

# Effect of Splinting and Exercise on Intraneural Edema of the Median Nerve in Carpal Tunnel Syndrome—An MRI Study to Reveal Therapeutic Mechanisms

Annina B. Schmid,<sup>1</sup> James M. Elliott,<sup>2,3</sup> Mark W. Strudwick,<sup>4,5</sup> Mary Little,<sup>6</sup> Michel W. Coppieters<sup>1</sup>

<sup>1</sup>Division of Physiotherapy, Centre of Clinical Research Excellence in Spinal Pain, Injury, and Health, School of Health and Rehabilitation Sciences, The University of Queensland, QLD 4072, St. Lucia (Brisbane), Australia, <sup>2</sup>Department of Physical Therapy and Human Movement Sciences, Feinberg School of Medicine, Northwestern University, Chicago, IL 60611, <sup>3</sup>School of Health and Rehabilitation Sciences, The University of Queensland, QLD 4072, St. Lucia (Brisbane), Australia, <sup>4</sup>Centre for Advanced Imaging, The University of Queensland, QLD 4072, St. Lucia (Brisbane), Australia, <sup>5</sup>Department of Medical Imaging and Radiation Sciences, Monash University, VIC 3800, Clayton, Australia, <sup>6</sup>Department of Occupational Therapy, The Princess Alexandra Hospital, QLD 4201, Woolloongabba (Brisbane), Australia

Received 9 October 2011; accepted 19 December 2011

Published online 9 January 2012 in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/jor.22064

**ABSTRACT:** Splinting and nerve and tendon gliding exercises are commonly used to treat carpal tunnel syndrome (CTS). It has been postulated that both modalities reduce intraneural edema. To test this hypothesis, 20 patients with mild to moderate CTS were randomly allocated to either night splinting or a home program of nerve and tendon gliding exercises. Magnetic resonance images of the wrist were taken at baseline, immediately after 10 min of splinting or exercise, and following 1 week of intervention. Primary outcome measures were signal intensity of the median nerve at the wrist as a measure of intraneural edema and palmar bowing of the carpal ligament. Secondary outcome measures were changes in symptom severity and function. Following 1 week of intervention, but not immediately after 10 min, signal intensity of the median nerve was reduced by ~11% at the radioulnar level for both interventions ( $p = 0.03$ ). This was accompanied by a mild improvement in symptoms and function ( $p < 0.004$ ). A similar reduction in signal intensity is not observed in patients who only receive advice to remain active. No changes in signal intensity were identified further distally ( $p > 0.28$ ). Ligament bowing remained unchanged ( $p > 0.08$ ). Intraneural edema reduction is a likely therapeutic mechanism of splinting and exercise. © 2012 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. *J Orthop Res* 30:1343–1350, 2012

**Keywords:** MRI; nerve and tendon gliding exercises; splinting; carpal tunnel syndrome; neurodynamics

Carpal tunnel syndrome (CTS) is a peripheral neuropathy at the level of the wrist. Despite considerable efforts, the pathophysiology of CTS is not yet fully understood.<sup>1</sup> There is however a well-established link between an elevated pressure in the carpal tunnel and the development of CTS.<sup>2,3</sup> When the pressure on a peripheral nerve is experimentally increased, a reduction of intraneural microcirculation occurs with subsequent breakdown of the blood nerve barrier and the formation of intraneural and extraneural edema.<sup>4</sup>

In CTS, swelling of the median nerve has been identified intra-operatively,<sup>5,6</sup> with ultrasound imaging<sup>7</sup> and with conventional magnetic resonance imaging (MRI).<sup>8,9</sup> If present for prolonged periods, intraneural edema may lead to potentially irreversible fibrotic changes.<sup>4</sup> These fibrotic changes are present in patients with severe CTS.<sup>9</sup> Edema reduction to prevent progression to a fibrotic stage is therefore a plausible target in the management of patients with mild to moderate CTS.

Besides advice, splinting and nerve and tendon gliding exercises are the most frequently performed non-invasive treatment modalities for CTS.<sup>10</sup> The beneficial effect of night splinting in a neutral wrist position

is commonly attributed to the avoidance of end-range positions associated with high carpal tunnel pressures.<sup>11,12</sup> Maintenance of a neutral wrist position is believed to promote adequate blood circulation with a subsequent reduction of edema.<sup>13</sup> Although further research is required, recent systematic reviews indicate that conservative management with nerve and tendon gliding exercises may be beneficial for patients with CTS.<sup>14,15</sup> It has been proposed that these exercises may improve restricted nerve gliding, reduce scar formation, and increase intraneural blood flow, which may also facilitate a reduction of intraneural edema and dispersion of inflammatory by-products.<sup>16–19</sup>

Albeit plausible, the therapeutic mechanisms by which splinting and nerve and tendon gliding exercises may influence signs and symptoms of CTS remain largely conjectural. This exploratory MRI study investigated whether splinting or nerve and tendon gliding exercises can indeed reduce intraneural edema of the median nerve in patients with CTS.

## METHODS

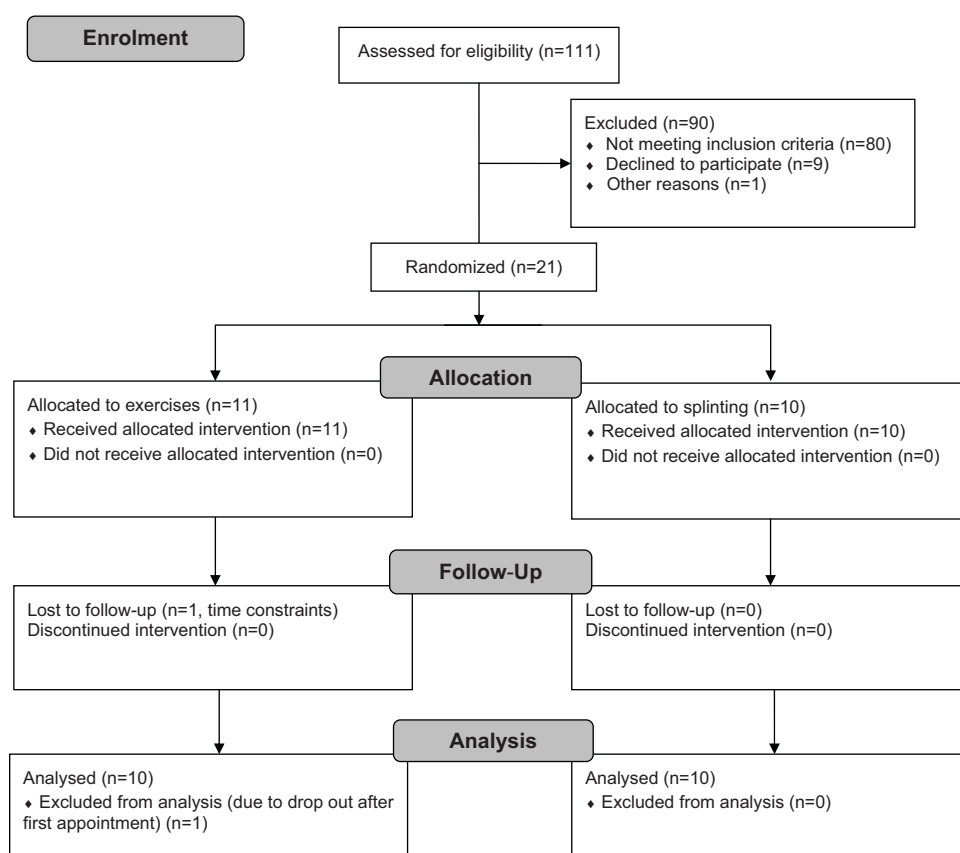
Patients who met clinical<sup>20</sup> and electrodiagnostic<sup>21,22</sup> criteria for mild or moderate CTS (S-Table 1) were randomly allocated to receive either night splinting ( $n = 10$ ) or nerve and tendon gliding exercises ( $n = 10$ ; Fig. 1). Allocation was stratified for CTS severity based on electrodiagnostic test results. Concealed random allocation was performed by an independent investigator using sealed envelopes. Demographic data (age, gender, symptom duration, and CTS severity) were collected at baseline. MRI scans were taken at baseline, immediately after 10 min of exercise or splinting,

Additional Supporting Information may be found in the online version of this article.

All authors declare no conflict of interest.

Correspondence to: Michel W. Coppieters (T: +61-7-3365-1644; F: +61-7-3365-1622; E-mail: m.coppieters@uq.edu.au)

© 2012 Orthopaedic Research Society. Published by Wiley Periodicals, Inc.



**Figure 1.** Flow diagram of the study.

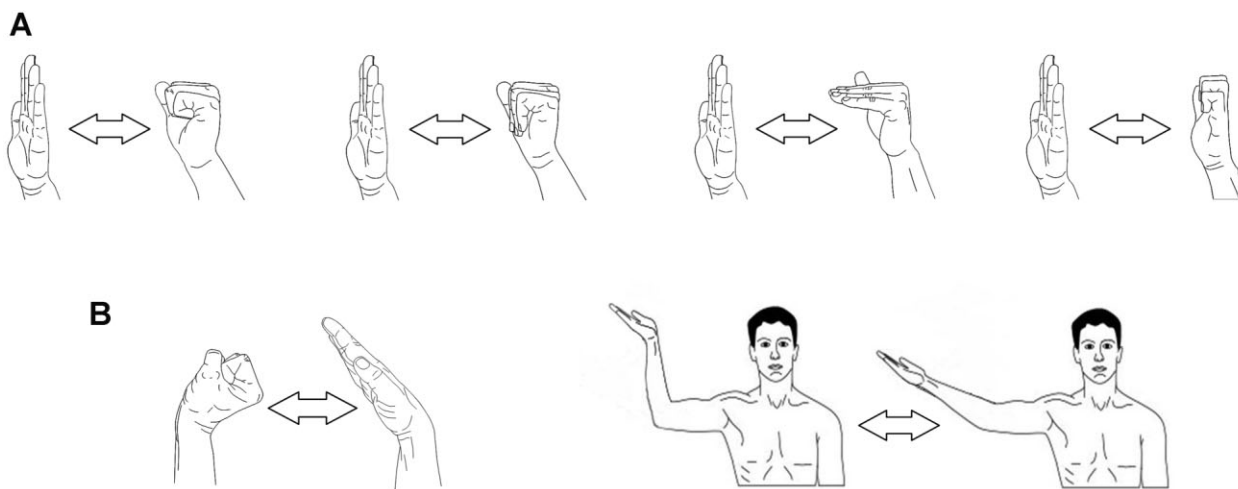
and after 1 week of intervention. All patients gave informed written consent prior to participating in the study and the study was approved by the human research ethics committee of the Princess Alexandra Hospital in Brisbane. A no-treatment group was removed from the original study design as it was deemed unethical to withhold treatment as intraneural edema does not reduce when no intervention is provided (see “Natural history” below).

Because no data were available in the current literature to calculate the sample size and because this study was exploratory in nature, it was decided a priori to study 10 patients per intervention group. To achieve this sample size, 21 patients were recruited from a list of patients awaiting electrodiagnostic testing at a neurology department of a public hospital. One patient discontinued the study after the first appointment due to time constraints. Patients with severe electrodiagnostic findings were excluded as severe CTS is characterized by fibrotic changes in the median nerve rather than edema.<sup>9</sup> Patients were also excluded if electrodiagnostic findings were indicative of peripheral neuropathies other than CTS, if another inflammatory disease was present, if a history of previous surgery or trauma to the upper limb or neck existed, if any kind of treatment for CTS was received in the 3 months before testing or if CTS was related to pregnancy or diabetes. Furthermore, patients with any contraindication to MRI examination were excluded from the study. The recruitment period lasted from August 2009 until August 2010.

### Intervention

Participants in the exercise group performed a 1-week home program of nerve and tendon gliding exercises. This program was instructed by a physiotherapist specialized in musculoskeletal management. For the tendon gliding exercises, the hand positions described by Wehbe et al.<sup>23</sup> were adopted in four separate exercises (Fig. 2A). The nerve gliding exercises were based on recent biomechanical insights.<sup>24,25</sup> Rather than progressively elongating the median nerve bed as described by Totten and Hunter,<sup>19</sup> exercises were selected which maximize nerve excursion while minimizing an increase in nerve strain (Fig. 2B).<sup>25</sup> In line with a large clinical trial evaluating a multimodal non-invasive treatment approach for CTS,<sup>26</sup> the exercises were preceded by one warming-up exercise that included forward and backward rolling of the shoulder girdle.

Ten repetitions of each exercise were performed per session. One session took approximately 2 min to complete. Participants were asked to complete 10 sessions per day. On the day of the 1-week follow-up assessment, no exercises were performed in order to evaluate the prolonged rather than immediate effects of exercise. Patients were instructed that exercises should not provoke any symptoms. If symptoms were provoked, it was recommended to continue the exercise regimen using a smaller range of motion. Each patient was contacted by phone after the first and third day to ensure that the prescribed exercise regime did not cause any discomfort. Exercise compliance was monitored with a diary.



**Figure 2.** A: Tendon gliding exercises as described by Wehbe et al.<sup>21</sup> B: Nerve gliding exercises for the median nerve were designed to maximize nerve excursion while minimizing nerve strain.<sup>23</sup> To achieve this, elongation of the nerve bed at one joint (loading) was counterbalanced by a simultaneous movement which reduces the length of the nerve bed in a neighboring joint (unloading). In the first exercise (left) a position of wrist extension (loading) and finger flexion (unloading) was alternated with wrist flexion (unloading) and finger extension (loading). Similarly, the second exercise (right) consisted of the alternation of elbow flexion (unloading) and wrist extension (loading) with elbow extension (loading) and wrist flexion (unloading).

Participants in the splinting group received a prefabricated wrist splint (Access Health, Blackburn, Australia) that they wore at night for 1 week. All patients irrespective of their treatment allocation were encouraged to continue with their normal daily activities.

#### Outcome Measures

MRI scans of the affected wrist (or most affected wrist in case of bilateral mild or moderate CTS) were performed using a purpose built transmit-receive wrist coil on a Bruker Medspec 4Tesla (4T) MR scanner<sup>27</sup> using Siemens Sonata gradients. Standard clinical 3D magnetization prepared gradient echo imaging sequences [MP-RAGE (TR 1400 TE 3.39 TI 700; matrix 192\*72, NSA 2, flip angle 15 degrees) and Dual Echo Steady State (DESS)<sup>28</sup> (TR 14.29 TE 3.92; matrix 192\*96, NSA 1, flip angle 30 degrees, water excitation)] were applied to generate high resolution T1 and T2 axial images. These images were reconstructed post-hoc in other planes for analysis. Slice thickness was set at 0.9 mm without gap with voxel volumes of 0.73 mm<sup>3</sup>.

Primary outcome measures were signal intensity changes of the median nerve and palmar bowing of the carpal ligament. Signal intensity of the median nerve on T2 weighted images is increased in CTS and is attributed to intraneural edema.<sup>9</sup> Enhanced signal on T2 weighted images is reflective of increased fluid content. A reduction in signal intensity is interpreted as a reduction in intraneural edema.<sup>8</sup> To determine the signal intensity of the median nerve, a region of interest comprising the central area of the median nerve in the shape of an ellipse measuring 80% of the width and length of the median nerve was evaluated for its average gray level using a custom written MATLAB program (MathWorks, Natick, MA). Since the border of the median nerve is not always distinct on MRI scans, the use of an ellipse covering a predetermined proportion of the median nerve prevented the inclusion of extraneural signal. The signal intensity was expressed as a ratio to the flexor carpi ulnaris muscle signal at the radioulnar level to avoid variations in signal intensity encountered with the surface coil.<sup>8</sup> Signal intensity was calculated at three levels: (i) at the distal

radioulnar joint where the pronator quadratus muscle was visible over the whole width of the radius (inlet of the carpal tunnel), (ii) at the center of the pisiform bone (mid-tunnel), and (iii) at the hook of hamate (outlet of the carpal tunnel).<sup>9</sup>

Palmar bowing of the carpal ligament is also increased in CTS<sup>29,30</sup> and is considered an indirect measure of increased carpal tunnel pressure.<sup>2,11</sup> MRI scans were analyzed by drawing a straight line between the hook of hamate and the trapezium (H-T line) using ImageJ software (Version 1.44 g, National Institutes of Health, Bethesda, MD). The bowing ratio of the ligament was defined as the perpendicular distance from the apex of the ligament to the H-T line divided by the length of the H-T line.<sup>29</sup> Since ligament bowing at the pisiform level has previously been shown to be normal in CTS, ligament bowing was only established at the level of the hook of hamate.<sup>31</sup>

All MRI scans were coded and an investigator blinded to the group allocation took all measurements (AS). To verify the inter-tester reliability of the measures, a second investigator blinded to group allocation independently evaluated all MRI scans (JE). Intra-class correlation coefficients (ICC[2,1]) and standard errors of measurement were calculated.

Questionnaires were included to evaluate changes in symptom severity and function. Changes in these two domains would normally constitute primary outcomes, but we considered them as secondary in this study because the primary aim was to reveal therapeutic mechanisms. Changes in symptom severity and function were included because a trend toward improvement or deterioration could assist in the interpretation of possible MRI changes. A decreased signal intensity may not only be interpreted as decreased intraneural edema (improvement), but also as decreased intraneural blood flow (deterioration).<sup>8</sup> Each patient completed the Boston carpal tunnel questionnaire, which consists of a symptom severity and a functional status sub-scale and is reproducible, internally consistent, valid and responsive to clinical change in patients with CTS.<sup>32</sup> Furthermore, the patient specific functional scale was administered,<sup>33</sup> which is a reliable and valid instrument to determine change in activities that are deemed difficult by the patient.<sup>34</sup> Two separate 10 cm

visual analogue scales (VAS) were completed for current level of pain and numbness (ranging from no pain/numbness to worst ever pain/numbness).

### Procedure

During the first session, participants completed the questionnaires and a MRI scan of the wrist was taken. In the following 10 min, participants in the exercise group performed three series of nerve and tendon gliding exercises under supervision of a clinician. Participants in the splinting group wore the splint for 10 min. Subsequently, the wrist was imaged a second time. After 1 week of home exercises or night splinting, patients completed the same questionnaires and underwent another MRI scan of their wrist.

### Statistical Analysis

Demographic and baseline data of the splinting and exercise group were compared with independent *t*-tests. The effect of the interventions on primary and secondary outcomes was analyzed using principles of intention-to-treat with two-way analyses of variance with one between group factor (GROUP with two levels (exercise and splinting)) and one repeated factor (TIME with three levels for MRI (baseline, immediate follow-up, 1 week follow-up) and two levels for questionnaires (baseline and 1 week follow-up)). Post-hoc comparisons were Bonferroni corrected for two pre-determined comparisons (baseline versus immediate follow-up; baseline versus 1 week follow-up).

Pearson's correlations were calculated between signal intensity of the median nerve and ligament bowing and pain intensity and numbness at baseline. Furthermore, correlations between the change in signal intensity and ligament bowing and pain intensity and numbness following 1 week of intervention were calculated. All analyses were performed in SPSS 15 (SPSS Inc, Chicago, IL). The level of significance was set at  $p < 0.05$ .

### Natural History

As it was a prerequisite that the MRI measures used in this study were stable over time, a separate experiment was conducted. This experiment was approved by the Medical Research Ethics Committee of The University of Queensland and all participants provided informed written consent. Five patients with mild to moderate CTS were recruited through the local print media (female: 3; age (mean (SD)): 53.4 (9.7) years; mild CTS: 1; moderate CTS: 4). Patients underwent two MRI scans of their affected wrist 1 week apart. They received no intervention during this period but received advice to remain active. The in- and exclusion criteria, MRI protocol, and outcome measures were identical to those described above. Paired *t*-tests demonstrated that MRI measures at 1 week follow-up were not different to those at baseline (mean (SD) decrease in signal intensity at the radioulnar level 1.6% (2.6%); signal intensity (at any level):  $p > 0.27$ ; ligament bowing:  $p = 0.81$ ). These results demonstrated that no systematic changes in MRI measures are to be expected within 1 week if no intervention is provided.

### RESULTS

The baseline patient characteristics were comparable between the two groups (Table 1). All participants received the treatment as allocated and adhered to the prescribed exercise program and splinting regime.

**Table 1.** Baseline Characteristics of the Splinting and Exercise Group

	Exercise	Splinting	<i>p</i> -value
Age in years (SD)	49.9 (12.5)	57.9 (16.3)	0.22
Gender (male/female)	5/5	7/3	0.28
Symptom duration in months (SD)	54.6 (47.6)	62.8 (56.1)	0.20
CTS severity			
Mild	4	3	0.79
Moderate	6	7	

There were no reported adverse effects and no adjustments to the exercise program were required. Inter-tester reliability of signal intensity measures was high, but somewhat lower for palmar ligament bowing (Table 2).

### Signal Intensity and Ligament Bowing

#### Signal Intensity of the Median Nerve

At the radioulnar level, the analysis of variance revealed no significant interaction effect for TIME  $\times$  GROUP [ $F(2,36) = 0.59$ ;  $p = 0.56$ ], demonstrating that both groups behaved similarly over time. There was no significant main effect for GROUP [ $F(1,18) = 1.61$ ;  $p = 0.22$ ] but there was a significant main effect for TIME [ $F(2,36) = 3.63$ ;  $p = 0.036$ ]. The signal intensity of the median nerve was 11.1% (SD = 15.4%) lower at 1 week follow-up [mean (SD) ratio = 1.20 (0.19)] compared to baseline [1.35 (0.27)] ( $p = 0.03$ ). At the hamate and pisiform level, no significant interaction effects for GROUP  $\times$  TIME were present [ $F(2,36) = 0.18$ ;  $p = 0.84$ ;  $F(2,36) = 0.03$ ;  $p = 0.97$ , respectively]. Similarly, no main effects for GROUP [hamate:  $F(1,18) = 1.22$ ;  $p = 0.28$ ; pisiform:  $F(1,18) = 0.001$ ;  $p = 0.97$ ] or TIME [hamate:  $F(2,36) = 0.81$ ;  $p = 0.45$ ; pisiform:  $F(2,36) = 2.98$ ;  $p = 0.063$ ] were identified. This indicated that signal intensity was comparable between groups and remained unchanged over time (Fig. 3, Table 3).

#### Ligament Bowing

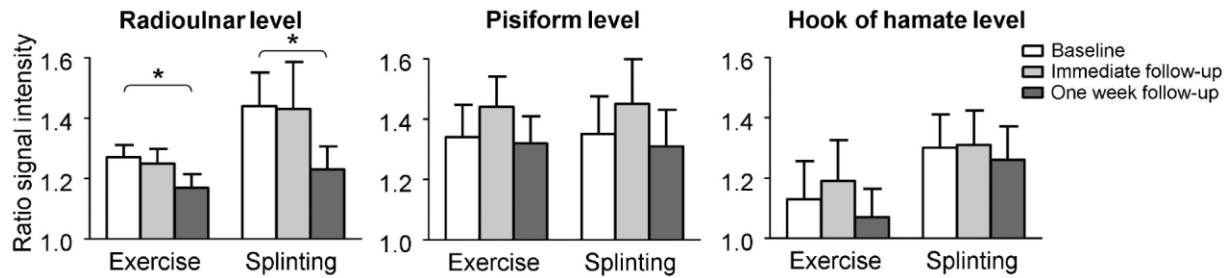
For carpal ligament bowing no significant interaction effect for GROUP  $\times$  TIME was identified [ $F(2,36) = 1.34$ ;  $p = 0.28$ ]. Similarly, there was no significant

**Table 2.** Reliability of Signal Intensity and Ligament Bowing Measurements

Level	ICC (2,1)	95% CI	SEM
Signal intensity			
Radioulnar	0.77	0.40–0.91	0.15
Pisiform	0.91	0.74–0.96	0.13
Hamate	0.93	0.82–0.97	0.11
Ligament bowing			
Hamate	0.62	0.26–0.83	0.02

ICC, intraclass correlation coefficient; CI, confidence interval; SEM, standard error of measurement.





**Figure 3.** Signal intensity ratio of the median nerve over time at the level of the radioulnar joint, the pisiform and the hook of hamate. \*Indicates statistical significance between baseline and 1-week follow-up measures ( $p < 0.03$ ). The error bars represent the standard error of the mean.

main effect for TIME ( $F(2,36) = 2.73$ ;  $p = 0.08$ ) or GROUP [ $F(1,18) = 0.002$ ;  $p = 0.96$ ] when comparing the exercise and splinting group (Table 3).

### Symptom Severity and Function

The analysis of variance for the exercise and splinting group did not reveal a significant interaction effect for TIME  $\times$  GROUP [ $F(1,17) < 0.88$ ;  $p > 0.36$ ] or a main effect for GROUP [ $F(1,17) < 1.42$ ;  $p > 0.25$ ] for symptom severity or function as determined by the Boston questionnaire and the patient specific functional scale. This indicated that there was no difference for these outcome measures between groups over time. There was however a significant effect of TIME for the Boston questionnaire [ $F(1,17) = 16.70$ ;  $p = 0.001$ ] and the patient specific functional scale [ $F(1,16) = 22.10$ ;  $p < 0.001$ ]. Post-hoc comparisons revealed that both groups improved significantly after 1 week intervention (all  $p < 0.004$ ;

Table 4). No significant interaction or main effects for pain intensity and numbness were found (all  $p > 0.16$ ).

### Correlation of Signal Intensity with Symptoms and Function

At baseline, signal intensity of the median nerve at the radioulnar ( $r = 0.68$ ;  $p = 0.001$ ) and pisiform level ( $r = 0.60$ ;  $p = 0.005$ ) correlated significantly with pain intensity. No significant correlations were present for signal intensity at the hamate level ( $p = 0.35$ ) or ligament bowing ( $p = 0.77$ ) and pain intensity. No significant correlations were found at baseline between signal intensity at any level or ligament bowing and numbness ( $p > 0.14$ ).

There was a significant correlation between the change in signal intensity of the median nerve at the radioulnar ( $r = 0.46$ ;  $p = 0.043$ ) and pisiform level ( $r = 0.61$ ;  $p = 0.004$ ) and the difference in numbness

**Table 3.** Signal Intensity and Ligament Bowing Ratios (mean (SD)) for the Exercise and Splinting Group

	Exercise			Splinting		
	Baseline	Immediate follow-up	One week follow-up	Baseline	Immediate follow-up	One week follow-up
SI RU	1.27 (0.13)	1.25 (0.15)	1.17 (0.14) <sup>a</sup>	1.44 (0.35)	1.43 (0.49)	1.23 (0.24) <sup>a</sup>
SI pisiform	1.34 (0.34)	1.44 (0.32)	1.32 (0.28)	1.35 (0.40)	1.45 (0.47)	1.31 (0.38)
SI hamate	1.13 (0.40)	1.19 (0.43)	1.07 (0.30)	1.30 (0.35)	1.31 (0.36)	1.26 (0.35)
Ligament bowing	0.17 (0.03)	0.16 (0.03)	0.16 (0.03)	0.17 (0.03)	0.17 (0.03)	0.16 (0.03)

<sup>a</sup>Statistical significance compared to baseline values. No significant differences were present between groups. SI, signal intensity.

**Table 4.** Mean (SD) for Symptom Severity and Function at Baseline and after 1 Week of Intervention

	Exercise		Splinting	
	Baseline	One week follow-up	Baseline	One week follow-up
Boston questionnaire	1.8 (0.5)	1.5 (0.6) <sup>a</sup>	2.0 (0.4)	1.7 (0.4) <sup>a</sup>
Pain intensity (VAS)	0.7 (1.3)	0.8 (1.4)	1.2 (2.1)	1.1 (1.1)
Numbness (VAS)	1.5 (2.2)	1.6 (2.4)	2.3 (2.7)	1.9 (2.1)
Patient specific functional scale	4.7 (2.9)	6.8 (2.9) <sup>a</sup>	5.0 (1.3)	7.9 (1.6) <sup>a</sup>

<sup>a</sup>Statistical significance compared to baseline values. No significant differences were present between groups.

over 1 week. No significant correlations were present between changes in signal intensity at the hamate level ( $p = 0.57$ ) or ligament bowing ( $p = 0.85$ ) and difference in numbness. Similarly, no significant correlations were present for changes in signal intensity at any level ( $p > 0.24$ ) or ligament bowing ( $p > 0.74$ ) and changes in pain intensity.

## DISCUSSION

The main finding of this study is that 1 week of either splinting or nerve and tendon gliding exercises reduced signal intensity of the median nerve at the inlet of the carpal tunnel in patients with CTS. A reduction in signal intensity of the median nerve in patients with CTS is considered to reflect a reduction in intraneural edema.<sup>8,9</sup> The mean reduction in signal intensity for both interventions was ~11%, whereas no reduction was observed if patients with CTS received advice to remain active without additional treatment. Three months after surgery, a similar decrease of ~11% at the inlet of the carpal tunnel has been demonstrated.<sup>8</sup> Although a direct comparison with surgery may not be warranted, we believe that the identified reduction after 1 week is substantial. No change in signal intensity was observed immediately following the first treatment session, which suggests a cumulative treatment effect over time.

No significant reduction in signal intensity of the median nerve was observed more distally in the carpal tunnel. There is however evidence to suggest that the inlet of the carpal tunnel is the most plausible region for a reduction in intraneural edema to occur following treatment. Swelling of the median nerve in CTS is most pronounced at the inlet of the tunnel<sup>5,35</sup> and the most prominent increase in signal intensity of the median nerve in CTS is also apparent at this level.<sup>8,30</sup> Signal intensity may even be reduced at the hamate level.<sup>8</sup>

Seradge et al.<sup>36</sup> demonstrated that hand exercises in patients with CTS lead to an immediate decrease of carpal tunnel pressure. Splinting has also been suggested to reduce carpal tunnel pressure.<sup>12</sup> Although palmar bowing of the carpal ligament is considered an indirect measure of carpal tunnel pressure,<sup>2,11</sup> no decrease in ligament bowing was observed following either intervention. Elevated carpal tunnel pressure and ligament bowing may not only be caused by intraneural or extraneural swelling, but structural changes such as thickened tenosynovial tissue or hypertrophy of the lumbrical muscles may also contribute.<sup>1</sup> It is unclear whether splinting and exercise can alter the structural factors especially within the short intervention period used in this study.

A decrease in signal intensity in the median nerve in patients with CTS is commonly attributed to a reduction in edema.<sup>8,30</sup> However, it could also reflect an unwanted reduction in intraneural blood circulation. Because neural ischemia contributes to the typical symptoms of CTS,<sup>4,37</sup> it would be logical that

symptoms and function would have worsened if the reduction in signal intensity had been reflective of reduced intraneural blood circulation. This worsening was not observed. Rather the opposite occurred as a mild improvement in symptom severity and function was reported. As outlined above, changes in symptom severity and function were secondary outcomes and included to better interpret possible changes in signal intensity. Considering the chronic nature of the symptoms and the short intervention period, a moderate trend rather than clinically meaningful changes were anticipated. Although statistically significant, the improvement in the Boston questionnaire did indeed not reach the previously established scores for a clinically meaningful change.<sup>38</sup> The significant improvement in the patient specific functional scale was however clinically meaningful.<sup>33</sup> We like to emphasize though that this study was designed to reveal possible therapeutic mechanisms of nerve and tendon gliding exercises and splinting, and not to evaluate the clinical efficacy of these interventions. The strong correlation between changes in signal intensity and changes in numbness provides further support that the changes in signal intensity should be interpreted as a reduction in intraneural edema rather than reduced blood circulation.

It may be somewhat surprising that two rather opposing treatment modalities (splinting and exercise) resulted in a comparable reduction in intraneural edema. Based only on the therapeutic mechanism uncovered in this study, there seems to be no preference for splinting or nerve and tendon gliding exercises. One may even argue that splinting is a safer option since provocative hand exercises may lead to a deterioration of MRI parameters indicative of edema.<sup>39</sup> Our study indicates however that the concern that nerve and tendon gliding exercises could increase intraneural edema due to irritation is unwarranted when non-provocative exercises are selected. A large clinical trial (197 patients) with a substantial follow-up (2-years) revealed that for patients awaiting CTS surgery, the addition of nerve and tendon gliding exercises to standard care lowered the percentage of patients requiring surgery from 71.2% to 43.0%.<sup>17</sup> As splinting was included in standard care, there is likely to be an advantage of incorporating nerve and tendon gliding exercises to a standard regime. As mentioned above, there may be additional local and remote effects of exercise that are not associated with splinting.<sup>16,40</sup> Incorporating nerve and tendon gliding exercises in standard care is in line with recommendations from a recent systematic review<sup>14</sup> and corresponds with current clinical practice.<sup>10</sup>

The findings of this study suggest that a reduction in intraneural edema is a therapeutic mechanism of both nerve and tendon gliding exercises and splinting. The chronicity of the symptoms of the patients involved in this study and the short treatment period propose that the reduction in intraneural edema is associated with the interventions rather than the result of the natural course of CTS. This is further supported

by the fact that signal intensity remained unchanged in patients who received no treatment. Studies in larger patient populations are needed to examine whether the identified short-term changes in intraneural edema can be maintained or even further improved long-term. The strong correlations observed in this study between MRI findings on the one side and baseline pain intensity and changes in numbness on the other side also warrant further investigations.

## ACKNOWLEDGMENTS

We would like to thank Wolbert van den Hoorn for designing the Matlab program. Annina Schmid was supported by the Endeavour Europe Award, Department of Education, Employment and Workplace Relations, Australian Government, and the International Post-graduate Research Scholarship, Australia. The study was funded through the Health Practitioner Research Scheme from Queensland Health, Australia and Project grant 511161 from the National Health and Medical Research Council (NHMRC) of Australia.

## REFERENCES

- Bland JD. 2005. Carpal tunnel syndrome. *Curr Opin Neurol* 18:581–585.
- Gelberman RH, Hergenroeder PT, Hargens AR, et al. 1981. The carpal tunnel syndrome. A study of carpal canal pressures. *J Bone Joint Surg Am* 63:380–383.
- Okutsu I, Ninomiya S, Yoshida A, et al. 2004. Measurement of carpal canal and median nerve pressure in patients with carpal tunnel syndrome. *Tech Hand Up Extrem Surg* 8:124–128.
- Mackinnon SE. 2002. Pathophysiology of nerve compression. *Hand Clin* 18:231–241.
- Phalen GS. 1966. The carpal-tunnel syndrome. Seventeen years' experience in diagnosis and treatment of six hundred fifty-four hands. *J Bone Joint Surg Am* 48:211–228.
- Tuncali D, Barutcu AY, Terzioglu A, et al. 2005. Carpal tunnel syndrome: comparison of intraoperative structural changes with clinical and electrodiagnostic severity. *Br J Plast Surg* 58:1136–1142.
- Mallouhi A, Pulzl P, Trieb T, et al. 2006. Predictors of carpal tunnel syndrome: accuracy of gray-scale and color Doppler sonography. *AJR Am J Roentgenol* 186:1240–1245.
- Cudlip SA, Howe FA, Clifton A, et al. 2002. Magnetic resonance neurography studies of the median nerve before and after carpal tunnel decompression. *J Neurosurg* 96:1046–1051.
- Kleindienst A, Hamm B, Hildebrandt G, et al. 1996. Diagnosis and staging of carpal tunnel syndrome: comparison of magnetic resonance imaging and intra-operative findings. *Acta Neurochir (Wien)* 138:228–233.
- Coppieters MW, Soon BTC. 2011. Non-invasive management of carpal tunnel syndrome. A national practice survey among Australian hand therapists. in press.
- Luchetti R, Schoenhuber R, Nathan P. 1998. Correlation of segmental carpal tunnel pressures with changes in hand and wrist positions in patients with carpal tunnel syndrome and controls. *J Hand Surg [Br]* 23:598–602.
- Weiss ND, Gordon L, Bloom T, et al. 1995. Position of the wrist associated with the lowest carpal-tunnel pressure: implications for splint design. *J Bone Joint Surg Am* 77:1695–1699.
- Sugimoto H, Miyaji N, Ohsawa T. 1994. Carpal tunnel syndrome: evaluation of median nerve circulation with dynamic contrast-enhanced MR imaging. *Radiology* 190:459–466.
- Medina McKeon JM, Yancosek KE. 2008. Neural gliding techniques for the treatment of carpal tunnel syndrome: a systematic review. *J Sport Rehabil* 17:324–341.
- Huisstede BM, Hoogvliet P, Randsdorp MS, et al. 2010. Carpal tunnel syndrome. Part I: effectiveness of nonsurgical treatments—a systematic review. *Arch Phys Med Rehabil* 91:981–1004.
- Coppieters MW, Butler DS. 2008. Do 'sliders' slide and 'tensioners' tension? An analysis of neurodynamic techniques and considerations regarding their application. *Man Ther* 13:213–221.
- Rozmaryn LM, Dovel S, Rothman ER, et al. 1998. Nerve and tendon gliding exercises and the conservative management of carpal tunnel syndrome. *J Hand Ther* 11:171–179.
- Hansford T, Blood H, Kent B, et al. 1986. Blood flow changes at the wrist in manual workers after preventive interventions. *J Hand Surg [Am]* 11:503–508.
- Totten PA, Hunter JM. 1991. Therapeutic techniques to enhance nerve gliding in thoracic outlet syndrome and carpal tunnel syndrome. *Hand Clin* 7:505–520.
- AAEM. 1993. Practice parameter for carpal tunnel syndrome (summary statement). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 43:2406–2409.
- AAEM. 2002. Practice parameter: electrodiagnostic studies in carpal tunnel syndrome. *Neurology* 58:1589–1592.
- Padua L, Lo Monaco M, Padua R, et al. 1997. Neurophysiological classification of carpal tunnel syndrome: assessment of 600 symptomatic hands. *Ital J Neurol Sci* 18:145–150.
- Wehbe MA, Hunter JM. 1985. Flexor tendon gliding in the hand. Part II. Differential gliding. *J Hand Surg [Am]* 10:575–579.
- Coppieters MW, Hough AD, Dilley A. 2009. Different nerve-gliding exercises induce different magnitudes of median nerve longitudinal excursion: an in vivo study using dynamic ultrasound imaging. *J Orthop Sports Phys Ther* 39:164–171.
- Coppieters MW, Alshami AM. 2007. Longitudinal excursion and strain in the median nerve during novel nerve gliding exercises for carpal tunnel syndrome. *J Orthop Res* 25:972–980.
- Coppieters MW, Vicenzino B, Soon BTC, et al. 2011. Comparative efficacy of a multimodal physiotherapy approach versus ultrasound for carpal tunnel syndrome: a protocol for a randomised, single blind clinical trial. Approved Project grant #511161 (2008–2011). Canberra, Australia: National Health and Medical Research Council.
- Zailaa A, Vegh V, Maillet D, et al. 2009. Quadrature radio frequency coil for magnetic resonance imaging of the wrist at 4T. *Concepts Magn Reson* 35B:191–197.
- Finn JP, Deshpande VS, Simonetti OP. 2006. Clinical magnetic resonance imaging. 3rd ed. Philadelphia: Saunders Elsevier.
- Tsujii M, Hirata H, Morita A, et al. 2009. Palmar bowing of the flexor retinaculum on wrist MRI correlates with subjective reports of pain in carpal tunnel syndrome. *J Magn Reson Imaging* 29:1102–1105.
- Uchiyama S, Itsubo T, Yasutomi T, et al. 2005. Quantitative MRI of the wrist and nerve conduction studies in patients with idiopathic carpal tunnel syndrome. *J Neurol Neurosurg Psychiatry* 76:1103–1108.
- Monagle K, Dai G, Chu A, et al. 1999. Quantitative MR imaging of carpal tunnel syndrome. *AJR Am J Roentgenol* 172:1581–1586.
- Levine DW, Simmons BP, Koris MJ, et al. 1993. A self-administered questionnaire for the assessment of severity of symptoms and functional status in carpal tunnel syndrome. *J Bone Joint Surg Am* 75:1585–1592.

33. Stratford P, Gill C, Westaway M, et al. 1995. Assessing disability and change on individual patients: a report of a patient specific measure. *Physiother Can* 47: 258–263.
34. Kowalchuk Horn K, Jennings S, Richardson G, et al. 2011. The Patient-Specific Functional Scale: psychometrics, clinimetrics, and application as a clinical outcome measure. *J Orthop Sports Phys Ther*. (Epub ahead of print).
35. Nakamichi KI, Tachibana S. 2000. Enlarged median nerve in idiopathic carpal tunnel syndrome. *Muscle Nerve* 23: 1713–1718.
36. Seradge H, Jia YC, Owens W. 1995. In vivo measurement of carpal tunnel pressure in the functioning hand. *J Hand Surg [Am]* 20:855–859.
37. Han SE, Boland RA, Krishnan AV, et al. 2009. Ischaemic sensitivity of axons in carpal tunnel syndrome. *J Peripher Nerv Syst* 14:190–200.
38. Leite JC, Jerosch-Herold C, Song F. 2006. A systematic review of the psychometric properties of the Boston Carpal Tunnel Questionnaire. *BMC Musculoskelet Disord* 7:78.
39. Brahme SK, Hodler J, Braun RM, et al. 1997. Dynamic MR imaging of carpal tunnel syndrome. *Skeletal Radiol* 26:482–487.
40. Bialosky JE, Bishop MD, Price DD, et al. 2009. A randomized sham-controlled trial of a neurodynamic technique in the treatment of carpal tunnel syndrome. *J Orthop Sports Phys Ther* 39:709–723.