

Electrodermal Measures of Jing-Well Points and Their Clinical Relevance in Endometriosis-Related Chronic Pelvic Pain

Andrew C. Ahn, M.D., M.P.H.,^{1,2} Rosa Schnyer, D.A.O.M., L.Ac.,^{1,3,4} Lisa Conboy, Sc.D.,^{1,3}
Marc R. Laufer, M.D.,⁵ and Peter M. Wayne, Ph.D.^{1,3}

Abstract

Objectives: To determine whether electrodermal measures at Jing-Well acupuncture points, “indicator” points located at the tips of fingers and toes are associated with clinical measures in adolescent women with chronic pelvic pain.

Design: The design of this study was a randomized sham-controlled trial. Analyses of electrodermal measures were based on longitudinal, multivariable analyses using generalized estimating equations.

Subjects and setting: The subjects were 14 young women (ages 14–22) with laparoscopically diagnosed endometriosis and chronic pelvic pain. Subjects were randomized to sham acupuncture or Japanese-style active acupuncture. Sixteen (16) treatments were administered over 8 weeks.

Outcome measures: Using a Hibiki-7 device, electrodermal impedance measures were obtained at all 24 Jing-Well points for each treatment visit. From these readings, measures of “imbalance” were determined by calculating statistical dispersion (statistical deviation and Gini coefficient) and level of asymmetry (left–right, top–bottom, and *yin–yang*). Clinical outcome measures were obtained at baseline, week 4, and week 8 and included level of pelvic pain, Endometriosis Health Profile, Pediatric Quality of Life, perceived stress, and inflammatory cytokine levels (interleukin-6 and tumor necrosis factor- α).

Results: Participants designated to the acupuncture group had, on average, a substantial decrease in statistical dispersion and asymmetry of Hibiki-7 values over the course of treatment compared to the sham group. Electrodermal asymmetry variables, specifically either *yin–yang* or left–right measure, were significantly associated with pelvic pain, Endometriosis Health Profile, Pediatric Quality of Life, and Perceived Stress even after adjusting for treatment designation. No associations between electrodermal balance measures and inflammatory cytokines were found.

Conclusions: Electrodermal measures may be significantly associated with clinical outcome and acupuncture treatments in adolescent women with chronic pelvic pain.

Introduction

FOR MORE THAN 50 YEARS, electrodermal instruments have been used for clinical diagnoses and are based on the premise that electrical measurements at strategic skin points reflect one’s health.¹ These electrical measures are frequently acquired at acupuncture points located on the extremities or

the ear. Depending on the technique, the electrical impedance is measured at a specified point or set of points to gain insight into a specific organ, disease state, or global health condition. Prognos (MedPrevent, Waldershof, Germany), Apparatus for Meridian Identification (AMI, Institute of Life Physics, Tokyo, Japan), Neurometer (Ryodoraku Research Center Ltd., Tokyo, Japan), Dermatron (Pitterling Electronic, Munich, Germany),

¹Division for Research and Education in Complementary and Integrative Medical Therapies, Harvard Medical School, Boston, MA.

²Division of General Medicine and Primary Care, Beth Israel Deaconess Medical Center, Boston, MA.

³New England School of Acupuncture, Watertown, MA.

⁴University of Texas, Austin, TX.

⁵Division of Gynecology, Children’s Hospital Boston, Boston, MA.

Hibiki-7 (Asahi Butsuruyooki Research Lab, Kita Kyoto, Japan), and AcuGraph (Meridia Technology Inc., Meridian, ID) are just a few examples of these electrodermal devices being applied to the clinical setting. Although these devices vary in their recommended testing sites, probe design, and electrical parameters, these devices share common barriers that continue to make them a subject of considerable controversy and skepticism. These barriers include the lack of a physiologic basis for the diagnostic method, the existence of multiple confounders associated with electrode–skin contact, and the lack of rigorous clinical studies to assess their validity.² Nevertheless, the manufacturers of these devices continue to assert the clinical usefulness of electrodermal diagnosis and cite clinical evidence—largely anecdotal—to support their claim.

According to many electrodermal proponents, the marker of good health is proper “balance” of energies across multiple meridians.^{3,4} This is assessed by identifying “abnormalities” in electrodermal readings at a particular meridian or “asymmetries” in measurements between the left and right meridians or between *yin* and *yang* meridians.^{5–9} The electrodermal readings are typically obtained at Jing-Well points located on the tips of the fingers and toes.^{2,10}

To our knowledge, however, electrodermal measurements have never been systematically evaluated in a prospective clinical trial where the electrodermal measures are gauged against standard outcome measures and where they are monitored over time to assess their correlation with the disease course. We recently completed a randomized controlled trial evaluating Japanese-style and sham acupuncture for the treatment of chronic pelvic pain in adolescents with surgically diagnosed endometriosis.¹¹ In this trial, a Hibiki-7 device was used at each acupuncture visit to measure electrical impedance at Jing-Well points located at the tip of fingers and toes. The device was used for both diagnostic and therapeutic purposes. Multiple clinical outcome measures were also obtained to assess the level of pelvic pain and quality of life for each subject. These collected data presented an opportunity to effectively and quantitatively evaluate the clinical utility of electrodermal measures for pelvic pain.

The objective of this study is to determine whether electrodermal measures at Jing-Points are associated with clinical measures in adolescent women with chronic pelvic pain. We hypothesize that electrodermal patterns, as determined by dispersion and asymmetry magnitudes across meridians, are associated with pelvic pain and quality of life. We also hypothesize that participants randomized to acupuncture treatments experience changes in electrodermal patterns over time, while individuals designated to the sham arm do not.

Materials and Methods

Randomized clinical trial

The pilot randomized controlled trial evaluating Japanese-style acupuncture for endometriosis-related pelvic pain was conducted through Boston’s Children Hospital and the New England School of Acupuncture from November 2005 to December 2007. Of 550 subjects approached for the study, a total of 18 subjects met eligibility criteria and were randomized to a treatment arm. Eligibility criteria for study participants included the following: age 13–22, diagnosis of stage 1, 2, or 3 endometriosis as determined by laparoscopic

surgery within the past 5 years, persistent pelvic pain with an intensity between 2 and 8 on a 10-point numerical scale, no prior experience with acupuncture, and living within 2 hours of the Boston metropolitan area. Subjects who were pregnant or lactating, had history of drug or alcohol abuse, used GnRH analogue such as DepoLupron within the 6 months prior to study participation, or had coexisting disabling physical or psychiatric conditions were excluded.

Ten (10) subjects were assigned to active acupuncture, while 8 subjects were assigned to sham acupuncture. Four (4) subjects (1 from the active group and 3 from the sham group) dropped out of the study. Participants assigned to both active and sham groups underwent a total of 16 acupuncture treatments: 2 per week for 8 consecutive weeks. Treatments were administered by a total of 7 licensed acupuncturists with specific training in Japanese style. All acupuncturists were New England School of Acupuncture graduates or faculty, and all treatments were done in their clinical offices. The active acupuncture treatment was a manualized approach to pelvic pain based on the Japanese-style acupuncture developed by Shima and Chace³ and Manaka.⁴ Treatment elements of the protocol are outlined in a companion publication¹² and include: (1) needling 8–12 points to activate and balance Extraordinary and Divergent acupuncture channels; (2) burning of moxibustion (warming herb) on both back *shu* acupuncture points and sacral areas; and (3) electrostimulation of reactive auricular acupuncture points using the Hibiki-7 device. Sham acupuncture was designed to mimic active treatments, and it employed a validated nonpenetrating “Streitberger” acupuncture device.¹³ To minimize any therapeutic effect, sham needles were positioned at nonacupuncture points and without meridian palpation. Sham moxibustion and sham ear stimulation were similarly modeled after active interventions and implemented within the sham treatments.

Clinical outcome measures were obtained at baseline and at 4 weeks, 8 weeks, and 6 months following commencement of acupuncture treatment. The primary outcome measure was change in pelvic pain after 8 weeks of treatment. Patients were asked to rate pain severity during their past 4 weeks that was not associated with menses and sexual activity from a scale of 0–10, with 0 equaling “absent” pain and 10 equaling “severe” pain. Additionally, health-related quality of life (HRQOL) was assessed with the use of four secondary outcome measures: (1) Endometriosis Health Profile-30; (2) Pediatric Quality of Life Inventory; (3) Perceived Stress Scale; and (4) a participant-generated list of 3 activities made difficult due to pelvic pain. The Endometriosis Health Profile-30 measures endometriosis-specific HRQOL.¹⁴ It consists of 30 items divided into 5 subscales (pain, control/powerlessness, emotional well-being, social support, self-image). Total scores range from 0 to 100, with a lower score reflecting fewer symptoms and better HRQOL. The Pediatric Quality of Life inventory is a less disease-specific instrument and measures HRQOL in children and adolescents ages 2–18.¹⁵ Total scores on the Pediatric QOL Inventory range from 0 to 100, with a higher score indicating better HRQOL. The Perceived Stress Scale is a measure of the degree to which situations in one’s life are appraised as stressful.¹⁶ Total scores range from 0 to 4, with lower scores indicating less perceived stress. Finally, a single question instrument was used to assess the degree to which

patients' pelvic pain interfered with daily activities.¹¹ Participants were asked to generate a list of three activities made difficult by their pelvic pain, and on a numerical scale of 0–10, rate how difficult each item is to perform (10, most difficult).

Inflammatory markers were also drawn at baseline, 4 weeks, and 8 weeks. Blood samples were tested for interleukin 6 (IL-6) and tumor necrosis factor α (TNF- α) using Quantikine high-sensitivity solid-phase enzyme-linked immunoassay (R&D Systems, Minneapolis, MN). These cytokines were chosen due to evidence showing that levels of IL-6 and TNF- α can help discriminate between patients with endometriosis and those without.¹⁷ Details regarding the methods and results for this clinical trial can be found in the primary publication.¹¹

Electrodermal measures

At each acupuncture visit and prior to each treatment, electrical impedances at Jing-Well points were measured using the Hibiki-7 device (Asahi Butsuruyooki Research Lab, Kita Kyoto, Japan). The Hibiki-7 is both a diagnostic and therapeutic instrument developed by Shigeji Naomoto in the 1980s.³ The device measures impedance by introducing electrical potentials from a metal cylinder (held by the subject) to a 2-mm metallic probe tip placed onto the acupuncture point (by the practitioner). Biphasic voltage spikes with peak-to-peak magnitudes of up to 100 V, pulse width of 400 μ sec, and frequency of 12–20 Hz are delivered. The voltage amplitudes are adjustable, and the device displays current amplitudes ranging from 0 to 100 μ A. The impedance values are normalized by calibrating the device to 100 μ A when the probe tip is contact with the metal cylinder. According to the Japanese technique, skin readings between 10 and 20 are considered "normal" while readings below 10 indicate excess and readings above 20 indicate deficiency.

In this clinical trial, all 24 Jing-Well points—six points for each hand and foot—were measured as part of the diagnostic approach for each subject. For finger Jing-Well points, the metal cylinder was held in the hand contralateral to the one being measured. For toe Jing-Well points, the cylinder was held in either hand. The order of testing was random. Practitioners were instructed to firmly place the probe tip on the skin without adjusting pressure, angle, or point locations. In addition, practitioners were told not to maintain the probe on a point for too long since the Hibiki-7 device theoretically begins treatment of the point after a certain period of time. All 16 sets of impedance values (one set for each treatment) were obtained in 13 of the 14 study participants. For the subject who did not complete all 16, 14 sets of impedance were obtained.

The success of patient blinding was assessed after the second and final acupuncture treatments with a self-administered instrument used in prior acupuncture trials.^{18,19} The instrument asks subjects to indicate the treatment group to which they believed they were assigned by circling the applicable statement: (a) I believe I am in the active acupuncture group; (b) I believe I am in the inactive, sham acupuncture group; (c) I am unsure what group I am in. If they chose response (a) or (b), they were also asked how confident they were of their answer on a 5-point Likert scale. The degree to which subjects were blinded to treatment allocation did not differ statistically between groups.

Statistical analysis

To derive measures of clinical relevance, we calculated the level of imbalance across all impedance measurements. This was achieved by formulating measures of statistical dispersion and asymmetry. Dispersion was defined as the variance in impedance values across the 12 meridians and was represented by two derived variables: standard deviation and the Gini coefficient. Both variables were calculated by initially averaging the Jing-Well impedances from the left and right side for each associated meridian.

The Gini coefficient is a nonparametric measure for statistical dispersion frequently used to determine the level of inequality in income distribution and size hierarchies in biological populations.^{20–23} A low Gini coefficient indicates more equal distribution, while a high Gini coefficient indicates more unequal distribution. The coefficient ranges from 0 to 1, with 0 corresponding to perfect equality and 1 corresponding to perfect inequality. For this study, the impedances for each set of meridians were placed in nondecreasing order and placed into the following formula:

$$Gini = \frac{2 \sum_{i=1}^n iy_i}{n \sum_{i=1}^n y_i} - \frac{n+1}{n}$$

where n is the number of meridians ($n = 12$), i is the order in which a meridian is placed, and y_i is the impedance for the corresponding meridian ($y_i \leq y_{i+1}$). In past electrodermal studies, statistical dispersion measures have been used as a clinical correlate.^{5,9}

Meridian asymmetry was represented by three variables: left–right, *yin–yang*, and top–bottom asymmetries. Left–right represented differences between the left and right impedance values; *yin–yang* represented differences between corresponding *yin–yang* meridians (e.g., Kidney and Urinary Bladder); and top–bottom represented differences between the upper and lower meridian (e.g., Stomach and Large Intestine). Each asymmetry value was calculated using a dissimilarity matrix where the absolute differences in impedances between all relevant comparisons were added up and averaged:

$$Asymmetry = \frac{1}{n} \sum_{i=1}^n |X_i - Y_i|$$

where n is the number of meridians ($n = 12$), X_i is the impedance values for i th left, top, or *yin* meridians, and Y_i is the impedance values for the corresponding i th right, bottom, or *yang* meridian, respectively. Like dispersion, asymmetry measures, particularly left–right asymmetry, have been used by electrodermal instruments to assess one's health status.³

To determine whether the Hibiki-7 measures were associated with the treatment designation or a clinical outcome, the imbalance measures were dichotomized two separate ways: (1) acupuncture versus sham and (2) responder versus nonresponders. "Responders" were defined as individuals who experienced a 30% or more improvement in pelvic pain over baseline at 8 weeks (primary outcome) regardless of intervention. To obtain a visual perspective of trends, the average meridian impedances, dispersion (standard deviation (SD)

and Gini), and asymmetry measurements (left–right, *yin–yang*, and top–bottom) were mapped across time and categorized according to these dichotomizations. To account for temporal variability, the dispersion and asymmetry measurements were averaged over a 2-week period at 4 and 8 weeks after the commencement of treatment. Generalized estimating equations were used to determine whether changes in dispersion and asymmetry variables over time were significantly associated with treatment designation (acupuncture versus sham) or clinical response (responder versus nonresponder). Electrodermal measures of dispersion and symmetry were assigned dependent variables while the dichotomized variable (treatment designation or clinical response) and the interaction term between the dichotomized variable and time were used as independent variables.

To statistically determine whether imbalance measures correlated with clinical outcome, generalized estimating equations were used to account for time and for repeated measures across individuals. Pelvic pain scores, Endometriosis Health Profile-30, Pediatric Quality of Life Inventory, and Perceived Stress Scale were individually designated as dependent variables while the treatment designation, statistical dispersion, and meridian asymmetry measures were entered as independent variables. Individual meridian values were also entered. Interaction terms between time (in weeks) and each dependent variable were created to account for potential relationships between temporal trends in outcomes and dependent variables. Because the clinical outcomes were an assessment of symptoms over the past 4 weeks, the electrodermal measures were averaged over four readings leading up to and including the 4-week and 8-week time point. A backward elimination approach was used where variables were entered into the model if a univariable relationship of $p < 0.10$ was found and variables with lowest significance (as determined by highest p -value) were sequentially removed. Variables were kept in the model if a statistical level of $p < 0.05$ was maintained.

Multivariable analyses for the cytokine laboratory tests (IL-6 and TNF- α), as dependent variables, were also performed. Because these tests were reflections of immediate inflammatory activity, the electrodermal measures entered into the model were instantaneous readings obtained on the day the cytokine tests were obtained.

Results

Baseline characteristics of the participants are summarized in Table 1. All subjects were diagnosed with stage I endometriosis, which is consistent with profiles of endometriosis in adolescent populations. On average, participants had greater top–bottom asymmetry than the other two asymmetry measures. As seen in Figure 1, the Jing-Well impedance profile showed abnormally elevated (>20) Hibiki-7 levels at the Spleen, Kidney, and Liver Jing-Well points in study participants. Of the 14 subjects, 6, 10, and 11 subjects had abnormally elevated Hibiki readings at the Spleen, Kidney, and Liver Jing-Well points, respectively. For other Jing-Well points, the mean Hibiki-7 values fell within “normal” (10–20) limits, although the large standard deviations indicate that not all subjects had normal levels at these points.

Participants designated to the acupuncture group had, on average, a substantial decrease in statistical dispersion and

TABLE 1. PARTICIPANT CHARACTERISTICS AT BASELINE

Baseline characteristics	Subjects (N = 14)
Demographics	
Age, y, mean (\pm SD)	17.9 (2.5)
Age, range	14–22
Hispanic or Latino	14%
White	100%
Clinical measures	
Stage of endometriosis	
Stage I	100%
Pain, mean	7.6 (1.9)
Endometriosis Health Profile	36.7 (18.6)
Pediatric QOL inventory	67.0 (12.8)
Perceived Stress Scale	1.6 (0.7)
Inflammatory cytokines	
IL-6, pg/mL, mean (\pm SD)	1.50 (0.54)
TNF- α , pg/mL, mean (\pm SD)	1.17 (0.95)
Electrodermal measures	
Dispersion	
Statistical deviation, mean (\pm SD)	11.4 (3.7)
Gini coefficient, mean (\pm SD)	0.32 (0.10)
Asymmetry	
Left–right	9.1 (4.8)
Top–bottom	13.8 (5.2)
<i>Yin–yang</i>	11.0 (4.5)

y, years; SD, standard deviation; QOL, quality of life; IL-6, interleukin 6; TNF- α , tumor necrosis factor α .

asymmetry of Hibiki-7 values over the course of treatment. As shown in Figure 2A and B, the variance in impedance measures across meridians diminished with time, largely attributed to changes in the Spleen, Kidney, and Liver Jing-Well points. Figure 2C further documents this observed trend by both standard deviation and Gini coefficient measures. In contrast, the Sham group had an increase in statistical dispersion over the same period of time. This difference in trend was statistically significant for standard deviation ($p = 0.02$) but not Gini coefficient ($p = 0.58$). Differences in trend between acupuncture and sham groups were also observed for all three asymmetry measures (Fig. 2D). The difference was statistically significant for left–right and *yin–yang* asymmetry ($p = 0.0002$, $p = 0.005$, respectively) but not top–bottom asymmetry ($p = 0.1$).

For subjects who reported a 30% improvement in their pelvic pain at 8 weeks, the average variance of Hibiki-7 Jing-Well measurements decreased over time, in contrast with those who did not have a 30% improvement (Fig. 3A and B). These trends were also seen with the two dispersion measures (particularly, the Gini coefficient), but were not as distinct as the changes observed with the acupuncture and sham groups (Fig. 3C) and were not statistically significant for either standard deviation or Gini coefficient ($p = 0.36$ and 0.63 , respectively). The three asymmetry measures generally showed similar patterns with a negative trend for responders and a positive trend for nonresponders, the one notable exception being the left–right asymmetry values for nonresponders where the trend was negative (Fig. 3D). No significant relationships between clinical response and trends in asymmetry measures were observed.

The univariable and multivariable analyses for the clinical outcome and inflammatory measures are shown in Table 2 and Table 3, respectively. Only statistically significant vari-

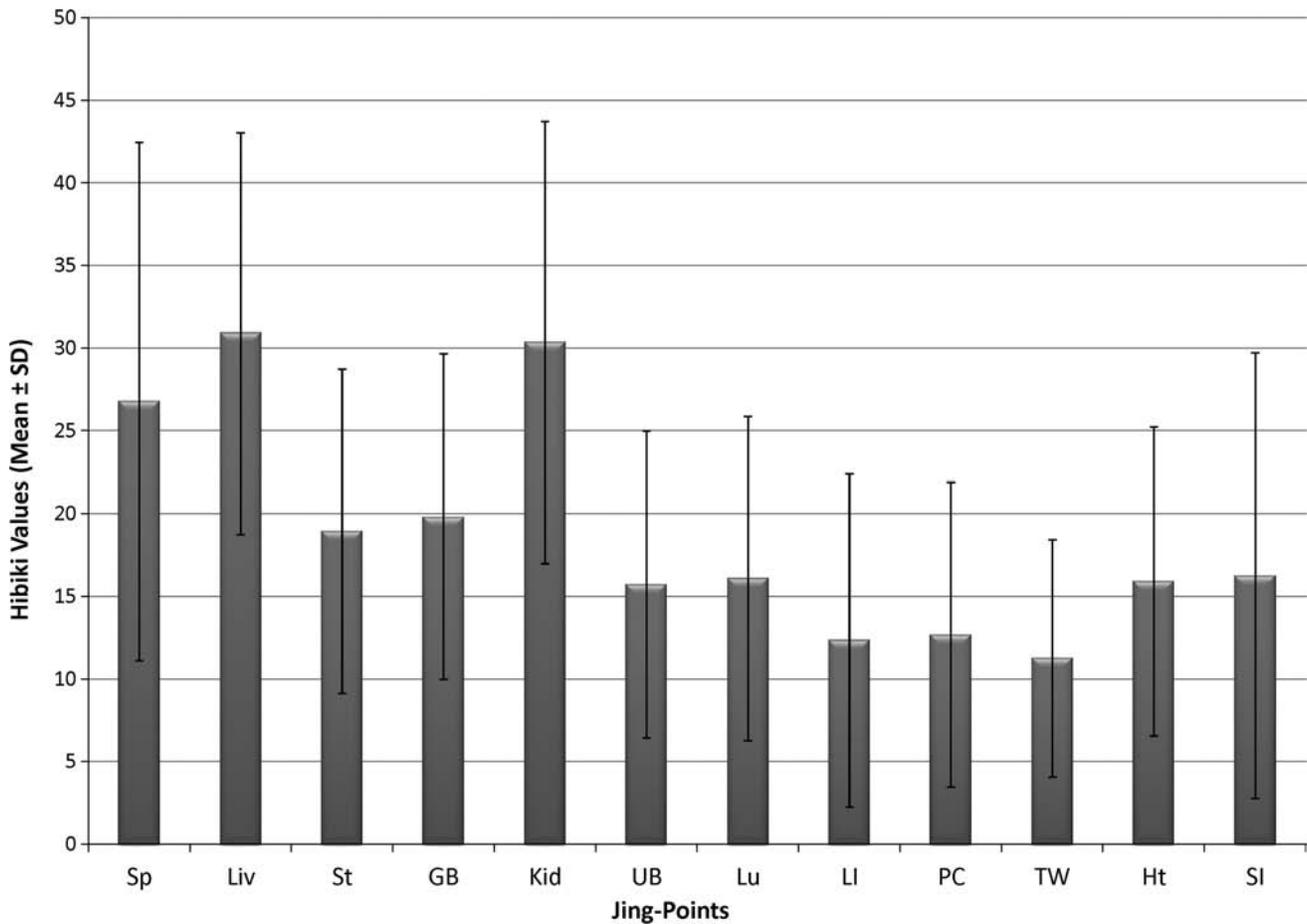


FIG. 1. Baseline electrodermal measures by meridian.

ables are listed. Treatment designation (acupuncture versus sham) is a significant variable for pelvic pain and all QOL measures, and, with the exception of Pediatric QOL, maintains its significance in multivariable analyses. Acupuncture is associated with improvements in pain, endometriosis HRQOL, and perceived stress and with reductions in TNF- α levels. The significance of the interaction term—treatment with time—in the univariable analyses suggests that treatment designation accounts for the temporal changes in clinical outcomes. However, the interaction term loses significance in the multivariable models and is attributable to the more robust association between electrodermal asymmetry variables and the outcome measures within the analyses. These results are similar to the results reported in the original publication¹¹ but differ statistically due to use of a different statistical model.

Electrodermal asymmetry variables, specifically *yin-yang* and left-right measures, were significantly associated with pelvic pain and QOL scores in both univariable and multivariable analyses. For pediatric QOL scores, *yin-yang* asymmetry was the only remaining variable after the backward elimination approach was completed. Top-bottom asymmetry and both statistical dispersion measures (statistical deviation and Gini coefficient) were significantly associated with pelvic pain in univariable analyses, but lost significance in multivariable modeling due to collinearity with treatment designation. No electrodermal imbalance

measures were significantly associated with inflammatory cytokines, and, conversely, no individual meridian measures remained significant in multivariable analyses of any of the clinical outcome measures assessed in this study.

Discussion

In this clinical trial of Japanese-style and sham acupuncture for chronic pelvic pain, subjects had elevated Hibiki-7 measures at the Liver, Spleen, and Kidney Jing-Well points at baseline. These abnormal values decreased over time with the active, but not sham, acupuncture treatments. These changes were reflected in the dispersion and asymmetry electrodermal measures. In univariable analyses, electrodermal imbalance measures were associated with pelvic pain and quality of life measures, but with multivariable modeling, the associations with the clinical outcomes were narrowed to designated treatment and to one of two asymmetry variables: *yin-yang* or right-left asymmetry. Other than a single meridian (left Kidney or right Stomach), electrodermal measures were not associated with IL-6 or TNF- α levels.

The clinical significance of the increased Hibiki values at the Liver, Spleen, and Kidney points is unclear. These Jing-Well points and their associated meridians are located on the inner aspect of the lower extremity. Consequently, the results can be interpreted as a technical effect stemming from the placement of the electrodes on the inner toes or the current

trajectory from the probe tip (toes) to the passive electrode (hands). However, the temporal reductions observed in these Hibiki values with the active and not sham interventions argue for a physiologic rationale that is not yet elaborated.

The idea that certain diseases or conditions are attached to particular electrodermal patterns is not new and is used to

advocate for the clinical utility of these electrodermal devices. For instance, in 1973, Bergsmann described statistically different voltage-current measurements at right Liver 9 in patients with "liver disturbances" compared to measurements at adjacent skin areas, the left Liver 9, or at right Liver 9 in healthy controls.²⁴ Saku also described statistically

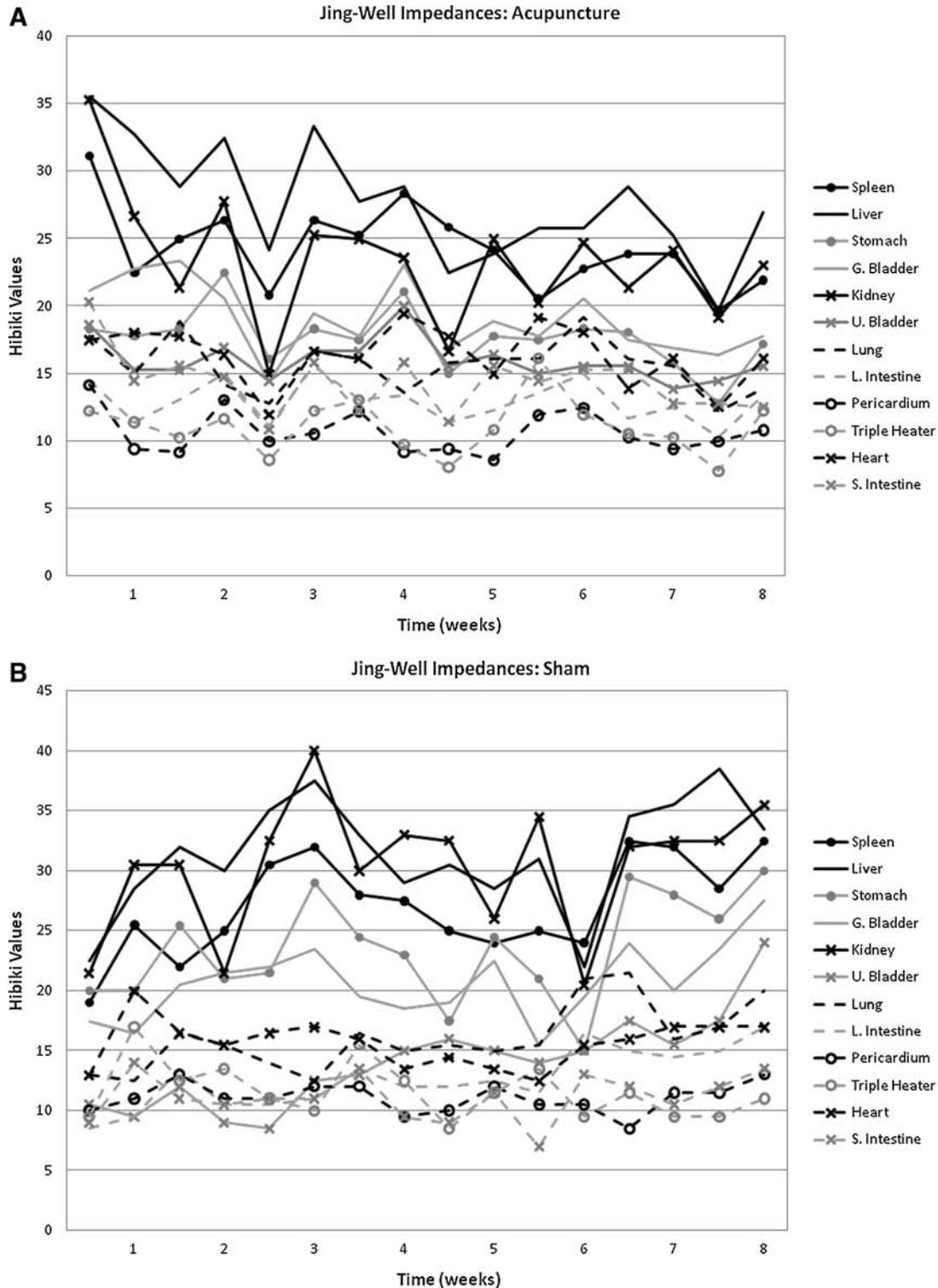


FIG. 2. Electrodermal measures by treatment arm. **A:** Jing-Well impedances over time: acupuncture. **B:** Jing-Well impedances over time: sham. **C:** Statistical dispersion over time. SD, standard deviation. **D:** Asymmetry measurements over time.

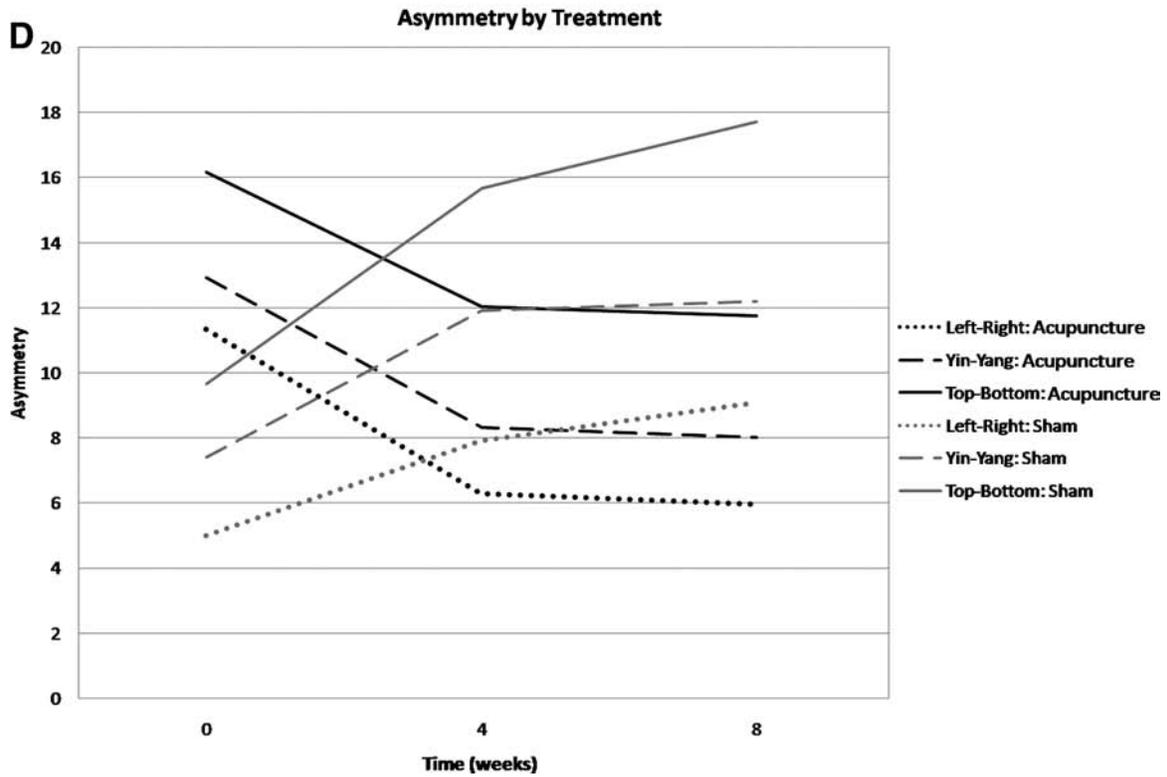
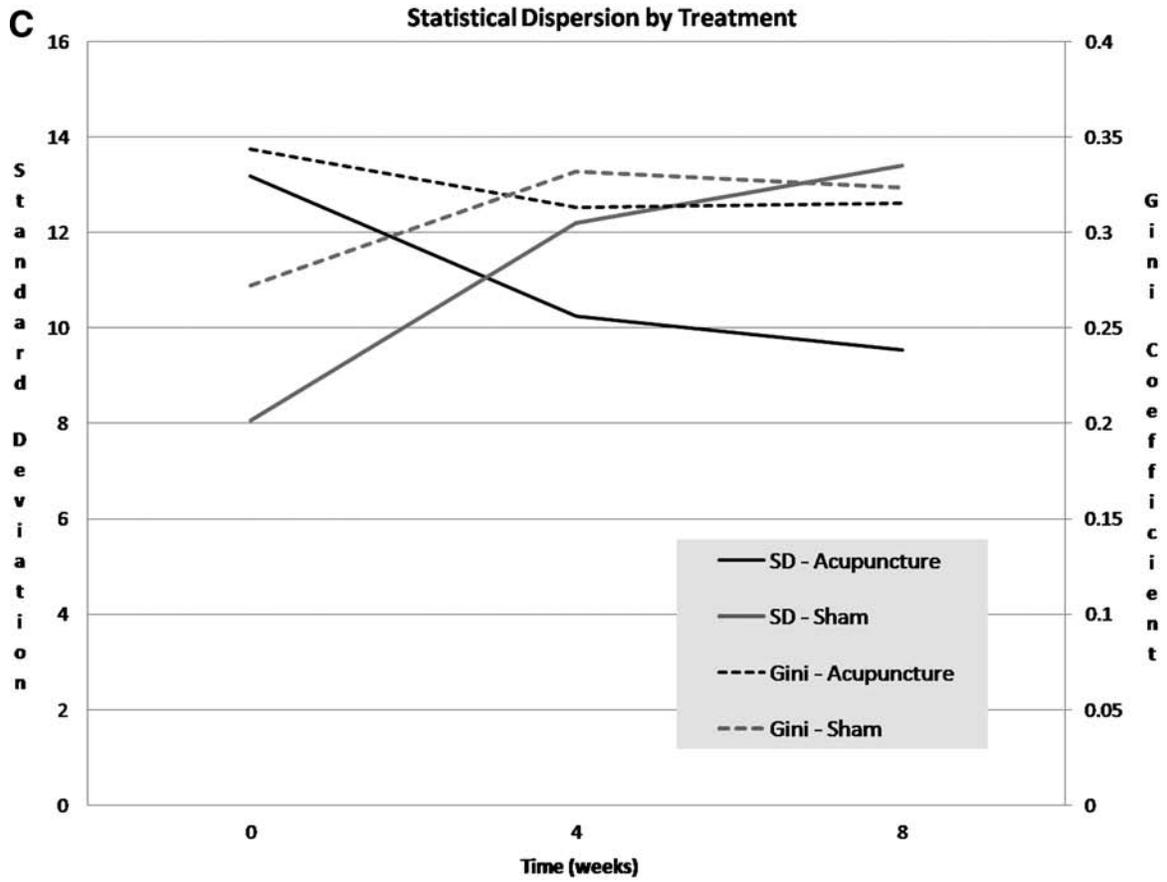


FIG. 2. (Continued).

significant differences in electrical impedance at auricular Heart points in patients with acute or old myocardial infarctions compared to healthy controls.²⁵ Other studies have similarly reported distinct electrodermal patterns in certain

medical conditions, but, like these two studies, were limited by the lack of objective confirmation for the disease.²⁶⁻³⁵ Although patients in our study were laparoscopically diagnosed with endometriosis, the lack of a healthy or non-

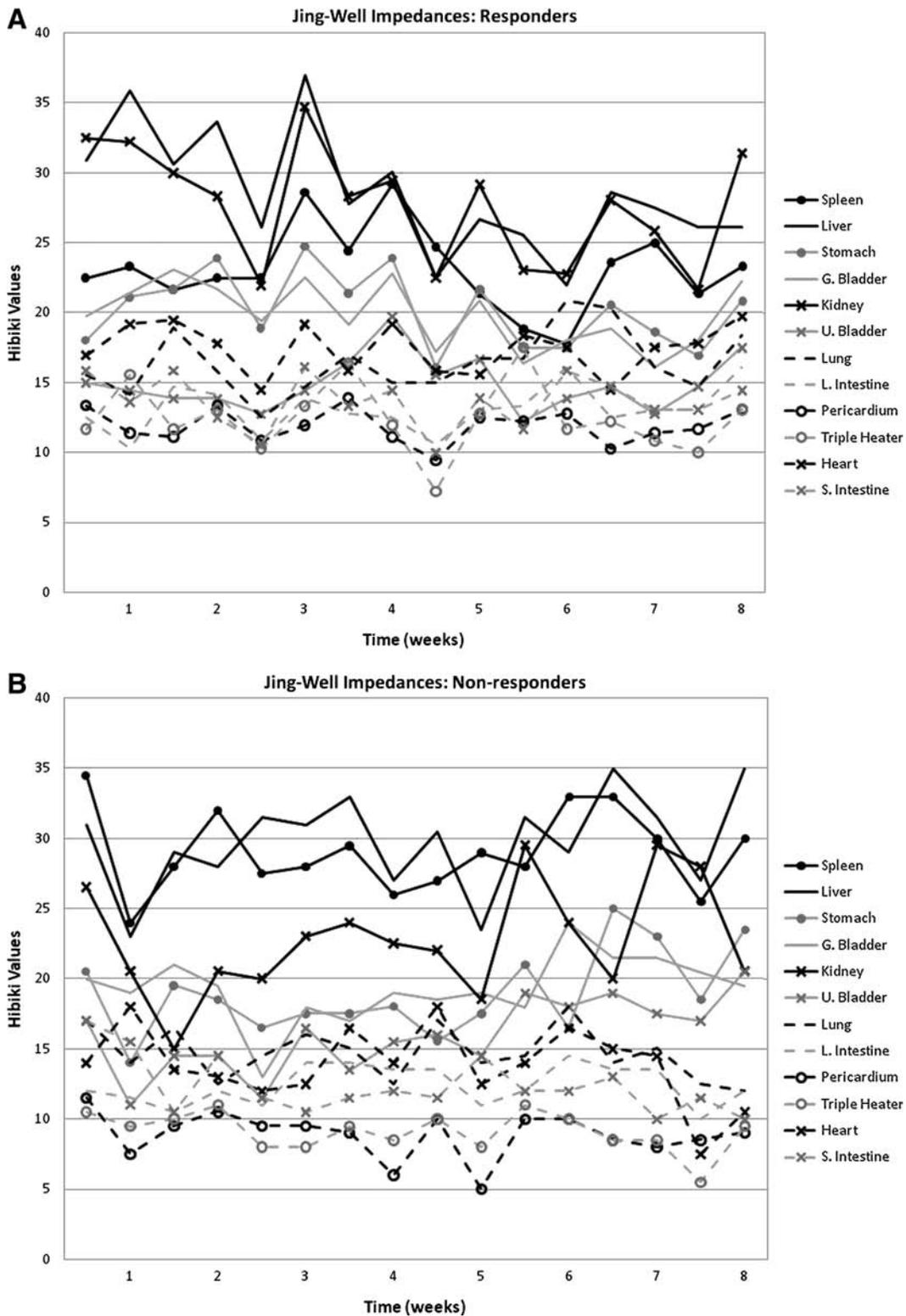


FIG. 3. Electrodermal measures by clinical response. **A:** Jing-Well impedances over time: clinical responders. **B:** Jing-Well impedances over time: clinical nonresponders. **C:** Statistical dispersion over time. SD, standard deviation. **D:** Asymmetry measurements over time.

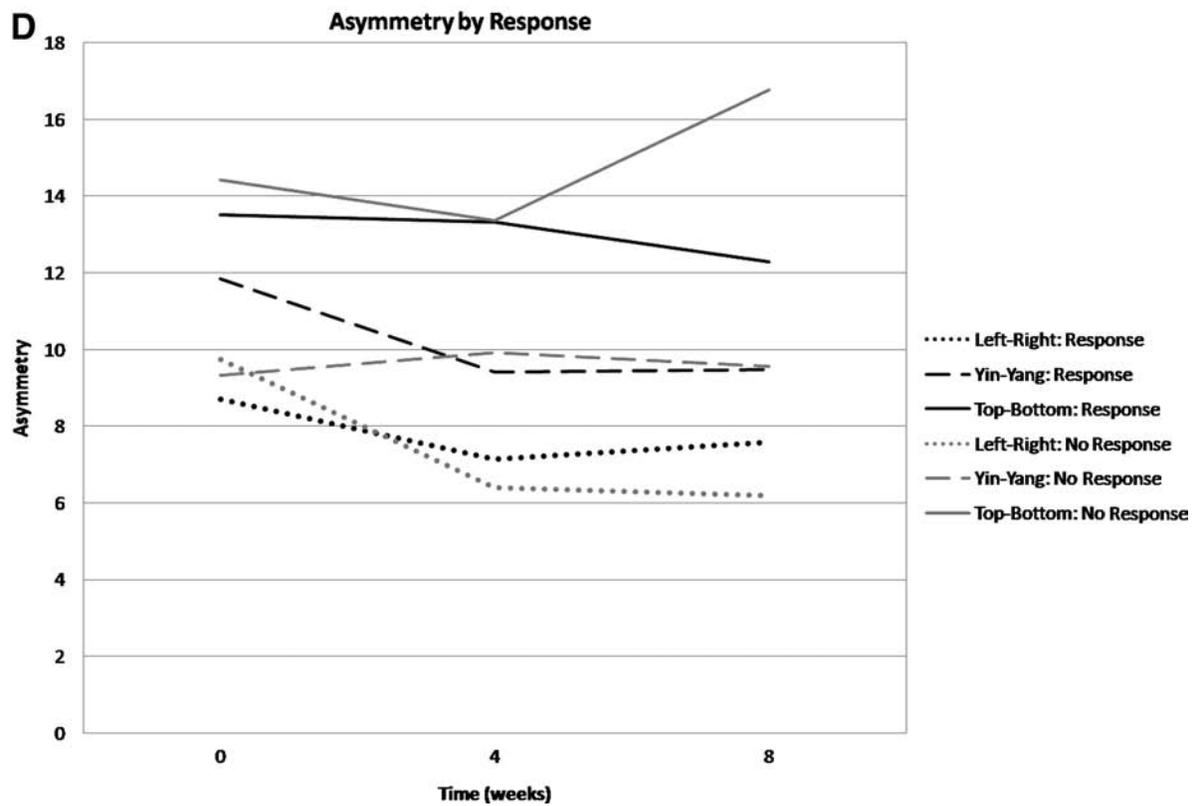
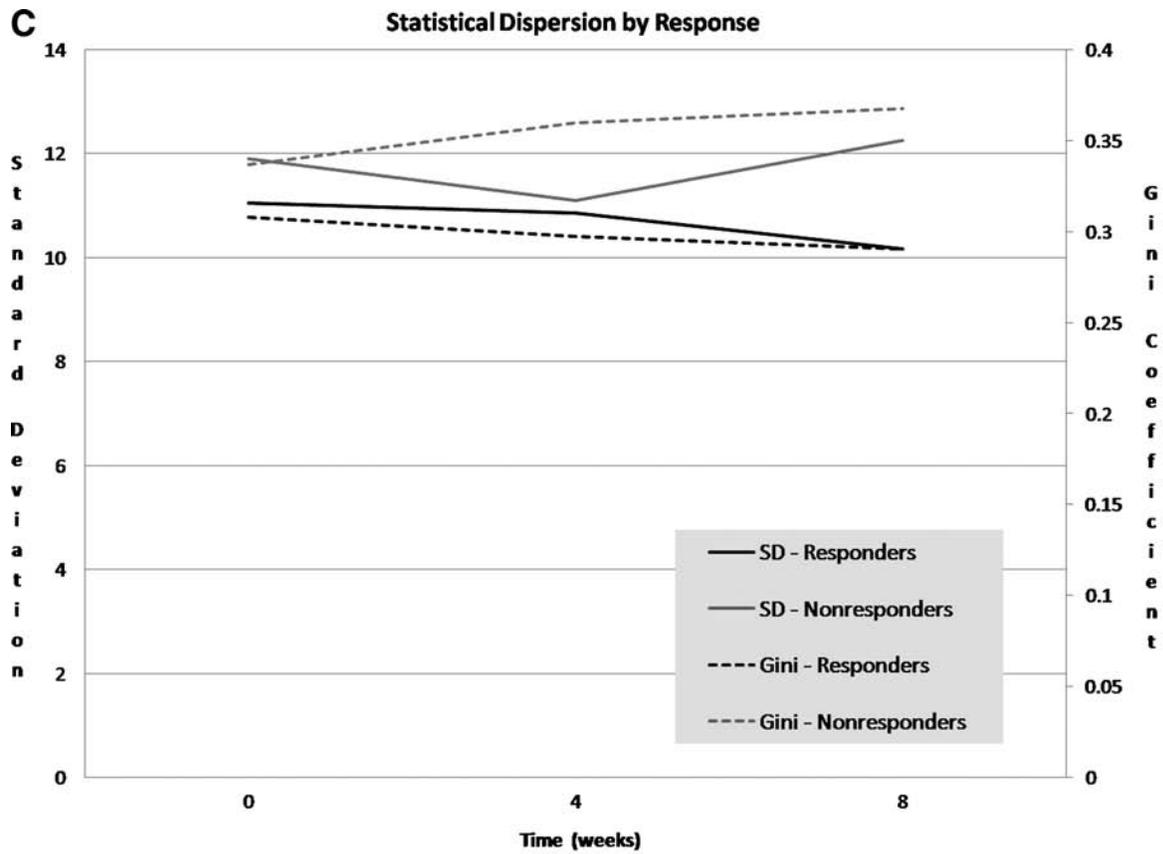


FIG. 3. (Continued).

TABLE 2. UNIVARIABLE ANALYSES: ASSOCIATIONS BETWEEN TREATMENT/ELECTRODERMAL MEASURES AND CLINICAL OUTCOME

Treatment and electrodermal measures	Pelvic pain over 4 weeks	Endometriosis HRQOL-30	Pediatric QOL	Perceived stress	IL-6	TNF- α
Intervention	-1.38	-19.64	8.47	-0.42	-0.91	-0.38
Treatment designation (sham as reference)	(<i>p</i> = 0.09)	(<i>p</i> < 0.0001)	(<i>p</i> = 0.013)	(<i>p</i> = 0.014)	(<i>p</i> = 0.085)	(<i>p</i> = 0.044)
Treatment*time	-0.47	-3.52	1.87	-0.08		-0.05
	(<i>p</i> < 0.0001)	(<i>p</i> < 0.0001)	(<i>p</i> = 0.0003)	(<i>p</i> = 0.002)		(<i>p</i> = 0.084)
Imbalance measures						
Standard deviation			-0.92			
			(<i>p</i> = 0.06)			
Std dev*time	-0.03					
	(<i>p</i> = 0.007)					
Gini coefficient	-1.27					
Gini*time	(<i>p</i> = 0.0003)					
Right-left asymmetry	0.31	1.92	-1.36	0.05		
	(<i>p</i> = 0.007)	(<i>p</i> = 0.012)	(<i>p</i> = 0.005)	(<i>p</i> = 0.063)		
Right-left*time	-0.04					
	(<i>p</i> = 0.015)					
Yin-yang asymmetry	0.30	1.55	-1.37			
	(<i>p</i> = 0.004)	(<i>p</i> = 0.024)	(<i>p</i> = 0.0008)			
Yin-yang*time	-0.03					
	(<i>p</i> = 0.025)					
Top-bottom asymmetry			-0.57			
			(<i>p</i> = 0.06)			
Top-bottom*time	-0.02					
	(<i>p</i> = 0.024)					
Meridian measures ^a						
Left-Sp*time	-0.01					
	(<i>p</i> = 0.005)					
Right-Sp*time	-0.01					
	(<i>p</i> = 0.0008)					
Left-Liv*time	-0.01					
	(<i>p</i> = 0.003)					
Right-Liv*time	-0.01					
	(<i>p</i> = 0.0018)					
Right-GB*time	-0.02					
Left Kidney						
			-0.39			
			(<i>p</i> = 0.002)			
Left-Kid*time					0.006	
					(<i>p</i> = 0.0065)	
Right-SI*time	-0.03					
	(<i>p</i> = 0.004)					

^aOnly univariable associations of *p* < 0.01 are listed under this category.

HRQOL, health-related quality of life; IL-6, interleukin 6; TNF- α , tumor necrosis factor α ; Sp, Spleen; Liv, Liver; GB, Gall Bladder; SI, Small Intestine.

healthy control precludes any reliable assessment of whether our observed electrodermal patterns are specific to women with endometriosis and chronic pelvic pain.

The decrease in asymmetry and dispersion seen with active acupuncture and not sham treatments is revealing and is significant for a number of reasons. These electrodermal measures are fundamentally rooted in Eastern medicine principles and aim to assess the activities of a theoretical meridian system. To observe quantitative changes in these measures with acupuncture compared to sham treatments suggests that there is a physiologic effect of acupuncture that likely goes beyond placebo. These effects are seen over a span of weeks and appear to peak and stabilize at 4 weeks (Fig. 2A–D). Furthermore, these documented changes are consistent with the schema espoused by acupuncture theory,

namely, that acupuncture restores balance and eliminates asymmetries.⁴ To see these intentional effects result from interventions performed on sites far from the Jing-Well points is intriguing and prompts further questions about the biological mechanisms of acupuncture. Nevertheless, the existence of a measure that is both quantitative and consistent with acupuncture theory may be helpful for basic research and needs further evaluation before any conclusions can be drawn.

Whether these electrodermal measures translate into meaningful clinical assessments, on the other hand, is a different question. Based on the graphical representation of electrodermal measures over time, clinical “responders” had a negative trend in both dispersion and asymmetry measures while “non-responders” had a positive trend (except for *yin-*

TABLE 3. MULTIVARIABLE ANALYSES: ADJUSTED ASSOCIATIONS BETWEEN TREATMENT/ELECTRODERMAL MEASURES AND CLINICAL OUTCOME

Dependent variables	Pelvic pain over 4 weeks	Endometriosis HRQOL-30	Pediatric QOL	Perceived stress	IL-6	TNF- α
Treatment designation (acup vs. sham)	-1.74 $p=0.007$	-19.8 $p<0.0001$		-0.42 $p=0.018$		-0.62 $p=0.001$
Right-left asymmetry		2.1 $p=0.0008$		0.05 $p=0.031$		
Yin-yang asymmetry	0.42 $p<0.0001$		-1.36 $p=0.0008$			
Yin-yang * time	-0.05 $p<0.0001$					
Left-Kidney * time					0.006 $p=0.007$	
Right-Stomach						-0.03 $p=0.005$

HRQOL, health-related quality of life; IL-6, interleukin 6; TNF- α , tumor necrosis factor α .

yang asymmetry). These differences, however, were not as robust as the ones seen between acupuncture and sham groups and could be interpreted as being confounded by treatment designation. In other words, "responders" are more likely to be designated to the acupuncture group than "nonresponders" and thus demonstrate reductions in imbalance measures. The multivariable analyses, however, show that asymmetry measures—specifically, the left-right and yin-yang variables—are independently associated with clinical outcomes even after accounting for treatment effects. In Pediatric QOL, yin-yang was the only significant variable. Because the general estimating equations model accounts for repeated measures in study participants, the timing of the test (at baseline, 4 weeks, and 8 weeks), the quantitative level of both clinical outcome and the Hibiki-7 measures, and multiple covariates, it is better suited to capture significant associations than a dichotomized analysis that arbitrarily chooses a single cutoff at a particular time-point (30% improvement at 8 weeks).

Based on the univariable analyses, pelvic pain is more commonly associated with electrodermal measures than the other clinical outcome measures. This may stem from components within the various Quality of Life assessments that have indirect relevance to the physiologic state of the body. For instance, the control/powerlessness, self-image, and social support subscales within the Endometriosis HRQOL-30 or the social health and school participation subscales within the Pediatric QOL may be poorly linked with electrodermal measures and thus contribute to fewer univariable associations. However, the fact that these QOL scores were significantly associated with general imbalance variables and not with specific meridian measures denotes the specificity of these imbalance variables (dispersion and asymmetry) to more global/qualitative assessments of health. Pain level can also theoretically reflect global health because there are psychologic and emotional components to it as well. This link between the general imbalance variables and global health is further supported by the lack of statistical association between any of the imbalance measures and inflammatory cytokine levels (a more specific outcome measure). The electrodermal measures of imbalance may play a surrogate role for qualitative measures, but additional studies

are needed to further assess the clinical validity of these electrodermal measures and the relative importance of the various imbalance measures.

This study has a number of limitations. First, with 14 participants, it has limited sample size and power. In addition, with the highly specific inclusion/exclusion criteria, the findings cannot be generalized to other stages of endometriosis or other causes of chronic pelvic pain. The second limitation, as mentioned in a related publication,¹¹ is that some of the instruments used to assess outcomes have not been specifically validated in adolescent populations. The Endometriosis Health Profile, for instance, has been validated for populations of adults older than 18 years, but not younger adolescents. Third, the derived imbalance measures in this study used simple statistics. It is possible that more complex, even nonlinear measures would better reflect clinical outcomes. Fourth, the results cannot be generalized to other clinical conditions or to other electrodermal devices. Fifth, the acupuncturists were not blinded to treatment designation and may have biased the electrodermal measurements. Sixth, the acupuncture group had higher electrodermal dispersion and asymmetry values at baseline compared to the sham group. It is conceivable that the observed temporal differences in electrodermal measurements between treatment groups could be attributed to this disparity. Finally, the technical limitations of the Hibiki-7 device remain largely unaddressed. How do stratum corneum moisture, electrode pressure, and variations in point localization affect the electrodermal readings? How do these factors affect interrater and intrarater reliability? Is there substantial temporal variability? In addition, the technical details of the Hibiki-7 device were not fully assessed, and the precision and proper calibration of the device have not been fully evaluated. While the device used for this study was not built specifically for scientific research, its use in this pilot study has generated findings that are interesting and suggestive enough (despite the problems discussed) to support further research into this area with a more technically sound electrodermal measurement device such as the Apparatus for Meridian Identification (AMI-Motoyama Institute of Life Physics, Tokyo, Japan) or the Prognos device (MedPrevent, Walderschorf, Germany). The measurements should be made by a technician blinded to treatment and patient outcomes.

Conclusions

Despite technical limitations to the Hibiki-7 device, we found significant associations between the electrodermal measures and both clinical outcome and treatment designation. These findings suggest that a physiologic basis for the Hibiki-7 electrodermal measurements may exist. To further assess the clinical utility of electrodermal devices, additional clinical and mechanistic studies are warranted.

Acknowledgments

We would like to acknowledge the acupuncturists who helped design the Japanese-style acupuncture protocol, Joseph Kay, L.Ac. and Diane Iuliano, L.Ac., the New England School of Acupuncture Japanese Department Chairs. This research was supported by grant numbers 5U19AT002022, K23-AT003238, and K24-AT004095 of the National Center for Complementary and Alternative Medicine (NCCAM). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NCCAM, National Institutes of Health.

Disclosure Statement

All authors of this paper—Andrew Ahn, Rosa Schnyer, Lisa Conboy, Marc Laufer, and Peter Wayne—have no commercial associations that would create a conflict of interest with this article and its content.

References

- Brewitt B. Quantitative analysis of electrical skin conductance in diagnosis: Historical and current views of bioelectric medicine. *J Naturopath Med* 1995;6:66.
- Ahn AC, Martinsen OG. Electrical characterization of acupuncture points: Technical issues and challenges. *J Altern Complement Med* 2007;13:817–824.
- Shima M, Chace C. *The Channel Divergences: Deeper Pathways of the Web*. Boulder, CO: Blue Poppy Press, 2001.
- Manaka Y, Itaya K, Birch S. *Chasing the Dragon's Tail: The Theory and Practice of Acupuncture in the Work of Yoshio Manaka*. Brookline, MA: Paradigm Publications, 1995.
- Ionescu-Tirgoviste C, Bajenaru O. Electric diagnosis in acupuncture. *Am J Acupunct* 1984;12:229–238.
- Ionescutirgoviste C, Pruna S. The acupoint potential, electroreception and bioelectrical homeostasis of the human body. *Am J Acupunct* 1990;18:15–24.
- Tsuei JJ, Chung C, Lam FM, Mi MP. Studies of bioenergy in healthy subjects. *Am J Acupunct* 1988;16:125–134.
- Voll R. Twenty years of electroacupuncture diagnosis in Germany: A progress report. *Am J Acupunct* 1975;3:7–17.
- Motoyama H. *Measurements of Ki Energy Diagnoses & Treatments: Treatment Principles of Oriental Medicine from an Electrophysiological Viewpoint*. Tokyo: Human Science Press, 1997.
- Dale RA. Acupuncture electrodiagnosis: Which acupoints can most easily provide the best diagnostic information. *Am J Acupunct* 1993;21:171–176.
- Wayne PM, Kerr CE, Schnyer RN, et al. Japanese-style acupuncture for endometriosis-related pelvic pain in adolescents and young women: Results of a randomized sham-controlled trial. *J Pediatr Adolesc Gynecol* 2008;21:247–257.
- Schnyer R, Iuliano D, Kay J. Japanese acupuncture in the treatment of chronic pelvic pain in adolescents: Protocol implementation and design in a prospective randomized controlled trial. 2008 (in review).
- Streitberger K, Kleinhenz J. Introducing a placebo needle into acupuncture research. *Lancet* 1998;352:364–365.
- Jones G, Kennedy S, Barnard A, et al. Development of an endometriosis quality-of-life instrument: The Endometriosis Health Profile-30. *Obstet Gynecol* 2001;98:258–264.
- Varni JW, Seid M, Kurtin PS. PedsQL 4.0: Reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. *Med Care* 2001;39:800–812.
- Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav* 1983;24:385–396.
- Bedaiwy MA, Falcone T, Sharma RK, et al. Prediction of endometriosis with serum and peritoneal fluid markers: A prospective controlled trial. *Hum Reprod* 2002;17:426–431.
- Wayne PM, Krebs DE, Macklin EA, et al. Acupuncture for upper-extremity rehabilitation in chronic stroke: A randomized sham-controlled study. *Arch Phys Med Rehabil* 2005;86:2248–2255.
- Kalish LA, Buczynski B, Connell P, et al. Stop Hypertension with the Acupuncture Research Program (SHARP): Clinical trial design and screening results. *Control Clin Trials* 2004;25:76–103.
- De Maio FG. Income inequality measures. *J Epidemiol Community Health* 2007;61:849–852.
- Cowell F. *Measuring Inequality*. 2nd ed. London: Prentice Hall, 1995.
- Rouvinen S, Kuuluvainen T. Tree diameter distributions in natural and managed old *Pinus sylvestris*-dominated forests. *For Ecol Manage* 2005;208:45–61.
- Berntson GM, Wayne PM. Characterizing the size dependence of resource acquisition within crowded plant populations. *Ecology* 2000;81:1072–1085.
- Bergsmann O, Woolley-Hart A. Differences in electrical skin conductivity between acupuncture points and adjacent skin areas. *Am J Acupunct* 1973;1:27–32.
- Saku K, Mukaino Y, Ying H, Arakawa K. Characteristics of reactive electropermeable points on the auricles of coronary heart disease patients. *Clin Cardiol* 1993;16:415–419.
- Prokhorov EF, Prokhorova TE, Gonzalez-Hernandez J, et al. In vivo dc and ac measurements at acupuncture points in healthy and unhealthy people. *Complement Ther Med* 2006;14:31–38.
- Yu H, Chang H, Liou S, et al. The correlation between skin electrical conductance and the score of Qi vacuity. *Am J Chin Med* 1998;3–4:283–290.
- Lee YH, Lee MS, Shin BC, et al. Effects of acupuncture on potential along meridians of healthy subjects and patients with gastric disease. *Am J Chin Med* 2005;33:879–885.
- Fox A. General practice management of gastrointestinal problems assisted by Vegatest techniques. *Br Homeopath J* 1993;82:87–91.
- Ionescu-Tirgoviste C, Bajenaru O, Zugravescu D. The electric potentials of the Jing distal points in diabetics with and without polyneuropathy. *Am J Acupunct* 1985;13:5–14.
- Krop J, Lewith GT, Gziut W, Radulescu C. A double blind, randomized, controlled investigation of electrodermal testing in the diagnosis of allergies. *J Altern Complement Med* 1997;3:241–248.
- Sedlacek PR, Clelland JA, Knowles C, et al. Electrical conductance at auricular acupuncture points during dysmenorrhea. *Clin J Pain* 1988;4:183–190.

33. Sullivan SG, Eggleston DW, Martinoff JT, Kroening RJ. Evoked electrical-conductivity on the lung acupuncture points in healthy-individuals and confirmed lung-cancer patients. *Am J Acupunct* 1985;13:261-266.
34. Usichenko TI, Lysenyuk VP, Groth MH, Pavlovic D. Detection of ear acupuncture points by measuring the electrical skin resistance in patients before, during and after orthopedic surgery performed under general anesthesia. *Acupunct Electrother Res* 2003;28(3-4):167-173.
35. Zukauskas G, Dapsys K, Ilgesviciute J, Vaitkus P. Quantitative analysis of bioelectrical potentials for the diagnosis of internal organ pathology and theoretical speculations concerning electrical circulation in the organism. *Acupunct Electrother Res* 1988;13(2-3):119-130.

Address correspondence to:
Andrew C. Ahn, M.D., M.P.H.

*Division for Research and Education in Complementary
and Integrative Medical Therapies
Harvard Medical School
401 Park Drive Suite 22A-West
Boston, MA 02215*

E-mail: aahn@hms.harvard.edu

