Validity of Transdermal Alcohol Monitoring: Fixed and Self-Regulated Dosing

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Background: To study the validity of transdermal assessment of alcohol concentration measured by a lightweight, noninvasive device.

Methods: Subjects wore a 227-g anklet that sensed transdermal alcohol concentrations (TACs) every 15 to 30 minutes, downloading results to a remote computer each day. Twenty-four subjects entered a laboratory and received a dose of 0, 0.28, or 0.56 g/kg of ethanol. Breath alcohol concentrations (BrAC) and TAC were measured every 15 to 30 minutes Twenty others [10 alcohol dependent (AD) and 10 not (NAD)] in the community who wore the anklet for 8 days kept a drinking log and provided a BrAC sample each day.

Results: In the laboratory, no zero-dose subject, and every subject receiving alcohol, had alcohol-positive TACs. The device distinguished low- and high-alcohol–dosing groups using peak ($t_{14} = 3.37$; $p < 0.01$) and area under the curve ($t_{14} = 3.42$; $p < 0.01$) of TACs. Within dosing groups, average TAC curves were broader (right-shifted) and had lower peaks than average BrAC curves. For community participants, self-reported number of drinks ($t_{18} = -3.77$; $p < 0.01$), area under the TAC curve ($t_{9.5} = -3.56$; $p < 0.01$), and mean TAC ($t_{9.9} = -3.35$; $p < 0.01$) all significantly distinguished the AD and NAD groups. However, individual transdermal readings were not reliably quantitatively equivalent to simultaneously obtained breath results.

Conclusions: Within the limits of the laboratory study, the device consistently detected consumption of approximately 2 standard drinks. On average, the device shows discriminative validity as a semiquantitative measure of alcohol consumption but individual readings often are not equivalent to simultaneous BrACs.

Key Words: Alcohol Monitoring, Transdermal, Insensible Perspiration, Sweat.

UNLIKE MANY OTHER substances of abuse (Eskridge and Guthrie, 1997), alcohol is quickly metabolized and excreted from the body (Wilkinson et al., 1977), complicating monitoring. Although daily breath testing for alcohol is sometimes used, daily clinic attendance can be burdensome, patients may miss days, and daily breath testing may fail to detect small to moderate amounts of alcohol consumption.

Several biomarkers, such as mean corpuscular volume (MCV) (Pol et al., 1990), carbohydrate-deficient transferrin (CDT) (Godart et al., 2005), and γ-glutamyl transferase (GGT) (Nemesanszky et al., 1988), have been studied to aid in the diagnosis of alcohol use disorders and monitoring for relapse during treatment. Although biomarkers can be an important part of monitoring for relapse among heavy drinkers, no biomarker currently in use is completely sensitive and specific for alcohol use (Conigrave et al., 2003; Neumann and Spies, 2003), and frequent blood draws may be impractical and expensive. Additional methods are needed for monitoring of alcohol consumption among treated patients.

After consumption, most alcohol is metabolized in the liver, some is removed through exhaled air, some leaves the body unchanged in the urine, and about 1% crosses the skin, in insensible perspiration and sweat (Swift, 2003); we refer to alcohol concentration in insensible perspiration and sweat as "transdermal alcohol concentration" or "TAC." The pharmacokinetics of alcohol elimination in insensible perspiration have been previously characterized (Brown, 1985). In the 1980s and 1990s, a sweat-patch test, which continuously collected sweat samples for 7 to 10 days, was tested in a controlled setting (Phillips and McAloon, 1980) and in community participants (Phillips, 1984a; Phillips et al., 1995). More recently, the WrisTAS™ (Giner Inc., Newton, MA) device has been tested in the laboratory, on individuals in a cocktail bar, in an inpatient substance abuse unit, and in free-ranging participants who

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wore the device for over 1 month (Swift, 2000; Swift et al., 1992). When well calibrated, it produces peak alcohol concentrations and area under the TAC curve that correlate highly with breath alcohol concentrations (BrAC) (0.6–0.7 and 0.8–0.9, respectively) (Swift, 2000, 2003).

An independently developed transdermal alcohol monitoring system (SCRAM^{TM}—Secure Continuous Remote Alcohol Monitor—Alcohol Monitoring Systems Inc., Highlands Ranch, CO) is a 227-g, noninvasive device worn around the leg. It measures and records (in an on-board memory) transdermal alcohol levels using fuel cell technology, at preset time intervals (i.e., every 30 minutes), and can store more than 140 sample results. The ankle monitor communicates by radio frequencies with a modem in the subject's home at preset times once or twice per day only if the wearer is within about 9 m. The modem uploads TACs to a secure website and authorized users can access the password-protected website from any Internet-connected computer, view all downloaded transdermal readings, and make changes to the frequency of anklet sampling or change the time of anklet-modem communication. The anklet has a maximum TAC reading of 80 mg/dl.

We sought to test the validity of this device, against the ''gold standard'' of breath alcohol readings, for fixed alcohol doses in a controlled laboratory setting and for self-regulated doses among community-living participants.

MATERIALS AND METHODS

A research protocol was designed by the researchers and funded by the developing company (Alcohol Monitoring Systems Inc.). By contract, the researchers were free to publish any results without prior approval by company representatives. Company representatives trained university personnel to use the SCRAM^{TM} system but were not involved in subject recruitment, protocol implementation, or manuscript preparation. Data were transmitted to the company's secure website via modem from the anklets, but personnel at the company were entirely blinded to subjects' group assignments, and data were retrieved directly from the website by the researchers. The company provided 5 SCRAM^{TM} units and the devices were used throughout the period of data collection without maintenance (except routine cleaning between subjects) or further calibration; 1 bracelet was returned to the company during the study because a subject cut the bracelet strap. The Colorado Multiple Institutional Review Board and the General Clinical Research Center's (GCRC's) Scientific Advisory Committee approved the research protocol and study consents.

Laboratory Study

Recruitment. We recruited subjects through advertisement in a local free newspaper, word of mouth, and distribution of a brochure. Inclusion criteria were: (1) 21 to 60 years of age, (2) a social drinker, (3) in good general medical health, and (4) giving informed written consent. Exclusion criteria were: (1) history of alcohol abuse, alcohol dependence, or treatment for alcoholism; (2) currently completely abstains from alcohol consumption; (3) had any disease potentially complicated by alcohol ingestion; (4) currently pregnant; and (5) currently being treated with metronidazole or disulfiram.

Initial Evaluation. A history, physical examination, and urine pregnancy test (female participants) were completed and the DSM Checklist (Hudziak et al., 1993) was administered by a board-certified psychiatrist with added qualifications in addiction psychiatry from the American Board of Psychiatry and Neurology. In general, the checklist provides questions regarding DSM-IV symptoms for disorders but in most categories, it does not include questions about impairment, whether the disorders are better accounted for by another mental health problem, or whether symptoms are because of the direct physiological effects of a substance or a general medical condition. As such, most diagnoses in this report represent symptom counts meeting the DSM-defined threshold number of symptoms for diagnosis by category.

Laboratory Protocol. Subjects meeting all inclusion and no exclusion criteria were scheduled for admission to the University of Colorado Hospital's outpatient general clinical research center (laboratory). Subjects were instructed to fast after midnight and not to consume any alcohol in the 24 hours prior to admission.

Once admitted to the laboratory, the subject's ankle was cleaned, the anklet was secured, baseline BrACs and TACs were determined (to ensure results were zero), and a blood sample was drawn (to test for signs of hepatic injury). All subjects were given 30% of their calculated total daily calories [by the Harris-Benedict equation (Kien and Ugrasbul, 2004)] for breakfast (15% protein, 30% fat, and 55% carbohydrates). Subjects ate breakfast over 15 minutes and deposited their car keys with the researchers. Keys were returned when BrAC was 0 mg/dl.

Subjects were assigned such that dosing groups were similar for age and gender on average; assignment was not random. One hour after completing breakfast, subjects were given a sugar-free, noncaffeinated beverage. For eight subjects, it contained no alcohol (no-dose group); for eight, 0.28 g/kg of ethanol administered as a 20% solution (low-dose group); and for eight, 0.56 g/kg of ethanol administered as a 20% solution (high-dose group). Study subjects were blinded to their dose but the researchers were not. The beverage was consumed over 10 minutes.

Breath alcohol concentrations were obtained with an Alco-Sensor III^{TM} (Intoximeters Inc., St. Louis, MO) (Gibb et al., 1984). The BrACs and TACs were sampled at 15- to 30-minute intervals following dosage administration. For the first 5 subjects, TACs and BrACs were measured every 30 minutes but not at identical times; for subsequent subjects all TACs and BrACs were timed to coincide exactly across subjects. Because we expected the TAC curve to be right-shifted (Brown, 1985), TAC sampling was continued for an additional 3 hours after the breathalyzer results returned to undetectable levels (0 mg/dl). To reach that level subjects remained in the laboratory approximately 3 to 11 hours after dose administration. Subjects were also given a light lunch (40% of daily calories with 15% protein, 30% fat, and 55% carbohydrates) exactly 4 hours after breakfast and if they were still present in the evening were given a light dinner. Subjects were allowed to be up with assistance when BrACs were greater than 40 mg/dl and up without assistance when BrACs were below 40 mg/dl. Subjects were paid $60.

Sample. Thirty-four subjects consented to participate but we admitted only 24; several were excluded because alcohol abuse or medical problems were discovered on initial evaluation.

Data Analysis. We graphed individual and average dosing group breathalyzer and TAC curves. By design, within- and between-group comparisons of low- and high-dose groups were completed (but not for the no-dose group). Between–dosing-group comparisons (for peak alcohol concentration and area under the alcohol concentration curve) were completed using independent *t*-tests (because of nonnormality, the Mann-Whitney test was also run; results are not presented unless significance was affected at $\alpha = 0.05$). Within–dosing-group comparisons (for breath vs transdermal results) used paired *t*-tests (because of nonnormality, we also used the Wilcoxon signed-rank test; again results are not presented unless significance was affected at $\alpha = 0.05$). Area under the curve (AUC) was calculated using both the spline and the trapezoid methods (Yeh and Kwan,

1978) (because the results were very similar, only the spline results are presented). Spearman correlations for peak alcohol concentration and AUC were calculated across and within the dosing groups. Bland-Altman analyses (Bland and Altman, 1986) were also used to compare breath and transdermal results.

Community Study

Recruitment. The community study compared TACs in 2 groups of subjects: (1) the alcohol-dependent group (AD) included 10 subjects recruited from a local community outreach program aimed at harm reduction for drug users not in treatment (Booth et al., 2004), and (2) the non–alcohol-dependent group (NAD) included 10 subjects recruited by advertisement in a local free newspaper and distribution of a brochure; interested participants in the community outreach program, who were not dependent on alcohol, were also enrolled into this group. The AD and NAD were recruited to provide groups that differed substantially in their level of alcohol consumption (Meyer et al., 2000). Inclusion criteria were: (1) at least 21 years of age, (2) English-speaking, (3) not in and did not now want treatment for an alcohol use disorder, and (4) gave informed written consent. Exclusion criteria were: (1) emotional problems that would interfere with participation in the study (i.e., currently psychotic, manic), (2) unstable living environment, (3) no home phone, (4) currently pregnant (by self-report), and (5) taking metronidazole or disulfiram.

Community Study Protocol

Day 1. The researchers attempted to schedule the in-home day 1 visit, when informed consent was obtained, during a natural break in alcohol consumption; intoxicated individuals were rescheduled. Subjects were assigned to the AD or NAD groups by results from the DSM-IV Checklist. The ankle monitor was secured to the subject's leg and the modem was plugged into the subject's phone line, BrAC was recorded, and a drinking log was given to subjects. The log contained a calendar with an outline of days/hours of participation. Subjects were asked to record any alcohol consumption (amount and brand of alcohol) next to the appropriate day/hour on the log; the definition of a standard drink was also written at the top of the drinking log. Subjects were paid $10 for this visit.

Day 2 to 7. The researchers met with each subject daily, obtained BrAC, and recorded the subject's drinking log information from the previous day. Subjects were paid $10 for each day they were available for interview and received a bonus if self-reported alcohol consumption for the previous day approximated results obtained from the transdermal alcohol monitor. This bonus was used to decrease underreporting, which has been seen in previous studies (Phillips, 1984a). Once subjects had reviewed their drinking log, the researchers left the residence and graphed the subject's self-reported alcohol consumption. The transdermal device provides a graph of TACs; only the researchers (and not subjects) had access to this information. The researchers visually compared the subject's self-reported alcohol consumption graph with the transdermal curve and immediately returned to the residence, where excellent approximations ($>75\%$ time and dose agreement) were rewarded with a $5 bonus, good approximations ($>50\%$ time and dose agreement) with a $2 bonus, and poor approximations ($<50\%$ time and dose agreement) earned no bonus.

Day 8. On day 8, the researchers followed day 2 to day 7 procedures. In addition, subjects were given a survey to assess subjective responses to wearing the device and then the ankle monitor and modem were removed. As in a previous survey on comfort (Phillips, 1984b), subjects marked the point on a 100-mm line to quantify their answers. The line was anchored by extremes such as "very comfortable" and "very uncomfortable."

Data Analysis. Area under the TAC curve (AUC-week) and mean TAC (Mean-TAC) were used as summary alcohol-level measures over the 8 days. The number of self-reported standard drinks consumed for the week was graphed and correlated with AUC-week and mean-TAC across and within the AD and NAD groups (because of nonnormality, Spearman correlations are reported). Between-group (AD and NAD) comparisons for the number of self-reported standard drinks consumed for the week, AUC-week, and Mean-TAC were completed using *t*-tests (Mann-Whitney tests were also completed; results are not presented unless significance was affected at $\alpha = 0.05$). Point estimates from breathalyzer tests were compared with the nearest-in-time TAC result using Bland-Altman analyses (with each subject providing 5–8 data points); Bland-Altman analyses for breath and TACs were also carried out for each individual. Finally, for the 6 comfort-survey questions independent *t*-test comparisons were completed (Mann-Whitney tests were also completed; results are not presented unless significance was affected at $\alpha = 0.05$).

RESULTS

Laboratory Participants

Baseline Characteristics. Table 1 shows baseline characteristics by group. Two individuals in the no-dose, 1 in the low-dose, and 1 in the high-dose group met criteria for lifetime major depression; although results are not presented, none met criteria for current major depression. No subject met lifetime or current criteria for mania, antisocial personality disorder, attention-deficit/hyperactivity disorder, or generalized anxiety disorder.

Transdermal Curves and Comparisons with Breath. Figure 1 depicts the average BrAC and TAC by dosing group in the laboratory study. As described previously (Brown, 1985), TAC is right-shifted; transdermal peaks occurred later and were lower. On average, peak TAC occurred 2 and 3 hours (low- and high-dose groups, respectively) after peak BrAC. There was wide individual variation in the relative heights of BrAC and TAC (1 curve shown—Fig. 2).

Within the laboratory study, individual graphs were examined for rates of false-positive (no-dose group) and false-negative (low- and high-dose groups) results. More than 80 samples were collected from the no-dose group (several prior to dose administration); all TACs and BrACs in this group were 0 mg/dl. In addition, all individuals in the low- and high-dose groups produced numerous TAC values >0 and demonstrated TAC curves with ascending, peak, and descending values.

Between–Dosing-Group Comparisons. Table 2 shows between–dosing-group comparisons for peak BrAC and TAC results and estimates of breath and transdermal AUC (laboratory study). Breathalyzer and transdermal testing significantly distinguished the 2 dosing groups (low- and high-dose) in the laboratory study using peak alcohol concentration and area under the alcohol concentration curve.

Within–Dosing-Group Comparisons. Table 2 also shows within–dosing-group comparisons of breath and transdermal results for the laboratory study. Peak TAC was significantly lower than peak BrAC in the low-dose group; this

Table 1. Subject Characteristics by Group

	Laboratory			Community Sample	
	No-dose ($N = 8$)	Low-dose ($N = 8$)	High-dose ($N = 8$)	Non-Alcohol Dependent ($N = 10$)	Alcohol Dependent ($N = 10$)
Age, mean (SD)	32.8 (12.8)	38.1 (14.4)	37.5 (12.6)	43.5 (10.3)	39.9 (9.6)
Female gender, % (*n*)	50 (4)	50 (4)	50 (4)	70 (7)	60 (6)
Weight in kilograms, mean (SD)	76.3 (9.3)	86.0 (27.8)	79.7 (17.5)	83.5 (24.7)	67.0 (14)
Height in centimeters, mean (SD)	170.9 (7.4)	171.5 (9.9)	174.5 (4.1)	165.6 (8.6)	165.6 (9.7)
Major depression lifetime, %	25	12.5	12.5	30	30
Antisocial personality disorder lifetime, (%) (does not require conduct disorder diagnosis be met)	0	0	0	10	40
Substance dependence lifetime (%)					
Cocaine	12.5	0	0	10	40
Cannabis	0	12.5	0	10	10
Nicotine	0	0	25	0	0
Amphetamine	0	0	0	0	10
Opioid	0	0	0	20	0

"No-dose," 250 ml beverage containing no alcohol; "Low-dose," 0.28 g/kg of ethanol; "High-dose," 0.56 g/kg of ethanol; SD, standard deviation.

difference was essentially significant in the high-dose group ($p = 0.052$). However, AUC for breath and transdermal alcohol tests were remarkably similar.

Bland-Altman Analyses. We also completed Bland-Altman analyses (Bland and Altman, 1986). As shown in Fig. 4A for each laboratory subject we averaged the peak breath and transdermal result (x-axis) and calculated the difference between peak breath and transdermal results (y-axis). For example, the point where $x = 41.5$ and $y = 15$ represents one individual who had an average peak BrAC and TAC of 41.5 mg/dl and a difference between peak BrAC and TAC of 15 mg/dl. This representation of the data allows a visual estimation of agreement between breath and transdermal results (difference between measurement techniques on the y-axis) at each subject's average breath-TAC (average on the x-axis). Perfect agreement between the breath and transdermal results at all alcohol concentration levels would result in a horizontal line (slope = 0) with an intercept of zero.

Figure 4 depicts the Bland-Altman analysis for the laboratory study using peak BrAC and TAC (Fig. 4A), and separately, breath and transdermal AUC (Fig. 4B). This analysis shows varying disagreement between peak BrAC and TAC and between breath and transdermal AUC. For peak alcohol concentrations, transdermal results tended to underestimate breath results, although this was not always the case. A predictable pattern for differences by AUC was not seen (Fig. 4B).

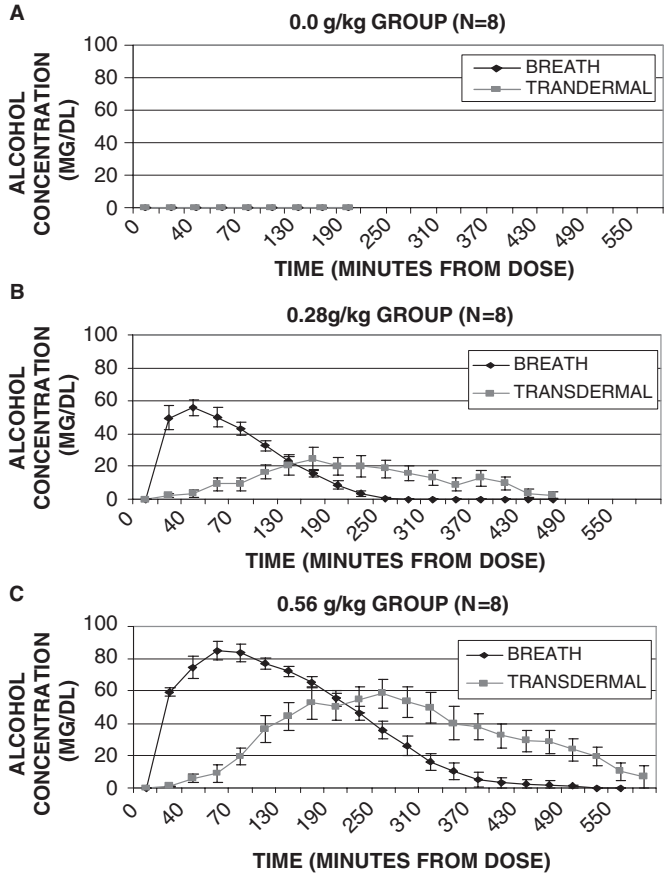

Fig. 1. Laboratory study—average transdermal and breath alcohol concentration (BrAC) curves (mg/dl) by dosing group. Recordings terminated after 3 hours at 0 mg/dl BrAC.

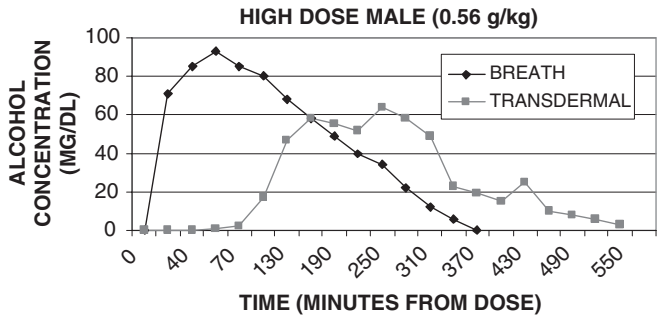

Fig. 2. Transdermal and breath alcohol concentration curve for one participant in the high-dose group in the laboratory study.

Table 2. Group Comparisons

	Laboratory Low-Dose ($N=8$) Mean (SD)	High-Dose ($N=8$) Mean (SD)	Statistic
Peak breath alcohol alcohol concentration (mg/dl)	56 (16.1) a	88 (13.3) b	a → b; $t_{14}=4.26$; $p<0.01$
			a → c; $t_7=2.76$; $p=0.03$
Peak transdermal alcohol concentration (mg/dl)	28 (21.0) c	64 (21.3) d	c → d; $t_{14}=3.37$; $p<0.01$
			b → d; $t_7=2.34$; $p=0.05$
Area under the curve (breath testing) (min · mg/dl)	6,090 (1,792) e	18,220 (4,681) f	e → f; $t_{14}=6.85$; $p<0.01$
			e → g; $t_7=0.05$; $p=0.96$
Area under the curve (transdermal testing) (min · mg/dl)	5,988 (4,876) g	19,062 (9,659) h	g → h; $t_{14}=3.42$; $p<0.01$
			f → h; $t_7=0.18$; $p=0.86$
	Community Sample: Non–Alcohol Dependent ($N=10$) Mean (SD)	Alcohol Dependent ($N=10$) Mean (SD)	Statistic
Self-reported # standard drinks (over 8 d)	20.5 (22.89)	70.8 (35.5)	$t_{18}=-3.77$; $p<0.01$
AUC-week (min · mg/dl)	52,770 (44,136)	362,915 (271,659)	$t_{9.5}=-3.56$; $p<0.01$
Mean-TAC (mg/dl)	6.6 (5.76)	34.7 (25.87)	$t_{9.9}=-3.35$; $p<0.01$

AUC-week, area under the transdermal alcohol concentration curve for 1 week; Mean-TAC, mean transdermal alcohol concentration for the week.

Although less informative than the Bland-Altman analysis (as correlation measures association and not agreement), the authors completed correlations between transdermal and breath results first across all 24 subjects in the laboratory study (peak alcohol concentration $r=0.84$; $p<0.01$; AUC $r=0.84$; $p<0.01$) and across the 16 subjects in the low-dose and high-dose community groups (peak alcohol concentration $r=0.49$; $p=0.06$; AUC $r=0.49$; $p=0.05$); correlations within each dosing group, considered separately, were nonsignificant.

Community Sample

Baseline Characteristics. Nondependent subjects were slightly older and there were more females than males in both groups (Table 1). Alcohol-dependent subjects, despite having the same average height as NAD subjects, weighed about 15 kg less, and 40% of them met criteria for lifetime (and current) cocaine dependence.

Transdermal Curves and Comparisons with Breath and Self-Report. Individual TAC curves were compared with self-reported alcohol consumption among community participants. All individuals who reported drinking during the week had positive TAC readings. The only subject who reported no drinking for the entire week had 331 TAC readings of 0 mg/dl (of 338) and a maximum reading of 1 mg/dl and did not have any positive TAC curves (with ascending, peak, and descending values).

Figure 3 shows data for one subject from the AD group; over the 8 days the subject reported consumption of 100 standard drinks. During the week, nearly all of the transdermal readings were positive for alcohol. Many readings were 80 mg/dl, the maximum possible reading for the anklet tested. On Tuesday and Wednesday, although the subject reported considerable drinking, TACs declined.

In general, self-reported alcohol consumption and transdermal alcohol readings showed good agreement by time. However, there were some instances where transdermal readings and self-reported alcohol consumption did not match; there were also several instances in which individuals provided breath alcohol tests that were inconsistent with self-reported alcohol consumption (both negative

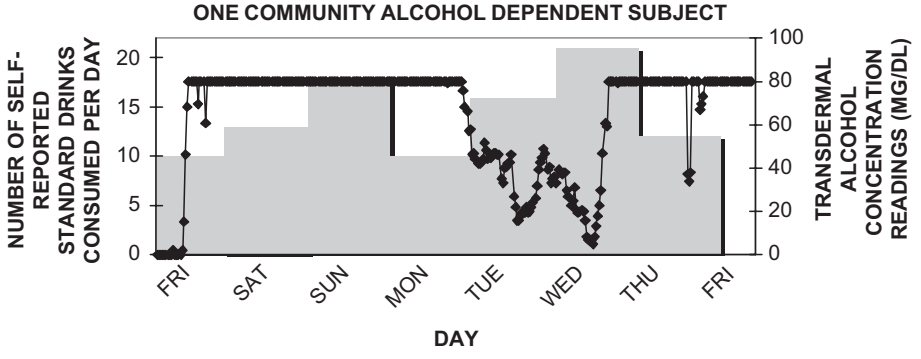

Fig. 3. Transdermal alcohol concentration (TAC) curve for one community sample participant in the alcohol-dependent group (line) and associated self-reported number of standard drinks consumed per day (bars). The maximum TAC measured by the SCRAM™ anklet is 80 mg/dl.

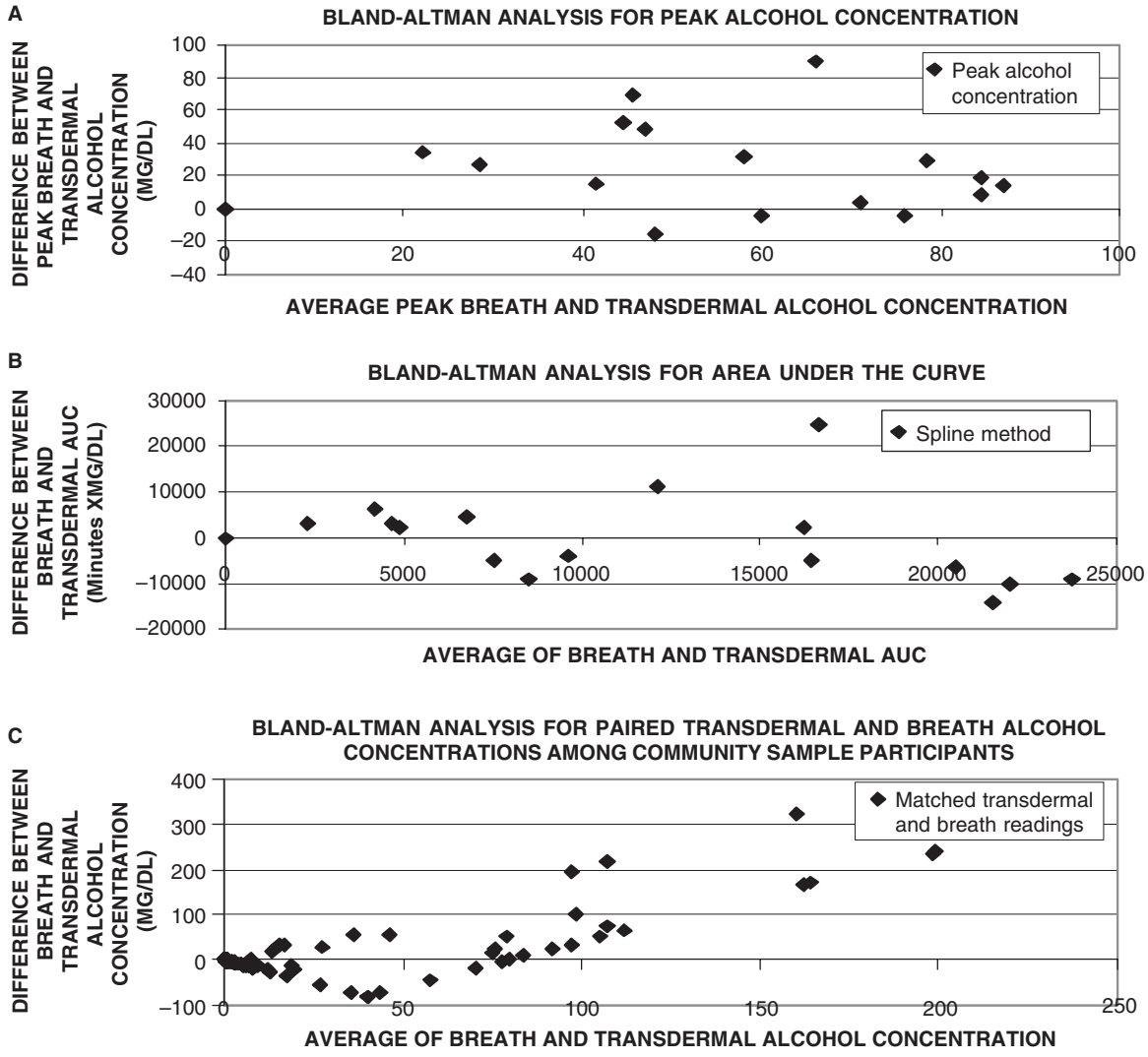

Fig. 4. (**A**) Bland-Altman analysis for the laboratory study [peak breath vs peak transdermal alcohol concentration (TAC)] and (**B**) Bland-Altman analysis for the laboratory study (area under breath and TAC curves). (**C**) Bland-Altman analysis for community sample participants (nearest-in-time breath and TACs).

breath tests when alcohol consumption was reported and positive breath tests when none was reported).

Between-Group Comparisons. Across the 8 days, self-reported number of drinks consumed, transdermal AUC, and mean TAC all differed significantly between the AD and NAD groups. The social drinking group (although nondependent by screening criteria) on average consumed about 20 standard drinks during the 8 days of testing, demonstrating at least moderate alcohol consumption in this group.

Bland-Altman Analyses. Bland-Altman analysis for community participants compared BrACs and nearest-in-time TACs (Fig. 4C). Again, many paired transdermal and breath samples differed by more than 20 mg/dl.

Next, for community participants, we correlated the number of standard drinks reported (for 8 days) with transdermal AUC (for 8 days) (across groups $r = 0.74$; $p < 0.001$; AD group $r = 0.57$; $p = 0.09$; NAD group $r = 0.31$; $p = 0.38$) and the mean TAC (across groups $r = 0.83$; $p < 0.001$; AD group $r = 0.56$; $p = 0.09$; NAD group $r = 0.64$; $p = 0.04$).

Survey on Comfort. Community sample participants were given a survey on comfort after wearing the anklet for approximately 1 week (Table 3). On average, those in both the AD and the NAD groups reported that the anklet was neither very comfortable nor very uncomfortable and caused some difficulty in physical activities such as sports or running. Many reported that others had noticed the device and asked questions about it but the device did not impede daily activities at home or outside the home, nor usual nighttime activities. Within-group means for each question were compared between the AD and NAD groups; no significant differences were found.

DISCUSSION

The study has 5 important findings: (1) Within the laboratory study, no false-positive tests were seen in the no-dose

Table 3. Comfort Survey Results: Community Sample Participants

Question	Anchor Points	Mean (SD) (Range) Non–Alcohol Dependent	Mean (SD) (Range) Alcohol-Dependent Group	Statistic *p* Value
I think this device is:	Very comfortable (0 mm) Very uncomfortable (100 mm)	44.5(39.4) (1–99)	54.4 (35.2) (12–99)	$t_{18} = -0.59$; $p = 0.56$
Compared to usual, while wearing the device, I could perform my daily activities at home (such as walking, showering, dressing, cooking) with:	No difficulty (0 mm) Great difficulty (100 mm)	14.4 (30.2) (1–96)	7.7 (15.3) (1–51)	$t_{18} = 0.63$; $p = 0.54$
Compared to usual, while wearing the device, I could perform my daily activities at work or outside my home (such as driving, working, shopping) with:	No difficulty (0 mm) Great difficulty (100 mm)	12.7 (30.6) (1–99)	2.6 (1.7) (1–7)	$t_{9.1} = 1.04$; $p = 0.31$
Compared to usual, while wearing the device, I could do physical activities (running, playing sports) with:	No difficulty (0 mm) Great difficulty (100 mm)	51.7 (47.4) (1–100)	28.4 (32.6) (0–93)	$t_{12.0} = 1.19$; $p = 0.26$
Compared to usual, while wearing the device, I could do my night-time activities (sleep, sex) with:	No difficulty (0 mm) Great difficulty (100 mm)	9.8 (21.0) (2–69)	29.6 (35.7) (2–100)	$t_{18} = -1.51$; $p = 0.15$
Other people saw the monitor and asked me questions about it:	Didn't happen (0 mm) Happened frequently (100 mm)	64.8 (40.8) (1–100)	49.8 (46.2) (0–100)	$t_{17} = 0.75$; $p = 0.47$

For each question, subjects were asked to mark the point on a 100 mm line that best represented how they felt; the line was measured for each question (0 to 100 mm) and means were calculated within each dosing group. SD, standard deviation. Because of nonnormality nonparametric tests were also completed but none of these analyses were significant at the $p = 0.05$ level.

laboratory group and of 16 subjects administered a dose of alcohol, none had a false-negative result by transdermal testing; (2) among the community participants, every subject reporting alcohol consumption during the week had positive transdermal alcohol readings; (3) the anklet was able to distinguish the low- and high-dose groups (laboratory) and the AD and NAD groups (community), suggesting that on average, summary measures of transdermal readings increase in a dose-dependent fashion; (4) Bland-Altman analyses suggest that individual TAC results (individual alcohol concentration readings, peak value, or AUC) cannot be reliably considered quantitatively equivalent to simultaneously obtained breath results; and (5) The device appears adequately comfortable for most users.

Agreement Between Self-Report and Transdermal Readings

In general, there was good agreement among community participants between self-reported alcohol consumption and transdermal results but it is important to note that there were some instances in which transdermal readings and self-reported drinking did not match. We know from previous studies that self-reports of drinking are generally reliable and are regularly used as a summary measure in research (Del Boca and Darkes, 2003), but that individuals may not always accurately record the timing and quantity of alcohol consumption from moment to moment; therefore, a comparison of self-reports and transdermal reports may be considered a test of reliability and not a test of validity. We observed behaviors that suggested some individuals had not taken as much care in recording their alcohol consumption as would have been preferred. In some cases, subjects did not fill out drinking logs but recalled the previous days' drinking from memory during their daily interview; others drank heavily and ultimately could not recall (had to estimate) the timing and amount of drinking. On several occasions breath tests for alcohol gave results inconsistent with the subject's self-reported alcohol consumption, providing objective evidence that self-report was sometimes inaccurate. Considering only the community study, it is impossible to know whether these episodes of disagreement between transdermal results and self-reported drinking indicate (1) poor self-reporting of the timing of alcohol consumption or (2) poor readings from the transdermal device. However, the laboratory study, in which time and amount of dosing are precisely known, strongly supports the validity of the device.

Comparison with Similar Devices

Unfortunately, comparisons with other existing devices such as the WrisTAS^{TM} were not completed in this study. However, despite the many similarities between the 2 devices there are a few obvious differences that merit comment. First, the WrisTAS^{TM} device is considerably smaller than the SCRAM^{TM}. Still on average, participants who wore the SCRAM^{TM} device for 1 week in our study found that it was neither very comfortable nor very uncomfortable. Although many reported that others had noticed the device and asked questions about it, wearing the device did not impede daily activities at home or at work. The device generally appears to be adequately comfortable for most

users although reducing its size may help to reduce the stigma associated with wearing the device and improve the patient's or probationer's overall satisfaction. Similar studies on the comfort of the WrisTAS™ do not appear to have been published to date. Second, the SCRAM™ system contains a passive method for downloading transdermal results through a modem stored at the subject's home. This system offers certain obvious advantages. Comparisons beyond this are difficult, and further studies that can elucidate the advantages and disadvantages of each device are merited.

Pharmacokinetics of Transdermal Alcohol. Although, in general, alcohol is known to rapidly diffuse across compartments, the elimination of transdermal alcohol is slowed; during absorption, TAC results were sometimes zero when breath results were not and during elimination, transdermal results remained positive after breath results had already returned to zero. This suggests the presence of a third compartment (such as fatty tissues), which takes up alcohol more slowly and holds alcohol after it is eliminated from the water compartment. Alternatively, this effect may relate in part to the anklet design. In an attempt to make the anklet water-resistant, only a small external outlet on the anklet covering was provided and this may not easily allow fresh air into the sampling chamber between readings. This may also partially explain the protracted transdermal readings.

Limitations. The device includes some antitampering elements. However, the device was tested with voluntary research subjects who had no incentive to attempt to tamper with the device. Thus, we cannot comment on how easily the device can or cannot be tampered with. We also did not explore factors that might influence transdermal readings (i.e., level of physical activity).

Potential Applications

The data from this study strongly support the validity of the SCRAM™ system as a method of monitoring alcohol consumption. Although individual readings from the device cannot be considered equivalent to blood alcohol concentrations, on average the device does provide meaningful information about relative alcohol concentrations. This device has several important potential applications. The anklet may be of use in clinical trials as an objective semiquantitative outcome measure (the device has a maximum alcohol reading of 80 mg/dl, suggesting that in very heavy drinking study populations, some information will not be captured). Criminal justice programs may use the device as a method to qualitatively identify drinking episodes, to monitor drinking among AD offenders to reduce recidivism, and to identify individuals in need of treatment [however, the device should not be used to approximate simultaneous blood alcohol concentrations (i.e., to charge an individual with driving under the influence of alcohol)]. Finally, after appropriate government approval, the device could be of use to clinicians treating AD patients.

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