A Miniature Skin-Attached Hot Flash Recorder

J. G. Webster[1], D. E. Bahr[1], M. C. Shult[1], D. G. Grady[2], J. Macer[2]

[1]Bahr Management, Inc., Middleton WI USA
[2]University of California, San Francisco CA USA

Abstract—**We are developing an innovative miniature ambulatory hot flash recorder that is precise, accurate, reliable, affordable and aesthetically appropriate. It is a small disposable adhesive patch with two electrodes. A nondisposable, miniaturized, coated circuit board snaps onto the electrodes. The unit records the frequency, timing, and amplitude of hot flashes by measuring skin conductance, using no external wires or telemetry. The recorder contains a hot flash event marker that the subject triggers whenever she experiences a hot flash. Because hot flash skin conductance changes slowly, we measure every 10 s. We use pulsed waveforms to take the data, and sleep mode to conserve battery life. Since electrodes polarize if current always travels in a single direction, we use pulses in alternate directions. Data are downloaded directly from the patch to data acquisition software for computer display. The new recorder will be a valuable tool for researchers.**

1. Introduction

There are currently about 36 million American women between the ages of 45 and 65 years. At least two thirds of these women will experience hot flashes and approximately 20% will seek medical relief for debilitating symptoms [1]. A hot flash is the sudden onset of intense heat and flushing in the upper torso and face, often followed by profuse sweating and chills [1]. The etiology of hot flashes is thought to be related to abnormalities of thermoregulation associated with changes in hormone levels that occur at menopause (Freedman, 1998), but the mechanism is not entirely clear.

Postmenopausal hormone therapy is highly effective treatment for hot flashes [2] and 10 million women in the US are currently taking some form of estrogen, either alone or in combination with progestin [3]. However, large randomized trials have recently shown that standard-dose hormone therapy is associated with increased risk for cardiovascular disease, venous thromboembolic events, and dementia [3–6]. Given the increased risks for serious diseases and other common side effects such as uterine bleeding and breast tenderness [7], many women would like to avoid using hormone therapy for treatment of hot flashes.

As reflected in recent NIH-sponsored workshops and conferences on Menopause (http://orwh.od.nih.gov/), there is intense interest in the research community regarding the etiology of hot flashes and in finding effective and safe treatment. However, research is currently hindered by the lack of a feasible, reliable and accurate objective measure of hot flash frequency and severity. Most studies currently use a 7-day self-reported hot flash diary [8]. This measure is subjective and can be inaccurate and unreliable because participants forget or fail to enter hot flashes in the diary (especially at night when many hot flashes occur), severity is self-reported on a coarse scale (mild, moderate, severe), and the exact timing of the hot flash is not recorded [9]. In addition, keeping a daily diary is labor-intensive and inconvenient and most participants are unwilling to do this for more than about a week.

Increases in skin conductance have been shown to be a good measure of the occurrence of hot flashes [10]. Skin conductance rises sharply from baseline at the onset of a hot flash, then slowly returns to baseline as depicted in Figure 1.

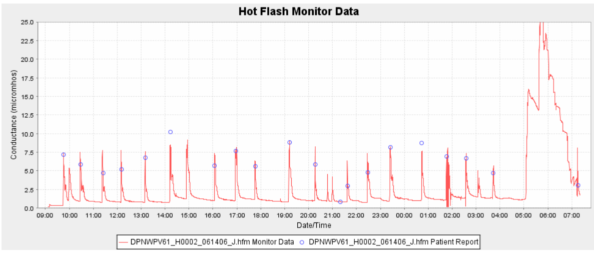

Fig. 1 Using electrodes containing gel C, baseline conductance in the participant shown is about 1.2 micromhos (µS). Typical hot flashes rise to about 7 µS and last about 2 min. The subject presses a button when she perceives a hot flash, which is recorded by the small circle shown on the 22 h record.

Ambulatory skin conductance monitors such as the BIOLOG are commercially available, but are not optimal for use in clinical research for several reasons. The device is heavy (200 g), bulky (3.3 × 7 × 13 cm), and cumbersome. Wires are used to attach the monitor, which is worn on the belt or in a case with a shoulder strap, to 2 ECG-type electrodes attached to the upper chest. The special electrode cream must be pasted into the dry electrode sponge by hand. The monitor cannot be worn under clothing or in the shower and the electrodes are awkward to attach and remove. Recording is limited to 24 h due to limited data storage capacity and there is no measure of severity (increased skin conductance duration or amplitude or their product). Because there is marked biologic variability between individual women and from week to week in a given individual in the frequency and severity of hot flashes, longer duration of monitoring would be optimal. In addition, the BIOLOG monitors are expensive, costing $2200 each and $2000 for the associated software. At this price and with these limitations, it is impractical to use the devices in adequately powered clinical trials.

II. Methods

A. *Hot flash monitor design and testing*

To address these problems, we have developed a medium sized prototype skin conductance monitor which is being tested in the bioelectrical laboratory and in ambulatory participants in clinical research studies at the University of California, San Francisco. We are presently miniaturizing the monitor so it can be skin attached. It measures the frequency, timing, and amplitude of the hot flashes. See Figure 1. After miniaturization it will be a discreet, nondisposable ambulatory recorder snapped onto disposable electrodes that is easy to attach and remove, precise, inexpensive, and aesthetically acceptable. It will be self-contained with no external wires and no telemetry transmission to an external receiver.

We have completed and manufactured 9 prototype hot flash measuring devices using skin conductance measurements with appropriate electrodes, wires, and circuitry to determine skin conductance. We have tested current commercially available ECG electrodes and found that they are not suitable for conductance monitoring. We have investigated the conductance vs. time curve for different ECG electrodes and found that their high salt concentration (about 4%) results in increased skin conductance that masks the increase caused by sweating during hot flashes. Thus we investigated electrodes with low salt concentration and found that they perform very well and produce results superior to the results obtained by the BIOLOG recorder and electrode cream. We have reproduced similar conductance patterns for simulated and real hot flashes. See Figures 1 and 2.

We have developed software for measuring, storing, processing, and displaying the data. See Figure 2. We display skin conductance changes as absolute changes and also as relative changes. Software will provide the frequency of hot flashes based on conductance changes, mean and range of hot flash duration, mean severity based on fractional change from baseline or area under the curve above baseline, and a severity score, which will be the product of frequency and duration.

B. *Electrode design and testing*

Our philosophy is that if we use an excellent sensor, then we will be able to use signal processing software to yield optimal results. If the sensor is bad, signal processing software may not correct the problem. Thus we have performed extensive testing on electrodes.

ECG electrodes do not work because they are designed to make good skin contact. Their approximately 4% salt diffuses into the skin and deliberately increases the conductance. Then when the hot flash opens the sweat ducts, the incremental parallel-added conductance is a tiny fraction of the total and produces a negligible change.

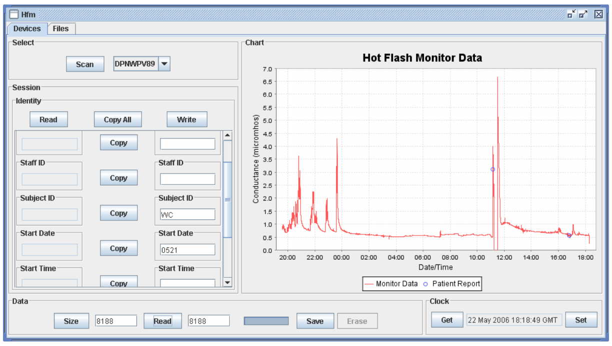

Fig. 2 Desktop computer software scans the monitor serial number, provides file labeling, downloads the data, saves them, displays them, erases the memory, and sets the clock. At the end of a 7-day test shown here, the conductive adhesive gel gives results as good as for day 2 of the same electrode (Shown below in Figure 3 bottom).

Thus we tested alternative electrodes designed with lower conductance and found excellent results with regard to low baseline and definitive increases with sweating. We also tested the cream recommended by BIOLOG and found that it yielded high baseline and erratic results.

We have tested electrodes with various adhesive tacks to ensure that the electrodes make good contact for several days, yet cause minimal irritation when removed.

We have tested solid backing materials and skin adhesives that breathe so that sweat does not accumulate in the solid gel. We have tested vinyl backing materials that do not breathe to prevent shower water from entering and accumulating within the solid gel.

Figure 3 shows a side-by-side comparison of gel A (poor results) with gel C (excellent results).

We have found gel C to be superior to gel A, BIOLOG gels, or 0.1% or 0.9% saline in hydrogels.

Skin conductance increases with time with a standard type of electrode and electrolyte. This is likely due to the fact that electrode salts and water diffuse into the skin, hydrating it and increasing its conductance. Also, the impermeable plastic in the electrode traps sweat under the electrode which further increases hydration.

Fig. 3 Side-by-side comparison of two electrodes worn by the same subject at the same time. Top: Biolog cream causes about 6 micromho (µS) baseline conductance. Sweating caused by exercise (marked by circles) causes about 30% change. Bottom: Conductive adhesive gel causes about 0.8 µS baseline conductance and has less motion artifact. Sweat caused by exercise causes 400% change. During shower (at about 16:00 hours), the recorder was detached (0 µS). After shower, electrode was wet, recording about 20 µS and recovering in about 1 h.

We have tested the time constant of the skin conductance to a step voltage of 0.5 V and find that the time constant is about 20 ms. We wait 20 time constants to ensure equilibrium, sample the skin conductance, then terminate the pulse after 400 ms. To save battery life we put the microprocessor to sleep and wait 10 s before taking the next sample. Hot a flash skin conductance change slowly over a period of about 2 min, therefore a measurement is only needed every 10 s. Because electrodes polarize if current always travels in a single direction, we apply pulses in alternate directions, positive and negative and electrically connect the electrodes together between pulses to discharge any residual charges. Because there is a slow drift and noise in skin conductance, we are writing computer programs to ignore slow drifts and average noise. The basic algorithm concept is to recognize hot flashes by their much higher slope. We will also use template matching. These programs will display raw data and also automatically identify and record frequency, timing, and amplitude using absolute conductances and/or their changes and/or percent changes in conductances or their changes.

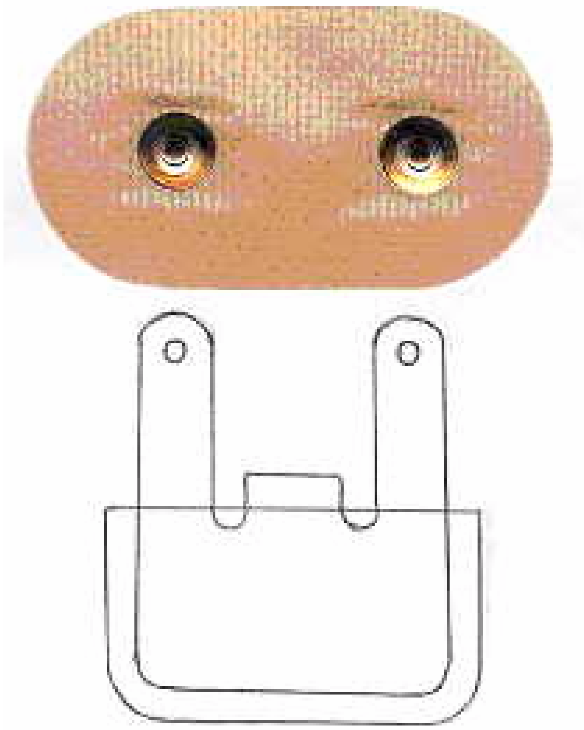

Fig. 4 Placement of the 2-electrode patch can be horizontal on the chest with hot flash miniature monitor snapped onto electrode studs by flex connections.

We have already tested modern chronic use skin adhesives in the size of a large Band-Aid similar to ScarSolution and find that the tack is too low for one-week use. We have not found an electrode tack that adheres adequately for 2 weeks and doesn't damage the skin. We tested several tacks similar to those used on ECG electrodes and find that they are satisfactory. We have found an adhesive that has improved tack, but is still well tolerated by the skin. As we move from our present Phase 1 prototype that is the size of a cell phone to the Phase 2 miniature skin-attached model, we will use a miniature lithium watch battery to power a low power amplifier, analog-to-digital converter, microprocessor, and memory mounted on flexible polyimide or polyester. We have tested a miniature magnet on the strap of a regular wristwatch that activates a miniature magnetic reed switch so the subject can manually record the time of perceived hot flashes by pressing the wrist magnet against the monitor. A light-emitting diode (LED) will flash to acknowledge the manual subjective recording. Figure 5 shows the final miniaturized hot flash recorder. Dimensions will be about 6 L × 2 W × 1 cm T.

At the conclusion of testing, the subject will remove the instrument and return it or mail it in a supplied packet to the clinical research team for data processing. The research technician will download the data into a personal computer using a JAVA data manager that can be used on multiple platforms such as Microsoft or Apple and the data can be imported by Excel, SAS, or any data base for data analysis. We have already developed software so that the investigator can perform data processing. After each use, the lithium battery will be removed from the device for recycling and the device disposed. We anticipate that the manufactured cost of these devices should not exceed a few tens of dollars each.

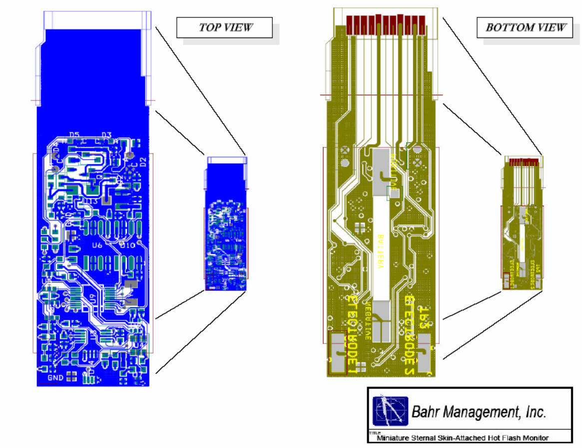

Fig. 5 We have designed a miniature skin-attached hot flash monitor that is 2 × 6 cm and will record skin conductance versus time for a week. Manufacture of 40 units begins in August 2006.

The initial medium sized prototype device 12 × 6 × 2 cm has been tested and revised by the engineers, it has been Phase 1 tested in women with frequent hot flashes at the University of California, San Francisco. The study participants are between 45 and 60 years old and have at least 10 hot flashes per day that occur both during the day and at night.

Acknowledgment

This publication was made possible by NIH Grant Number R43AT003183-01 from the National Center for Complementary and Alternative Medicine (NCCAM).

References

1. Kronenberg F. (1990): ‘Hot flashes: epidemiology and physiology’, *Ann. N. Y. Acad. Sci*. **592** 52-86
2. Maclennan A, Lester S, Moore V.(2001): ‘Oral estrogen replacement therapy versus placebo for hot flushes: a systematic review’, *Climacteric*. **4**(1) 58-74
3. Rossouw JE, Anderson GL, Prentice RL, et al. (2002): ‘Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial’, *JAMA*. Jul 17 **288**(3) 321-33
4. Shumaker SA, Legault C, Rapp SR, et al. (2003): ‘Estrogen plus progestin and the incidence of dementia and mild cognitive impairment in postmenopausal women: the Women's Health Initiative Memory Study: a randomized controlled trial’, *JAMA*. May 28 **289**(20) 2651-62
5. Anderson GL, Limacher M, Assaf AR, et al. (2004): ‘Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial’, *JAMA*. Apr 14 **291**(14) 1701-12
6. Shumaker SA, Legault C, Kuller L, Rapp SR, et al. (2004): ‘Conjugated equine estrogens and incidence of probable dementia and mild cognitive impairment in postmenopausal women: Women's Health Initiative Memory Study’, *JAMA*. Jun 23 **291**(24) 2947-58
7. Greendale GA, Reboussin BA, Hogan P, et al. (1998): ‘Symptom relief and side effects of postmenopausal hormones: results from the Postmenopausal Estrogen/Progestin Interventions Trial’, *Obstet. Gynecol*. Dec **92**(6) 982-8
8. Sloan JA, Loprinzi CL, Novotny PJ, et al. (2001): ‘Methodologic lessons learned from hot flash studies’, *J. Clin. Oncol.* Dec 1 **19**(23) 4280-90
9. Miller, H. G., Li, R. M. (2004): ‘Measuring hot flashes: Summary of a national institute of health workshop’, *Mayo Clinic Proc*. June **79**(6) 735-7
10. Freedman, R R. (1998): ‘Biochemical, metabolic, and vascular mechanisms in menopausal hot flashes’, *Fertility and Sterility* **70** 332-7

Address of the corresponding author:

Author: J. G. Webster
Institute: Bahr Management, Inc
City: Middleton WI
Country: USA
Email:Webster@engr.wisc.edu