



## Operator differences in thermal quantitative sensory testing



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Small fibre peripheral neuropathies often present a significant diagnostic challenge as standard nerve conduction studies cannot evaluate A $\delta$  and C-fibre function. Thermal threshold quantitative sensory testing (QST) using the method of limits is an indirect assessment technique that can help in this situation. This has been augmented by the recent determination of normative age-dependent values in a large, age-diverse cohort at our centre (Hafner et al., 2015).

In that study, we tested for but found no evidence of machine differences when the same operator was testing a small cohort in a crossover design. However, the possibility remained for operator differences to account for some variability between repeat tests on the same machine that was not sufficiently addressed in this previous work, given its small sample size. Therefore, we conducted the present study to establish if operator differences could be detected when subjects were crossed over using the same machine with a larger cohort.

This study was approved by the local ethics committee and complied with the 2013 update of the Declaration of Helsinki. All subjects provided written informed consent.

Thirty-two normal volunteers aged 17–66 years (median age 29.5 years) participated. The modified Marstock method of limits (Fruhstorfer et al., 1976) was used to record thermal thresholds for warm (WDT) and cool detection (CDT) at the thenar eminence of the right hand and over the dorsolateral aspect of the right foot. Initial data were collected on individuals after randomisation to

one of two investigator groups (operator RB-F in group 1, operators SC or AL in group 2) using the same Medoc Thermal Sensory Analyser II Machine (Medoc, Ramat Yishai, Israel). All tests were performed in the same room with the subject supine using identical scripted instructions. The testing methodology was performed as reported previously (Hafner et al., 2015). A thermode with a temperature range between 0 °C–50 °C using the Peltier effect was applied to each area of skin examined. After a temperature adaptation period at 32 °C, subjects pressed a button in response to the first sensation of temperature change. Five trials were conducted per modality per site and the results averaged to yield the final threshold value.

Subjects then underwent repeat testing by an investigator belonging to the alternate group blinded to the results of previous testing at least 21 days after the first test in order to minimise learning effects. All investigators were formally trained on machine operation. However, the Group 2 investigators (SC and AL) possessed extensive clinical experience with thermal threshold QST, whereas RB-F had performed less than five clinical studies using this method prior to the commencement of this study.

Statistical analysis was performed using SAS (SAS Institute Inc., Cary, NC, USA). T-tests were used to test for intra-subject differences between operators, and for period and carryover effects (an effect of the operator for the first test that carries over to the second test). One subject was excluded from all analyses due to outlying values.

We did not find evidence for a difference in mean temperature thresholds between operators. The estimates for the difference in mean operator effects (Group 1 minus Group 2), confidence

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**Table 1**  
Operator (Group 1 minus Group 2), carryover and period effect size results (first test minus second test). Mean temperature differences are in °C. ICC >0.75 is taken as excellent, 0.60–0.75 as good, 0.40–0.59 as fair and <0.40 as poor (Shrout and Fleiss, 1979).

Limb	Temp.	Difference in mean operator effects (95% CI) (°C); P-value	P-value for difference in carryover effects	Difference in mean period effects (95% CI) (°C); P-value	Intraclass correlation coefficient (grade)
Hand	Warm	−0.04 (−0.26–0.18); P = 0.73	0.16	0.12 (−0.10–0.34); P = 0.28	0.68 (Good)
	Cool	0.02 (−0.09–0.12); P = 0.74	0.30	0.04 (−0.06–0.15); P = 0.42	0.84 (Excellent)
Foot	Warm	0.06 (−0.99–1.12); P = 0.90	0.20	0.14 (−0.92–1.19); P = 0.79	0.58 (Fair)
	Cool	0.14 (−0.20–0.47); P = 0.41	0.24	−0.10 (−0.43–0.24); P = 0.56	0.86 (Excellent)

intervals (CIs) and P-values are shown in Table 1. The difference and their CIs were small in comparison to the size of the observed thresholds. Similarly, there was no evidence for a difference in carryover effects between the patients tested, dependent on the investigator administering the first test or period effects between the first and second tests (Table 1).

Thermal threshold testing, employing cool and warm detection, is a one of few readily available methods in the armamentarium of diagnostic neurophysiological testing for small fibre neuropathies. By contrast, the determination of thermal pain thresholds is less reliable in this regard due to the relatively increased variability of measurements therein (Ng Wing Tin et al., 2014). Microneurography remains a research tool. It is particularly advantageous in that it is non-invasive, well tolerated by subjects and for its relative ease of administration. Furthermore, intra-rater (Knutti et al., 2014) and inter-observer reliability (Geber et al., 2011) has been shown to be good-to-excellent using the method of limits in recent studies of similar design. Though it may be a less sensitive tool than intraepidermal nerve fibre density (IENF) measurement by skin biopsy, an accurate diagnosis of small fibre neuropathy might depend on abnormal QST results in a small but significant proportion of affected persons in whom IENF density is not reduced (Devigili et al., 2008).

The results of our study suggest that differences between examiners, carryover or period effects do not contribute significantly to variation in measurements when conditions are standardized and the testing interval is at least three weeks. The lack of apparent observer variation despite the disparity in the level of practical technical experience between examiner groups is also notable, being relatively infrequently detailed in the QST literature (Moloney et al., 2011). This however is contingent on operators receiving adequate preparatory training on equipment use.

Further studies are needed to examine whether differences in observers remain insignificant when testing persons with known small fibre neuropathy, as there is known to be more intra-individual variability on serial testing (Bravenboer et al., 1992; Moravcová et al., 2005), and absolute threshold values in these individuals are significantly larger compared to those in our cohort. However, our study findings are encouraging for the

broader implementation of this testing modality in practice both in clinical and research settings, where collaboration between multiple operators and/or serial testing may be necessary.

### Conflict of interest

None.

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