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OPTIMAL STIMULATION DURATION OF TENS IN THE MANAGEMENT OF OSTEOARTHRITIC KNEE PAIN

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Objective: **This study examined the optimal stimulation duration of transcutaneous electrical nerve stimulation (TENS) for relieving osteoarthritic knee pain and the duration (as measured by half-life) of post-stimulation analgesia.**

Subjects: **Thirty-eight patients received either: (i) 20 minutes ($TENS_{20}$); (ii) 40 minutes ($TENS_{40}$); (iii) 60 minutes ($TENS_{60}$) of TENS; or (iv) 60 minutes of placebo TENS ($TENS_{PL}$) 5 days a week for 2 weeks.**

Methods: **A visual analogue scale recorded the magnitude and pain relief period for up to 10 hours after stimulation.**

Results: **By Day_{10}, a significantly greater cumulative reduction in the visual analogue scale scores was found in the $TENS_{40}$ (83.40%) and $TENS_{60}$ (68.37%) groups than in the $TENS_{20}$ (54.59%) and $TENS_{PL}$ (6.14%) groups ($p < 0.000$), such a group difference was maintained in the 2-week follow-up session ($p < 0.000$). In terms of the duration of post-stimulation analgesia period, the duration for the $TENS_{40}$ (256 minutes) and $TENS_{60}$ (258 minutes) groups was more prolonged than in the other 2 groups ($TENS_{20}$ = 168 minutes, $TENS_{PL}$ = 35 minutes) by Day_{10} ($p < 0.000$). However, the $TENS_{40}$ group produced the longest pain relief period by the follow-up session.**

Conclusion: **40 minutes is the optimal treatment duration of TENS, in terms of both the magnitude (VAS scores) of pain reduction and the duration of post-stimulation analgesia for knee osetoarthritis.**

Key words: knee osetoarthritis; pain; TENS.

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INTRODUCTION

Osteoarthritis (OA) is the most prevalent form of arthritis in the USA (1) and its prevalence increases with age (2). It is estimated that about 15.8 million of Americans are afflicted with OA (3). It occurs mostly in people over the age of 65 years (4) and the knee is the most commonly affected site in the lower limb (1). The main complaints of patients suffering from OA are pain, stiffness, crepitation, instability, loss of function, joint enlargement and impaired muscle strength (5, 6). As the condition progresses, the pain level increases while patients' physical performance deteriorates. Effective management of osteoarthritic pain may allow patients with OA to regain a certain mobility level and thereby maintain a reasonably normal life. Transcutaneous electrical nerve stimulation (TENS) is one of the commonly used physical modalities for managing OA knee. Previous studies have examined the effectiveness of TENS for managing OA knee pain (7–12), but some of the results were controversial. According to a recent meta-analysis carried out by the Philadelphia Panel (13), the relative differences between treatment group and placebo group varied greatly from one study to another. The relative difference reported by Taylor et al. was 40% (7), compared with 10.6% in the findings of Lewis et al. (12). In summary, the pooled estimate showed that TENS produced a 41% pain reduction relative to a placebo treatment.

Among the studies reporting positive findings, Taylor et al. (7) allowed patients with knee OA to control the stimulation duration themselves. After 4 weeks of treatment, active TENS produced a significantly greater reduction than placebo TENS in subjective pain scores ($p = 0.030$), but not in the consumption of medicine or in ambulatory performance ($p > 0.05$). Ambulatory performance was assessed by asking the subjects how far they could walk without being stopped by pain. However, the stimulation duration varied from 30 to 60 minutes in various patients; some patients even used the TENS machine continuously throughout the day. Lewis et al. (9) further demonstrated that active TENS with a similar stimulation duration of 30 to 60 minutes produced a significantly longer duration of pain relief than placebo TENS ($p < 0.01$). However, using the same treatment protocols, they found no significant difference in the pain scores and knee functions between active TENS and sham TENS in a later study ($p > 0.05$) (12). Grimmer (11) found that the high rate TENS (80 Hz, a single treatment session lasting for 30 minutes) resulted in a significant reduction in knee stiffness ($p = 0.03$) and a significantly longer time of stiffness relief ($p = 0.004$) compared with the placebo.

From the above review, it is evident that the stimulation duration of TENS was not well controlled in some of the previous studies. It could vary from 30 to 60 minutes a day, or even up to almost continuous stimulation throughout the day, within a single study. In fact, there is no consensus in the literature with regard to the optimal stimulation duration of TENS. As suggested by Long & Hagfors (14), stimulation duration is a parameter that could influence the duration of post-stimulation analgesia. The underlying mechanism is not known. However, recent research studies have shown that TENS

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Table I. *Demographic data of the patients with knee osteoarthritis (OA) (mean, SD)*

	$TENS_{20}$	$TENS_{40}$	$TENS_{60}$	$TENS_{PL}$
Number	10	10	10	8
Age (years)	69.2 (5.7)	63.2 (8.4)	63.5 (5.6)	66.1 (9.3)
Gender				
Male	1	1	1	1
Female	9	9	9	7
Body height (m)	1.5 (0.1)	1.5 (0.1)	1.5 (0.1)	1.5 (0.1)
Body weight (kg)	64.5 (6.5)	67.2 (7.1)	66.3 (5.2)	66.5 (5.8)
History of OA knee (years)	3.6 (1.4)	4.5 (1.4)	4.2 (1.6)	4.0 (1.6)
Baseline VAS scores	4.4 (1.2)	5.2 (1.1)	5.5 (1.3)	4.9 (1.0)

$TENS_{20}$: Transcutaneous electrical nerve stimulation for 20 min; PL = placebo..

analgesia involves the activation of the endogenous opioid system (15). It should be pointed out that the release of endogenous opioids takes time, and that the analgesic effects of endogenous opioids can last for some time before they decay. One could postulate that the accumulation or depletion of endogenous opioids can influence the amplitude and the duration of the *post*-stimulation analgesia of TENS. It is therefore important to determine the optimal stimulation duration that will achieve the best analgesic effect of TENS.

For repeated applications of TENS over a 2-week period, previous studies in our laboratory demonstrated a 30% reduction in acute experimental pain and a 48.8% decrease in chronic low back pain. Such levels of pain reduction were significantly higher than those of placebo stimulation (16, 17). Cheing & Hui-Chan (18) further demonstrated that repeated applications of TENS for 4 weeks also produced a cumulative analgesic effect for OA knee pain. The stimulation duration was 60 minutes in all the studies and the analgesic effect was demonstrated to be cumulative over the treatment period. As the stimulation duration of TENS used in clinical settings is usually less than 60 minutes, we set out to examine whether shorter stimulation duration can also produce similar cumulative effects. The two purposes of this study were to determine:

- the optimal treatment duration of TENS for OA knee pain, and
- the duration (as measured by half-life) of post-stimulation analgesia

In order to examine the time course of the analgesic effect of TENS in detail, *post*-treatment pain levels were recorded for up to 10 hours in this study.

METHODS

Subjects

Patients diagnosed with knee OA by orthopedic surgeons were recruited from the outpatient physiotherapy department of Queen Elizabeth Hospital in Hong Kong. The inclusion criteria were patients aged from 50 to 80 years, with at least grade II OA changes shown in X-ray according to the Kellgren & Lawrence (19) scale and with knee OA as the only cause of the present knee pain and the sole reason for receiving physiotherapy. The subjects were independently ambulatory within the community, able to report their subjective pain level by visual analogue scale (VAS) during walking and suffered from moderate knee pain with the baseline VAS scores ranging from 3.0 to 7.0 out of 10. The exclusion criteria were prior knee surgery, having received a steroid injection and TENS treatment 2 months prior to this study. Subjects who had cardiac pacemakers were also excluded (20). Forty patients were recruited initially. Two patients from the placebo group dropped out of the study, 1 because of hospital admission due to renal problems and the other due to work commitments. The patients' relevant demographic data are presented in Table I. Among the 38 patients who completed the study, 34 were female and 4 were male. The mean age of all patients was 65.5 years (ranging from 51 to 79 years). They had suffered from pain due to knee OA for 2–7 years. All patients showed grade II OA changes on radiographs.

Instrumentation

TENS (model 120Z; ITO, Tokyo) was used in the study. The calibration of the pulse frequency, pulse duration and current intensity of the active TENS unit was carried out by the use of an oscilloscope (21). The electronic circuit of the sham unit was disconnected, so that when the machine was turned on, the indicator lamp was on but there was no electrical current output.

A VAS was used to record patients' subjective reports of OA knee pain. The VAS consisted of a 10-cm horizontal line, anchored with "no pain" at the left end (i.e. threshold intensity) and "pain as bad as it could be" at the right (i.e. maximally tolerable intensity). This scale has been demonstrated to be valid (22), reliable (22, 23) and generalizable (24, 25). As most subjects complained of knee pain during walking, VAS scores for knee pain during walking were recorded.

Experimental procedures

After informed consent had been obtained, demographic data including gender, age, body weight, body height and history of knee pain were recorded. The subjects were stratified by gender and randomly divided into 4 groups. During the treatment, they lay supine on a plinth with both knees supported by a pillow at approximately 15° from full knee extension, which is a relaxed position for the knee joint.

Four rubber electrodes (2 cm × 3 cm) from a dual channel TENS unit were placed with aqueous gel on the acupuncture points around the knee: Extra 31, 32, St. 35, Gb. 34 and Sp. 9 (26, 27). Acupuncture points were used in this study because they were likely to maximize the body's intrinsic opioid response (28, 29). The stimulation frequency was set at 100 Hz with a pulse width of 200 μs in a continuous mode. Patients from the 3 active TENS groups felt "strong but comfortable" tingling parathesia during the stimulation. Patients from the placebo group received treatment from the sham stimulation unit and they were told that there was no sensation during the treatment.

The TENS treatment was given 5 days per week for 2 consecutive weeks. For each treatment session, the *pre*-stimulation intensity of knee pain was first recorded by VAS, then at 20-minute intervals in the initial *post*-stimulation hour at the clinic. The patients were then asked to record the *post*-stimulation VAS scores at 2-hour intervals for up to 10 hours at home. As the pain level for some patients did not return to the *pre*-stimulation level even when they returned to the clinic for the next treatment session, the *post*-stimulation pain relief period was presented in terms of the "half-life" of the analgesic effect of TENS. The time to

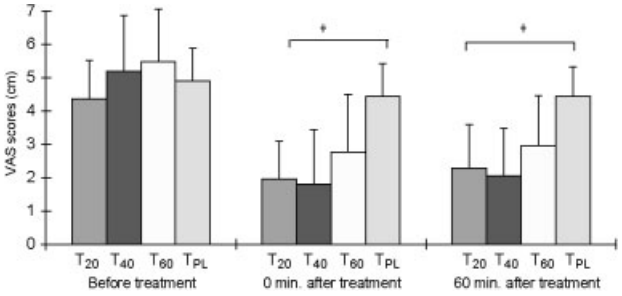

Fig. 1. Immediate analgesic effects of transcutaneous electrical nerve stimulation (TENS) in Day_1. Each histogram column represents the group mean of VAS scores. For within-group comparisons, there was a significant change before and after stimulation for all 4 groups (# all $p < 0.01$). For between-group comparisons, there was a significant group difference immediately after stimulation ($p = 0.003$) and at 60 minutes after the treatment ($p = 0.009$). *Post-hoc* analysis showed that lower VAS scores were observed in the 3 active TENS groups (i.e. $TENS_{20}$, $TENS_{40}$ and $TENS_{60}$ groups), in contrast to the negligible change in the $TENS_{PL}$. However, no significant difference was found among the 3 groups.

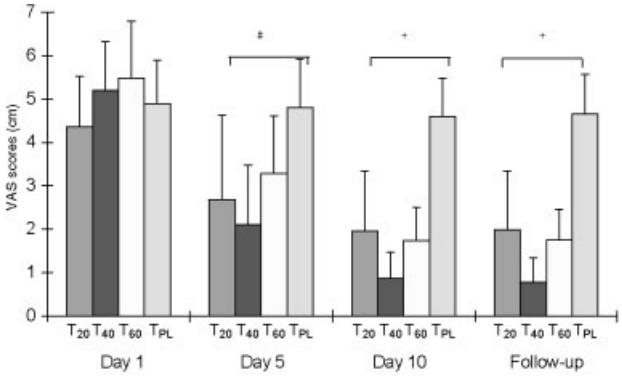

Fig. 2. Pre-stimulation VAS scores recorded in Day_1, Day_5, Day_{10} and the follow-up session. The between-group difference in VAS scores was significant by Day_5 (#$p = 0.004$), Day_{10} (+$p = 0.000$) and at the follow-up sessions (+$p = 0.000$). The 3 active TENS groups showed significantly lower VAS scores than the placebo group in these 3 treatment sessions. When comparing only the 3 active TENS groups, the VAS scores of the $TENS_{40}$ group was significantly lower than the $TENS_{20}$ group by Day_{10}, but was similar to the $TENS_{60}$ group. However, in the follow-up session, the $TENS_{40}$ group demonstrated significantly lower VAS scores than both the $TENS_{20}$ and $TENS_{60}$ groups.

reach the "half-life" was defined as the time required for the pain scores to recur at half of the pain level between the *pre-* and immediate *post-*stimulation scores. In order to study the carry-over effect of TENS, a follow-up session was carried out 2 weeks after the end of the treatment period.

Data analysis

Data analysis was performed with the use of the SPSS statistical package (Version 10.0, SPSS, Chicago, IL) and the level of significance was set at 0.05. A number of repeated measures ANOVAs were employed to test the differences in the VAS scores among the 4 groups, between various time periods, and across treatment sessions. Details of each ANOVA will be described in the text along with the results. As several ANOVAs had been carried out, the "Sharpened Bonferroni" (30) procedure was used to adjust for individual alpha level, keeping the overall significance level at 0.05. This procedure has been shown to give substantially higher statistical power than the usual Bonferroni correction when multiple testing is performed. Linear regression was used to analyse the relationship between the pre-stimulation VAS scores and treatment sessions. We also compared the time to reach half-life of TENS analgesia of the 4 groups over the 10 treatment sessions. However, "half-life" was never reached within the studied period for some of the patients. Their observations constituted so-called "censored data" and hence survival analysis techniques were needed for the analysis. Specifically, the log-rank test was used for the comparison. All statistical powers presented are observed powers.

RESULTS

Demographic data

There was no significant difference in the demographic data among the 4 groups (all $p > 0.05$, Table I). Twenty-eight patients suffered from bilateral knee pain and 10 suffered from a unilateral problem. For subjects with bilateral knee pain, only the more painful knee was treated in the study.

Immediate analgesic effects of TENS on Day_1

The VAS scores of the 4 groups obtained *before*, immediately (0 minutes) *after* and 1 hour (60 minutes) *after* stimulation on Day_1 are shown in Fig. 1 and analysed using a 4 × 3 (group × time) repeated measures ANOVA. The baseline measurement of VAS scores before treatment showed no significant difference among the 4 groups ($F = 1.65$; $df = 3,34$; $p = 0.196$; power = 0.393). As there was significant interaction between time period and treatment group ($F = 5.80$; $df = 6,68$; $p < 0.001$; power = 0.982), further analyses of the VAS scores at the 3 time periods for the 4 groups were performed separately.

For within-group comparisons, there were significant differences between the *pre-* and *post-*stimulation VAS scores within each of the 4 groups. There was a 47.93% reduction of VAS scores in the $TENS_{20}$ group (from 4.36 to 2.27; $F = 23.0$; $df = 2,18$; $p < 0.001$; power >0.99), a 60.31% reduction in the $TENS_{40}$ group (from 5.19 to 2.06; $F = 28.5$; $df = 2,18$; $p < 0.001$; power >0.99) and a 45.89% reduction in the $TENS_{60}$ group (from 5.47 to 2.96; $F = 34.3$; $df = 2,18$; $p < 0.001$; power >0.99). Interestingly, there was a 9.41% reduction in the $TENS_{PL}$ group that was also significant even after the Sharpened Bonferroni correction (from 4.89 to 4.43; $F = 7.10$; $df = 2,14$; $p = 0.007$; power = 0.86). For between-group comparisons, there was a significant (again with Sharpened Bonferroni adjustment) difference immediately after stimulation ($F = 5.77$; $df = 3,34$; $p = 0.003$; power = 0.93) and also 60 minutes after the treatment ($F = 4.47$; $df = 3,34$; $p = 0.009$; power = 0.84). *Post-hoc* analysis showed that lower VAS scores were observed in the 3 active TENS groups (i.e.$TENS_{20}$, $TENS_{40}$ and $TENS_{60}$ groups) than in the placebo group, but no significant difference was found among the 3 active groups.

Cumulative effect of repeated TENS applications over 2 weeks

The average VAS scores for the 4 groups recorded on Day_1,

Table II. *Time (minutes) to reach half-life of transcutaneous electrical nerve stimulation (TENS) analgesia over the 10 days of treatment (mean ± SE)*

	$TENS_{20}$ ($n = 10$)	*N*	$TENS_{40}$ ($n = 10$)	*N*	$TENS_{60}$ ($n = 10$)	*N*	$TENS_{PL}$ ($n = 8$)	*N*
Day_1	162 ± 62	1	380 ± 77	3	352 ± 62	3	163 ± 73	1
Day_2	182 ± 58	1	316 ± 72	3	372 ± 61	1	148 ± 49	0
Day_3	178 ± 37	0	346 ± 63	2	270 ± 47	0	160 ± 79	1
Day_4	270 ± 50	1	350 ± 63	3	376 ± 67	4	58 ± 19	0
Day_5	196 ± 55	0	152 ± 47	0	330 ± 62	1	188 ± 68	1
Day_6	204 ± 40	0	246 ± 69	0	420 ± 64	2	253 ± 95	0
Day_7	198 ± 28	0	384 ± 66	3	348 ± 52	2	85 ± 28	0
Day_8	174 ± 38	0	336 ± 67	3	338 ± 64	2	150 ± 68	1
Day_9	196 ± 50	1	244 ± 49	0	360 ± 65	1	148 ± 72	1
Day_{10}	168 ± 32	0	256 ± 35	0	258 ± 49	0	35 ± 7	0

N = number of observations showing half-life being longer than 10 hours after stimulation.

Day_5, Day_{10} and in the follow-up session are summarized in Fig. 2 and analysed using a 4 × 4 (group × day) repeated measures ANOVA. Again, since there was significant interaction between "day" and "group" ($F = 4.89$; $df = 9,102$; $p < 0.001$; power >0.99), the VAS scores of the 4 testing "days" were analysed separately for each of the 4 treatment groups and then for the 4 groups at each time period separately.

From Day_1 to Day_{10}, the cumulative reduction (within-group comparisons) in the average *pre*-stimulation VAS scores was by 54.59% (from 4.36 to 1.96; $F = 27.68$; $df = 2,18$; $p < 0.001$; power >0.99) for the $TENS_{20}$ group; 83.40% (from 5.19 to 0.86; $F = 52.55$; $df = 2,18$; $p < 0.001$; power >0.99) for the $TENS_{40}$ group; and 68.37% (from 5.47 to 1.73; $F = 48.15$; $df = 2,18$; $p < 0.001$; power >0.99) for the $TENS_{60}$ group; but only 6.14% (from 4.89 to 4.59; $F = 7.26$; $df = 2,14$; $p = 0.532$; power = 0.87) for the $TENS_{PL}$ group. From Day_{10} to the follow-up session, the VAS remained more or less unchanged in each of the 4 groups. After adjustment for alpha, the between-group difference in VAS scores was significant by Day_5 ($p = 0.012$; power = 0.90), Day_{10} ($p < 0.003$; power >0.99) and at the follow-up session ($p < 0.003$; power >0.99). Specifically, the 3 active TENS groups demonstrated significantly lower VAS scores than the placebo group in these 3 treatment sessions. Further analysis using linear contrast showed that among the 3 active TENS groups, the between-group difference in VAS scores reached significance by Day_{10}. Interestingly, the VAS scores of the $TENS_{40}$ group were similar to those of the $TENS_{60}$ group, with both groups being significantly lower than the $TENS_{20}$ group. By the follow-up session, the $TENS_{40}$ group had significantly lower VAS scores than both the $TENS_{20}$ and the $TENS_{60}$ groups.

Half-life of the analgesic effect of TENS

The time taken to reach half-life for the 4 groups is summarized in Table II and analysed using survival analysis due to the presence of censored data (i.e. "half-life" was not reached even after 10 hours for some of the patients). On Day_1, the time taken (minutes) to reach half-life (±SE) by the $TENS_{40}$ and the $TENS_{60}$ groups was longer than that taken by the $TENS_{20}$ and the $TENS_{PL}$ groups ($TENS_{20}$: 162 ± 62; $TENS_{40}$: 380 ± 77; $TENS_{60}$: 352 ± 62; $TENS_{PL}$: 163 ± 73), but this between-group difference did not reach statistical significance (log-rank test; $p = 0.096$; power = 0.27). By Day_{10}, the "half-life" for the 4 groups was: $TENS_{20} = 168 \pm 32$; $TENS_{40} = 256 \pm 35$; $TENS_{60} = 258 \pm 49$; $TENS_{PL} = 35 \pm 7$; and the difference was statistically significant (log-rank test; $p < 0.001$; power = 0.32) even after adjustment of alpha. The half-life of the $TENS_{40}$ group on Day_{10} was similar to that of the $TENS_{60}$ group and was longer than the $TENS_{20}$ and $TENS_{PL}$ groups. Over the 10 days of stimulation, 17% of the $TENS_{40}$ group and 16% of the $TENS_{60}$ group demonstrated a half-life of TENS analgesia longer than 10 hours. In contrast, only 4% of the $TENS_{20}$ group and 6% of the $TENS_{PL}$ group had a half-life longer than 10 hours.

Regressing of pre-stimulation VAS scores on treatment sessions

Repeated stimulations of TENS produced a cumulative inhibitory influence on the *pre*-stimulation VAS scores from Day_1 to Day_{10}. Table III shows the results of regressing the daily *pre*-stimulation VAS scores on the 10 treatment sessions. There was a moderate negative linear relationship for the $TENS_{40}$ and the $TENS_{60}$ groups ($TENS_{40}$: $r = -0.716$, $p < 0.000$, power >0.99; $TENS_{60}$: $r = -0.672$, $p < 0.000$; power >0.99) and a fair relationship for the $TENS_{20}$ group ($TENS_{20}$: $r = -0.334$, $p = 0.001$; power = 0.94). As shown by the slope of the regression lines, the VAS scores decreased faster in the $TENS_{40}$ group than in the $TENS_{60}$ and the $TENS_{20}$ groups (slope: $TENS_{20} = -0.213$; $TENS_{40} = -0.423$; $TENS_{60} = -0.380$). For the $TENS_{PL}$ group, there was almost no relation-

Table III. *Linear regression of the VAS scores across treatment sessions*

	Constant (y-intercept)	Slope	*p**	r
$TENS_{20}$	3.998	−0.213	0.001	−0.334
$TENS_{40}$	4.718	−0.423	0.000	−0.716
$TENS_{60}$	5.357	−0.380	0.000	−0.672
$TENS_{PL}$	4.894	−0.028	0.447	−0.086

p-value for testing the slope = 0.

ship between the VAS scores and the treatment session (T_{PL}: r = −0.086, $p = 0.447$; power = 0.12), which indicated that there was only minimal placebo effect in the present study.

DISCUSSION

Immediate effects of 1 treatment session

After 1 session of stimulation, a differential reduction in the VAS scores was found among the 4 groups. The between-group difference in the subjective pain sensation was significant immediately after TENS ($p = 0.003$, Fig. 1). This difference was maintained even up to 60 minutes after the TENS treatment ($p = 0.009$). The between-group difference came from the 3 active TENS groups, which showed significantly lower VAS scores than those of the placebo group. The gradual offset of TENS analgesia is consistent with our findings in previous studies. Cheing & Hui-Chan (18) demonstrated that 60 minutes of TENS produced maximum reduction in OA knee pain *after*, but not *during* the stimulation. This reduced the *pre*-stimulation VAS score to 67.3% during TENS and further to 64.1% 60 minutes *after* TENS. Similar results were found in patients with low back pain (31).

It could be argued that the involvement of endogenous opioids in TENS analgesia results in a typical time course of gradual onset and offset, as shown in both animal and human studies. In rats, Wang et al. (32) showed that 30 minutes of TENS produced inhibition on the tail flick test. The antinociceptive effect developed gradually and peaked at the end of the treatment period. It outlasted the treatment time, then returned gradually to the *pre*-stimulation level 30 minutes after the termination of stimulation. Such a gradual onset and offset analgesic pattern could at least partly be explained by a neurochemical mechanism. To elaborate, Han et al. (15) demonstrated that acupuncture-like TENS increased the release of met-enkephalin-arg-phe, whereas conventional TENS (high frequency and low intensity) enhanced the release of dynorphin A in human subjects. The gradual onset of TENS analgesia could thus be explained by the time lag in releasing the endogenous opioids. Similarly, the gradual offset could be due to the prolonged effect of the endogenous opioid substances before decaying.

Half-life of the analgesic effect of TENS after 1 single treatment session

How long does the post-stimulation analgesic effect of TENS last in human subjects? As reported by various studies, it usually persists from 5 minutes up to 18 hours post-stimulation (33). The present study is the first one using the time to reach half-life to address the duration of *post*-stimulation analgesic effect of TENS. On Day_1, the average time (minutes) to reach half-life for the $TENS_{40}$ and $TENS_{60}$ groups was longer than that of the $TENS_{20}$ and $TENS_{PL}$ groups ($TENS_{20} = 162$; $TENS_{40} = 380$; $TENS_{60} = 352$; $TENS_{PL} = 163$). As the stimulation duration increased, the half-life tended to last longer; however, the group difference did not reach statistical significance level ($p = 0.096$). After a single session of TENS, more patients in the $TENS_{40}$ and $TENS_{60}$ groups showed a half-life longer than 10 hours than did patients in the $TENS_{20}$ and the $TENS_{PL}$ groups ($TENS_{20}$: 10%; $TENS_{40}$: 30%; $TENS_{60}$: 30%; $TENS_{PL}$: 16.7%).

The present study was the first to address *post*-stimulation analgesic effects for up to 10 hours. The concept of half-life of the analgesic effect of TENS was also unique to this study. The idea of calculating the half-life of the analgesic effect of TENS came from the observation that some of the patients' pain levels did not return to the *pre*-stimulation levels even after 24 hours. The half-life of TENS analgesia is a useful measuring tool to reflect the effective pain relief period after receiving TENS.

Repeated applications of TENS for 10 sessions over 2 weeks

Upon repeated daily stimulation for 2 weeks, the drop in the VAS scores reached statistical significance ($p \leq 0.001$) within each of the 3 active TENS groups, but not in the placebo group. The VAS scores in these groups remained similar from Day_{10} to the follow-up session (Fig. 2). This finding illustrates that the cumulative analgesic effect of TENS achieved in the treatment period seemed to be carried over for at least 2 more weeks. However, in the follow-up session, the cumulative effect of TENS was significantly maintained better in the $TENS_{40}$ group.

Longer stimulation duration, such as 40 or 60 minutes of TENS produced a more long-lasting analgesic effect than 20 minutes of TENS. It is interesting to note that 20 minutes of TENS and 60 minutes of placebo stimulation produced similar analgesic effects. The half-life of the $TENS_{40}$ group was similar to that of the $TENS_{60}$ group and this value was longer than that of the $TENS_{20}$ or the $TENS_{PL}$ group from Day_1 to Day_{10} (Table II). Nevertheless, the half-life of TENS analgesia did not increase significantly within any treatment group across sessions. One possible explanation is that the *pre*-stimulation pain level of a particular treatment session had already decreased after each treatment session. Note that there was a cumulative reduction greater than 50% in the *pre*-stimulation VAS scores for the 3 active TENS groups over the 10 treatment sessions, as compared to the baseline measurement (Fig. 2). Details aside, repeated applications of TENS did not prolong the absolute duration of the half-life of TENS analgesia throughout the 10 days of treatment.

The half-life of TENS analgesia could be determined by the half-life of the analgesic action of the endogenous opioids. Han et al. (15) showed that TENS increased the release of the endogenous opioids into the cerebrospinal fluid. One could argue that when TENS is terminated, these opioid substances will gradually decay, so pain will recur. Indeed, the pharmacokinetic characteristics of an opioid can influence the onset and duration of its analgesic effect (34), with a half-life that can vary from minutes to hours. Longer stimulation duration may increase the amount of any endogenous opioids released, which could in turn result in a longer period of pain relief. However, overly prolonged stimulation could deplete the release of endogenous opioids. This is why it is important to search for the optimal TENS duration. The results of the present study

unequivocally showed that the analgesic effect plateaued after 40 minutes of TENS. In fact, further increase in the stimulation duration beyond 40 minutes did not result in greater or longer analgesic effects.

This study further demonstrated a cumulative reduction in OA knee pain after repeated applications of active but not placebo TENS. The cumulative effect of TENS after repeated stimulation in the present study was consistent with that reported for electrically induced experimental pain (16) and chronic low back pain (17). The mechanisms underlying the cumulative TENS analgesic effect are unclear. It is likely to be related to possible plastic changes in the neuronal pathway.

Most physiotherapy clinics are very busy and the usual treatment time of TENS is about 20 minutes for patients suffering from OA knee pain. Based on the present findings, 20 minutes of TENS is not the optimal treatment duration for the relief of OA knee pain. The difference in analgesic effects produced by various stimulation durations was not obvious immediately after a single session of treatment. However, repeated stimulations for 10 sessions over a 2-week period demonstrated that longer stimulation duration (40 minutes and 60 minutes) of TENS produced significantly greater reductions in VAS scores than 20 minutes of TENS or placebo stimulation. In addition, the half-life of the $TENS_{40}$ and the $TENS_{60}$ groups was significantly longer than that of the $TENS_{20}$ and $TENS_{PL}$. By the follow-up session (2 weeks after treatment terminated) the $TENS_{40}$ group even showed significantly lower VAS scores than the $TENS_{60}$ group. Therefore, 40 minutes of TENS is the optimal treatment duration for relieving OA knee pain.

As a conclusion, single sessions of 20 minutes, 40 minutes or 60 minutes of TENS produced similar magnitudes of analgesic effect immediately after stimulation, with 40 minutes and 60 minutes of TENS tending to produce analgesic effects with a longer half-life. After 10 sessions of repeated stimulations, 40 minutes and 60 minutes of TENS produced a cumulative analgesic effect on OA knee pain, which was significantly more effective than 20 minutes of TENS and placebo stimulation in terms of both the magnitude (VAS scores) and duration (half-life) of post-stimulation analgesia. Furthermore, the cumulative analgesic effect manifested by the $TENS_{40}$ group was significantly greater than those seen in the other 2 active TENS groups in the follow-up session, i.e. 2 weeks after termination of the treatment. We therefore advocate that 40 minutes is the optimal treatment duration of TENS to be used for the relief of OA knee pain.

REFERENCES

1. Scott JC, Hochberg MC. Arthritis and musculoskeletal disorders. In: Brownson RC, Remington PL, Davis JR, eds. Chronic disease epidemiology and control. Washington: Am Pub Health Ass., 1993, pp. 285–305.
2. Badley EM, Tennant A. Changing profile of joint disorders with age: findings from a postal survey of the population of Calderdale, West Yorkshire, United Kingdom. Ann Rheum Dis 1992; 51: 366–371.
3. Lawrence RC, Hochberg MC, Kelsely JL. Estimates of the prevalance of selected arthritic and musculoskeletal diseases in the United States. J Rheumatol 1989; 16: 427–441.
4. Davis MA. Epidemiology of osteoarthritis. Clins of Geriatric Medicine 1988; 4: 241–255.
5. Altman RD. Osteoarthritis: aggravating factors and therapeutic measures. Postgr Med 1986; 80: 150–163.
6. Cooke TDV, Dwosh IL. Clinical features of osteoarthritis in the elderly. Clin Rheum Dis 1986; 12: 155–172.
7. Taylor P, Hallett M, Flaherty L. Treatment of osteoarthritis of the knee with transcutaneous electrical nerve stimulation. Pain 1981; 11: 233–240.
8. Smith CR, Lewith GT, Machin D. TENS and osteoarthritic pain. PHSIA 1983; 69: 266–268.
9. Lewis D, Lewis B, Sturrock RD. Transcutaneous electrical nerve stimulation in osteoarthritis: a therapeutic alternative? Ann Rheum Dis 1984; 43: 47–49.
10. Jensen H, Zesler R, Christensen T. Transcutaneous electrical nerve stimulation (TNS) for painful osteoarthrosis of the knee. Int J Rehabil Res 1991; 14: 356–358.
11. Grimmer K. A controlled double-blind study comparing the effects of strong burst mode TENS and high rate TENS on painful osteoarthritic knees. Aust J Physiother 1992; 38: 49–56.
12. Lewis B, Lewis D, Cumming G. The comparative analgesic efficacy of transcutaneous electrical nerve stimulation. Br J Rheumatol 1994; 33: 455–460.
13. Philadelphia Panel evidence-based clinical practice guidelines on selected rehabilitation interventions for knee pain. Phys Ther 2001; 81: 1675–1700.
14. Long DM, Hagfors N. Electrical stimulation in the nervous system: the current status of electrical stimulation of the nervous system for relief of pain. Pain 1975; 1: 109–123.
15. Han JS, Chen XH, Sun SL, Xu XJ, Yuan Y, Yan SC, Hao JX, Terenius L. Effect of low- and high-frequency TENS on Met-enkephalin-Arg-Phe and dynorphin A immunoreactivity in human lumbar CSF. Pain 1991; 47: 295–298.
16. Liu J, Hui-Chan CWY. Long-term afferent conditioning produces cumulative inhibitory influence on pain sensation and flexion reflex. Proceedings of 10th Annual Spinal Cord Injury Research Symposium 1994, 8.
17. Cheing GLY, Hui-Chan CWY. Repeated application of transcutaneous electrical nerve stimulation (TENS) produce cumulative effects on chronic clinical pain but not acute experimental pain in chronic low back pain patients. The 8th World Congress on Pain 1996; 8: 85.
18. Cheing GLY, Hui-Chan CWY. Repeated afferent conditioning produced cumulative effect on osteoarthritic knee pain. The 28th Annual Meeting of the Society for Neuroscience 1998; 24: 884.
19. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthritis. Ann Rheum Dis 1957; 16: 494–502.
20. Cheing, GLY, Hui-Chan CWY. The motor dysfunction of patients with osteoarthritic knee in a Chinese population. Arthritis Care Res 2001; 45: 62–68.
21. Walsh DM, McAdams ET. TENS: Clinical Applications and Related Theory. New York: Churchill Livingstone, 1997.
22. Price DD, MsGrath PA, Rafii A, Buckingham B. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. Pain 1983; 17: 45–56.
23. Wade JB, Price DD, Haber RM, Schwartz SM, Hart RP. An emotional component analysis of chronic pain. Pain 1990; 40: 303–310.
24. Price DD, Harkins SW. The combined use of visual analogue scales and experimental pain in providing standardized assessment of chronic pain. Clin J Pain 1987; 3: 2–11.
25. Harkins SW, Price DD, Braith J. Effects of extraversion and neuroticism on experimental pain, clinical pain, and illness behaviour. Pain 1989; 36: 209–218.
26. Wensel LO. Acupuncture in medical practice. Virginia: Reston Publishing Company, 1980, pp. 15–62.
27. Stux G, Pomeranz B. Basics of Acupuncture. New York: Springer-Verlag, 1988.
28. Andersson SA, Holmgren E. On acupuncture analgesia and the mechanisms of pain. Am J Chin Med 1975; 3: 311–318.

29. Melzack R, Stillwell GK, Fox EJ. Trigger and acupuncture points for pain: correlations and implications. Pain 1977; 3: 3–23.
30. Hochberg Y, Benjamini Y. More powerful procedure for multiple significance testing. Stat Med 1990; 9: 811–818.
31. Cheing GLY, Hui-Chan CWY. Transcutaneous electrical nerve stimulation: Non-parallel antinociceptive effects on chronic clinical pain and acute experimental pain. Arch Phys Med Rehab 1999; 80: 305–312.
32. Wang JQ, Mao L, Han JS. Comparison of the antinociceptive effects induced by electroacupuncture and transcutaneous electrical nerve stimulation in the rat. Int J Neurosci 1992; 65: 117–129.
33. Woolf CF. Segmental afferent fibre-induced analgesia: transcutaneous electrical nerve stimulation (TENS) and vibration. In: Wall PD, Melzack R, eds. Textbook of Pain. London: Churchill Livingstone, 1991, pp. 884–896.
34. Lipman AG. Clinically relevant differences among the opioids analgesics. Am J Hosp Pharm 1990; 47 Suppl 1: S7–13.