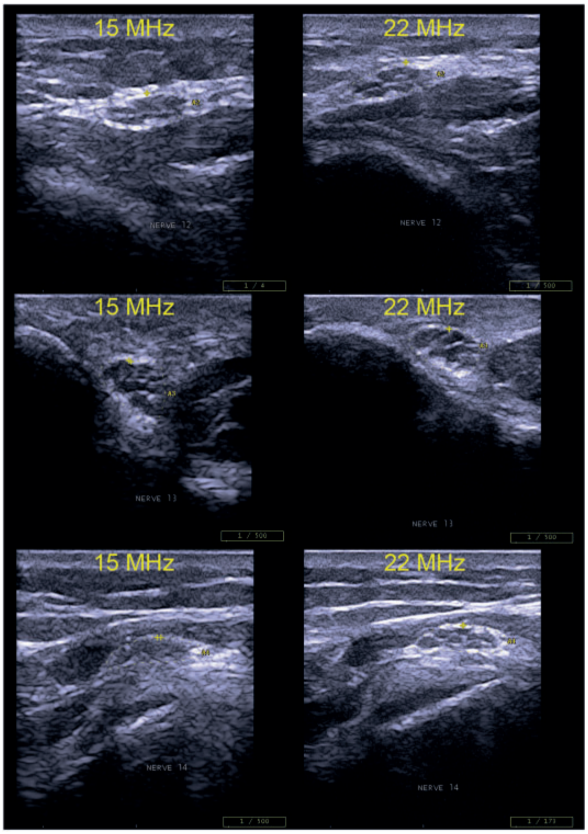

Figure 1. Ultrasonographic pictures of the intraneural architecture depicted with 15 MHz (left) and 22 MHz transducer (right) (Esaote MyLabOne®); top: proximal to the medial epicondyle; middle: medial epicondyle; bottom: distal to the medial epicondyle.

To compare the findings of the 15 MHz with the 22 MHz transducer, the fascicles of the intraneural microanatomy within the ulnar nerve at each site were counted by an experienced neurologist who did not take part in performing the ultrasonographic studies from recorded images. He was blinded to the frequency of the scanner as well as all other aspects of the site.

Statistical analyses

Non-normally distributed variables (CSA) were log-transformed to achieve normality, before entering the analyses. Since the measurements of CSA of the ulnar nerve at different locations and at different sides are correlated, we determined the effect of age, sex, hand dominance, weight, height, side and location using multilevel analysis.

Age, sex, hand dominance, weight and height were entered in a generalized linear mixed model as between-subjects effects, and side (non-dominant versus dominant) and location were entered as within-subject effects. Robust covariance estimations were used, and a random intercept for subjects was inserted to account for differences between participants.

Differences in fascicle count using the 15 MHz and 22 MHz transducer were analysed with generalized estimation equations (GEE), using a log link function, exchangeable working correlation matrix, robust estimator and the generalized score statistic. Age, sex, hand dominance, weight and height were entered as between-subject effects, and transducer, side and location were entered as within-subject effects. For all analyses, a significance level of 5% was used.

Results

We included 15 men with a mean age of 42 years (range 26–60) and 15 women mean age 40 years (range 21–61). Mean height in men was 185 cm and in women 171 cm. Mean weight in men was 81 kg and in women 69 kg (Table 1).

With the 22 MHz transducer we found the smallest CSA of 5.4 mm^2 (SD 1.2) at Guyon's Canal at the distal wrist crease on the non-dominant side in women aged 18–29 and the largest CSA of 12.1 mm^2 (2.2) at the epicondyle of the non-dominant side of men aged 51–65 (Table 2). Similar results for CSA were obtained with the 15 MHz and 22 MHz transducers (Online Table S1). A significant effect was found between CSA and age; with increasing age, the CSA increased. In addition, the CSA was significantly larger at the medial epicondyle but smaller at the mid-forearm and Guyon's canal, compared with the mid-upper arm (Table 3). There were no significant differences between men and women regarding CSA, or between the dominant and non-dominant sides. Furthermore, no significant effects of hand dominance, weight and height could be demonstrated.

Table 1. Participant characteristics of the healthy volunteers.

Characteristic	Men	Women	Total
Number	15	15	30
Age (range) (years)	42 (26–60)	40 (21–61)	41 (21–61)
Hand dominance			
Right	13	15	28
Left	1	0	1
Bimanual	1	0	1
Height (SD) (m)	1.85 (0.07)	1.71 (0.05)	1.78 (0.09)
Weight (SD) (kg)	81 (11)	69 (13)	75 (14)
BMI (SD) (kg/m^2)	24 (3)	24 (4)	24 (4)

Data presented as number or mean (SD); SD: standard deviation; BMI: body-mass index.

Overall, significantly more fascicles were visible with the 22 MHz transducer than with 15 MHz, corrected for side and location (Online Table S2 and Table 4). Additionally, significantly more fascicles were counted in men compared with women. A significant effect of weight was found, showing that a higher weight is related to less fascicles. Finally, there were significantly more fascicles visible distal to the medial epicondyle compared with the mid-upper arm location.

Discussion

We applied an ultra-high definition 22 MHz ultrasound transducer to gather normative data on the CSA of the ulnar nerve for this new, high frequency and to establish its additional value compared with a 15 MHz transducer. This was accomplished by looking at the intraneural architecture, namely the visibility and the number of fascicles, which might offer more insight into the pathophysiology of ulnar nerve compression in the future.

The CSA measured with the 22 MHz transducer ranged between 5.4–12.1 mm^2, with SD ranging between 0.6–4.2 mm^2, and was similar to measurements with the 15 MHz transducer. The mean CSA of the ulnar nerve, as well as the SD in our volunteer population, is larger than the normative values measured with lower frequencies reported previously (Cartwright et al., 2007; Yalcin et al., 2013). This is interesting because we found no significant correlation with weight or height as the other studies have. Yalcin et al. (2013) found a correlation with height, whereas the higher correlation in Cartwright et al.'s (2007) article was with weight. Our study population was, on average taller and heavier, but with a lower mean body-mass index (BMI). The main advantage of our study is the equal distribution of the study population across different age groups and sexes. A final explanation for the absence of a significant correlation between CSA and weight or height might be that our analyses took the multilevel data structure into account. Therefore, multiple testing problems did not occur, which might be a reason why other studies did find a significant correlation on some, but not all, associations (Cartwright et al., 2007).

One subject had increased CSA of the ulnar nerve around the medial epicondyle without any clinical symptoms, even though, according to the normative data from other studies, those values would meet the

Table 2. Cross-sectional area of the ulnar nerve measured with the 22 MHz transducer (mm^2).

			Men		Women	
Age	*N*		Dominant	NonDom	Dominant	NonDom
18–29	10	Mid-humerus	7.1 (1.0)	8.1 (2.2)	7.7 (1.5)	7.3 (2.8)
		2 cm prox. to epicondyle	8.7 (1.8)	8.3 (2.6)	8.2 (1.7)	8.2 (2.2)
		Epicondyle	8.5 (1.8)	9.4 (2.3)	9.2 (2.3)	8.4 (1.6)
		2 cm dist. from epicondyle	8.0 (2.4)	7.8 (2.9)	7.7 (2.3)	7.1 (1.9)
		Mid-forearm	7.1 (1.2)	7.0 (2.0)	5.6 (1.4)	6.3 (1.2)
		Guyon's canal	6.7 (1.2)	6.6 (1.9)	6.1 (1.3)	5.4 (1.2)
30–49	10	Mid-humerus	8.2 (2.1)	7.9 (2.4)	7.6 (0.7)	8.0 (2.3)
		2 cm prox. to epicondyle	8.0 (2.5)	8.0 (2.5)	7.9 (1.2)	8.5 (2.0)
		Epicondyle	8.4 (1.4)	8.2 (2.3)	10.4 (2.0)	10.3 (1.4)
		2 cm dist. from epicondyle	7.3 (1.2)	7.7 (2.6)	8.1 (1.8)	8.7 (1.7)
		Mid-forearm	7.1 (1.5)	7.3 (2.4)	7.6 (2.2)	7.3 (1.5)
		Guyon's canal	6.7 (0.6)	7.1 (1.3)	6.0 (1.1)	6.3 (1.2)
50–65	10	Mid-humerus	9.5 (2.0)	10.0 (1.5)	7.5 (1.4)	9.5 (2.7)
		2 cm prox. to epicondyle	10.8 (1.2)	9.6 (1.3)	7.4 (1.0)	8.5 (1.8)
		Epicondyle	11.6 (4.2)	12.1 (2.2)	8.4 (1.0)	9.7 (1.8)
		2 cm dist. from epicondyle	8.5 (1.5)	9.2 (1.9)	8.2 (2.2)	8.7 (1.5)
		Mid-forearm	7.6 (1.8)	8.0 (2.8)	6.9 (0.9)	7.4 (1.3)
		Guyon's canal	7.3 (1.1)	9.1 (1.7)	5.9 (1.4)	6.7 (1.0)
Total 18–65	30	Mid-humerus	8.2 (1.9)	8.7 (2.2)	7.6 (1.2)	8.3 (2.6)
		2 cm prox. to epicondyle	9.2 (2.1)	8.6 (2.2)	7.8 (1.3)	8.4 (1.9)
		Epicondyle	9.5 (3.0)	9.9 (2.7)	9.3 (1.9)	9.4 (1.7)
		2 cm dist. from epicondyle	7.9 (1.7)	8.3 (2.2)	8.0 (2.0)	8.2 (1.8)
		Mid-forearm	7.3 (1.4)	7.4 (2.3)	6.8 (1.6)	7.0 (1.3)
		Guyon's canal	6.9 (1.0)	7.6 (1.9)	6.0 (1.2)	6.1 (1.2)

Results presented as mean (SD).
N: number of participants; NonDom: non-dominant arm; prox.: proximal; dist.: distal.

Table 3. Relation of ulnar nerve CSA with age, sex, hand dominance, weight, height, side and location.

	Estimate	SE	*p*-value
Intercept	0.879	0.172	**<0.001**
Between-subjects effects			
Age (>50 years = reference)			
31–50 years	−0.053	0.013	**<0.001**
≤30 years	−0.070	0.015	**<0.001**
Sex (female = reference)	0.017	0.017	0.309
Hand dominance (left = reference)	0.003	0.031	0.933
Weight	0.001	0.001	0.305
Height	0.011	0.109	0.918
Within-subject effects			
Arm (non-dominant = reference)	−0.011	0.010	0.276
Location (mid-humerus = reference)			
Proximal to epicondyle	0.020	0.017	0.225
At epicondyle	0.069	0.018	**<0.001**
Distal from epicondyle	−0.003	0.018	0.868
Mid-forearm	−0.056	0.017	**0.001**
Guyon's canal	−0.088	0.016	**<0.001**

CSA: cross-sectional area; Estimate: parameter estimate of log transformed CSA; SE: standard error. Bold print indicates statistically significant *p*-values.

Table 4. Relation number of fascicles with age, sex, hand dominance, weight, height, side and location.

	Estimate	SE	*p*-value
Intercept	1.398	1.07	0.192
Between-subjects effects			
Age >50 years = reference)			
31–50 years	−0.189	0.125	0.132
≤30 years	−0.241	0.123	0.050
Sex (female = reference)	0.275	0.086	**0.001**
Dominance (left = reference)	0.159	0.131	0.225
Weight	−0.013	0.002	**<0.001**
Height	0.492	0.683	0.472
Within-subject effects			
Transducer (22 MHz = reference)	−0.124	0.031	**<0.001**
Arm (non-dominant = reference)	0.030	0.020	0.135
Location (mid-humerus = reference)			
Proximal to epicondyle	0.088	0.098	0.372
At epicondyle	−0.174	0.109	0.111
Distal from epicondyle	0.192	0.082	**0.020**
Mid-forearm	0.144	0.087	0.098
Guyon's canal	0.124	0.092	0.179

Estimate: parameter estimate of number of fascicles; SE: standard error.
Bold print indicates statistically significant *p*-values.

criteria for being pathologic (Cartwright et al., 2007; Yalcin et al., 2013, 2014). Therefore, in individual cases, even clearly elevated CSA values do not have to be pathological and do not necessarily represent an indication for surgery. In this healthy and symptom-free volunteer, the microanatomy of the individual fascicles of the ulnar nerve did not show any abnormalities except for the CSA.

With higher age the CSA increased significantly in our study, which is in line with the results of Ozturk et al. (2008), but in contrast to the results of Cartwright et al. (2007) and Yalcin et al. (2013), who, furthermore, found significant differences in CSA between men and women at different sites. This was not verified by our data as well as another study that also did not find any difference between men and women (Ozturk et al., 2008). The difference in findings might be caused by different relations between height and weight and between men and women within the study populations, which were unfortunately not clearly reported in previous studies. Another possible explanation for these differences could be the less accurate statistical methods in the previous studies.

The CSA was significantly larger at the medial epicondyle, but smaller at the mid forearm and Guyon's canal, compared with mid-upper arm, which indicates that the ulnar nerve becomes thinner the more distal the measurement. This finding is consistent with general anatomical knowledge because the nerve splits up into motor and sensory branches more distally.

Overall, significantly more fascicles were visible with the 22 MHz transducer than with 15 MHz, corrected for side and location (Tables 4 and Online Table S2), which demonstrates that it is easier to identify the fascicles with the ultra-high resolution. Earlier studies found fewer fascicles when using 5 to 13 MHz probes (Ozturk et al., 2008).

Additionally, significantly more fascicles were counted in men compared with women.

Another significant effect with weight was found, showing that higher weight is related to less visible fascicles. These findings are new because earlier studies have not looked precisely at intraneural architecture. Second, the depth of the nerves may have an influence because the higher the ultrasound frequency, the more difficult it is to see the deeper tissues within the surrounding fat. Therefore, the frequency that can be used to look at nerves with high definition may be technically limited, one of the reasons for performing this study being to establish the feasibility and added value of the 22 MHz transducer. Finally, there were significantly more fascicles visible distal to the medial epicondyle compared with the mid-upper arm location, which is in line with the expected anatomical splitting and branching of the nerve as it runs distally.

We found asymptomatic ulnar nerve subluxation at the cubital tunnel in several subjects, which has also been described in earlier publications (Cartwright et al., 2007; Kim et al., 2005; Yalcin et al., 2013).

A strength of this study is that non-normal data were transformed before entering the analyses. Also, in contrast to many other studies, we performed statistical analyses that take the multilevel structure of the data into account. In this way, all statistical analyses were corrected for correlations between the measurements within one subject.

A limitation of this study is the sample size of 30 participants. However, the primary aim of this study was to gather normative data, so an a priori sample size calculation could not be performed. Another limitation is that the ultrasonography was performed by two ultrasound technicians (both experienced in peripheral nerve ultrasound). This might have introduced some variability, but previous studies using lower frequency transducers showed high inter-observer agreement (Tagliafico and Martinoli, 2013), and the inter-observer variability is expected to be low.

The application of an ultra-high-resolution transducer of 22 MHz to display more detailed intraneural architecture of the ulnar nerve is feasible. We observed significantly more fascicles with the 22 MHz transducer compared with 15 MHz, but no major differences in the cross-sectional diameter of the ulnar nerve were observed between the two transducers. Further studies are necessary to determine the reliability of the 22 MHz transducer and to gather more information on the clinical implications of the intraneural architecture of the ulnar nerve and its putative relation to pathology, and post-traumatic or postoperative recovery.

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Ethical approval The study protocol was approved by the institutional review board of the University of Groningen, The Netherlands (METC2012.235).

Informed consent Written informed consent was obtained from all volunteers for their anonymized information to be published in this article.

ORCID iD Mike Ruettermann https://orcid.org/0000-0003-1649-6824

Supplemental material Supplemental material for this article is available online.

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