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PROTRACTED LOW-DOSE IONIZING RADIATION EFFECTS UPON PRIMATE PERFORMANCE

Donald J. Barnes, M.A.

Rayford P. Patrick, Lieutenant Colonel, USAF

Michael G. Yochmowitz, Captain, USAF

Robert J. Yaeger, Sergeant, USAF

Neal E. Lof, B.S.

Kenneth A. Hardy, M.S.

Robert W. Bastien, Sergeant, USAF

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USAF SCHOOL OF AEROSPACE MEDICINE Aerospace Medical Division (AFSC) Brooks Air Force Base, Texas 78235



NOTICES

This final report was submitted by personnel of the Weapons Effects Branch, Radiation Sciences Division, USAF School of Aerospace Medicine, Aerospace Medical Division, AFSC, Brooks Air Force Base, Texas, under job . order 7757-05-22.

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The animals involved in this study were procured, maintained, and used in accordance with the Animal Welfare Act of 1970 and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources - National Research Council.

This report has been reviewed by the Information Office (OI) and is releasable to the National Technical Information Service (NTIS). At NTIS, it will be available to the general public, including foreign nations.

This technical report has been reviewed and is approved for publication.

DONALD J. BARNES, M.A. Project Scientist

DONALD N. FARRER, Ph.D.

Supervisor

ROBERT G. MCIVER

Brigadier General, USAF, MC

Commander

Editor: ARTHUR B. DAVIS

Supervisory Editor: MARION E. GREEN

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UNCLASSIFIED SECURITY CLASSIFICATION OF THIS PAGE(When Data Entered) 20 ABSTRACT (Continued) the monkeys' behavior was monitored during the 72-hour radiation exposure period. Ability to control the PEP was found to be relatively unimpaired, but all animals displayed classic prodromal symptoms including productive emesis.

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PROTRACTED LOW-DOSE IONIZING RADIATION EFFECTS UPON PRIMATE PERFORMANCE

INTRODUCTION

The Air Force nuclear survivability program was implemented to insure that each USAF system be capable of surviving in environments generated by the detonations of nuclear weapons. As aircrewmembers are integral to manned systems, a key part of the overall nuclear survivability program is the prediction of human response to nuclear environments.

For surviving aircraft, the most significant nuclear component in crew vulnerability analyses is nuclear radiation. Concurrent weapon effects such as electromagnetic pulse (EMP) appear to have little influence on human capabilities, while others such as the thermal pulse can be countered with hardware, e.g., cockpit thermal shields and PLZT segments for ilashblindness-retinal burn protection. Nuclear radiation is not easily countered by the aircraft and poses a potential threat to mission success.

According to Gerstner (6), the threshold for human reaction to nuclear radiation is about 100 roentgens (67 rads-midline). Above this level, reaction incidence increases rapidly until the trigger level of 300 roentgens (201 rads-midline) where "...each individual person seems to display fully the severity of the initial reaction peculiar to his degree of susceptibility; up to 600 roentgens, no appreciable further increase in severity occurs." At this trigger level, Gerstner expects 20% of exposed humans to be asymptomatic, 20% to experience mild reactions (i.e., brief spells of fatigue, anorexia, and nausea), 50% to experience moderate reactions including vomiting and marked weakness, and 10% to experience severe reactions leading to profuse vomiting and even possible prostration. Other discussions of human reactions are presented by Zellmer (18) and Hempelmann et al. (7).

Modern manned weapons systems are complex mechanisms which demand high degrees of operator proficiency. Such highly trained personnel must be capable of successfully performing complex tasks over long periods of time in the presence of physiological and psychological stresses. Therefore even small amounts of radiation stress could adversely impact mission completion.

Much of the information presently available to crew survivability/vulnerability analysts is based on clinical observations of cancer patients undergoing radiotherapy, nuclear accident victims, and survivors of Hiroshima and Nagasaki. This information is supplemented and complemented by experimental investigations using animal subjects. (The hazardous nature of radiation precludes use of human subjects.) Extrapolation of clinical observations to healthy, highly motivated and highly

trained aircrewmembers is tenuous. Of course, extrapolation from animal subjects to aircrewmembers is also hypothetically based and requires special assumptions. The experimentalist maintains an advantage, however, of being able to design experiments which correlate very closely to the operational situation. Using interspecies modeling techniques, these experimental data can be used to estimate radiation impact upon aircrew performance.

Past experimental research has largely been devoted to high-dose, pulsed radiation (neutron and gamma) exposures which generally resulted in relatively drastic changes in performance (2, 3, 4). Basic laboratory simulations of operational parameters led to reasonable estimates of crew vulnerability given such high-dose environments. Emphasis is currently being placed upon low levels of gamma radiation delivered at low dose rates. Such environments yield milder physiological reactions as well as more subtle performance effects.

Low-dose radiation effects upon performance have not been well defined. The available cata have been obtained from a variety of behavioral tasks, radiation types, and dose rates, and often cannot be compared. For example, Riopelle (16) found no evidence of a behavioral change using a task requiring a delayed response in monkeys exposed to 400-rad whole-body X-rays. Within the same dose range, Kaplan et al. (9) found no decrement in the retention of highly discriminative tasks. Leary and Ruch (10), and McDowell and Brown (12), respectively, observed a decline in cage activities in the 400 and 544-700 rad whole-body range of X-rays. Brown et al. (5) exposed rhesus monkeys performing discrete tasks over a 12-hour period to 300 rads (whole body) of gamma radiation and observed increased reaction times and decreased response accuracies in some subjects. In the latter experiment, serious attempts were made to correlate laboratory with operational parameters. The dose rates mentioned in these experiments were not comparable, thereby casting serious doubt upon the general applicability of these data.

The experiment reported herein is a continuation of the effort to design radiation experiments that more closely approximate operational conditions. The radiation profile, feeding schedule, mission duration, work loading, and task similarity were carefully tailored to approximate as closely as possible mission parameters of a manned aircraft on an airborne command and control type of mission. Extensive behavioral data were accumulated, processed, and analyzed to define normal preexposure performance and to assess performance in a low-intensity radiation environment. Emesis and other observable behavioral aspects of the radiation reaction were also recorded.

A second objective of this effort was the development and evaluation of new methods of representing the subjects' performance and detecting minimal changes in such performance. Earlier studies utilized relatively crude performance metrics and used only one preexposure baseline as a standard of comparison. For the catastrophic performance changes evoked

by high-level pulsed radiation exposures, these methods were adequate. However, subtle changes may have been masked by normal subject variability on a day-to-day basis, as well as by "learning curve" trends.

EXPERIMENTAL METHODOLOGY

This experiment was designed to simulate the mission parameters, crew work schedule, and other characteristics of a manned aircraft engaged in a 72-hour mission. The radiation profile used in this experiment is shown in Figure 1. It was based on the hypothesis that soon after

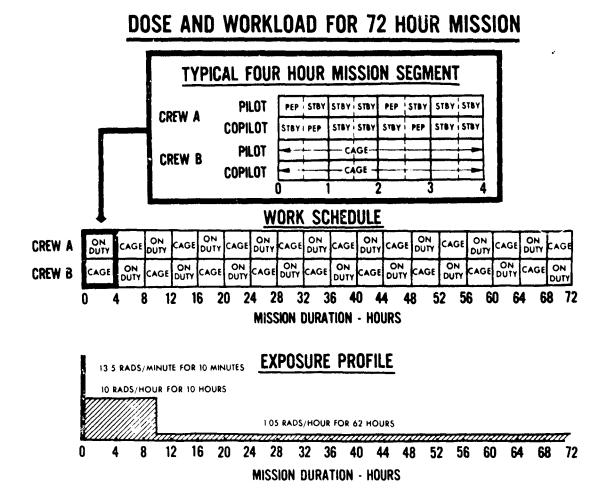


Figure 1. Radiation dose and workload for a 72-hour mission.

takeoff, the aircraft penetrated a radioactive cloud generated by the detonation of a megaton-class enemy weapon (14). The immersion dose from such a penetration was estimated to be 135 rads accumulated over a 10-minute period. It was further hypothesized that the aircraft was not fitted with a protective filter and that some of the radioactive cloud material was drawn into the aircraft via the environmental control system, while some adhered to external aircraft surfaces. All of this material contributed to irradiation of the crewmembers throughout the remainder of the mission. The dose rate from such exponentially decaying radioactive material was approximated by dose rates of 10 rad/hour for 10 hours, followed by 1.05 rad/hour for 62 hours. The total hypothetical radiation dose accumulated by the aircrew then was 300 rads.

The radiation in this scenario was limited to gamma. Neutron flux and X-radiation are associated with prompt output of the nuclear detonations and are not considered significant factors here. The late-time radioactive cloud accidentally penetrated by the aircraft is of major concern. The cloud consisted of decaying fission products emitting photons with an average energy of about 1 MeV.

An additional concern for an aircraft with an unfiltered air supply penetrating radioactive clouds is the possible effects of beta radiation upon exposed skin surfaces. The beta radiation dose for exposed skin for the radioactive material ingested into the cockpit for these hypothesized situations could cause some irritation, erythema, and potential blistering to exposed skin over a long mission. This potential hazard cannot be easily simulated in the laboratory and is therefore not included in this effort.

The hypothetical crew workload during the mission is also shown in Figure 1. The aircraft is manned by two crews, each with a duty schedule of 4 hours on and 4 hours off. During each 4-hour tour of duty, each crewmember controls the aircraft for two 30-minute periods. During the remainder of the 4 hours, the aircraft is assumed to be on automatic pilot, and the crewmembers are relatively idle.

We are unaware of existing criteria for estimating the food-intake of operational personnel. For experimental purposes, it was assumed that the aircrew consumed a meal 1 hour prior to the mission and subsequent flight lunches during off-duty periods.

All of the above mission parameters (except the beta radiation exposure) were carefully considered and their simulation attempted in this experiment. The radiation exposure profile was duplicated within the accuracy of our sensors. The decaying fission product gamma radiation was simulated using a cobalt-60 source which emits photons with energies representative of fission-product photons. The work cycle and mission duration were based on the hypothetical profile of Figure 1. The experimental subjects (rhesus monkeys) were fed 1 hour prior to exposure and again when relieved from each experimental session. Task proficiency

was achieved by extensive preexposure training and baselining of the subjects. The Primate Equilibrium Platform (PEP) was selected to simulate manual aircraft control.

The PEP is a platform gimballed about two axes (Fig. 2), and controlled by a joystick. The primates were trained to control the horizontal position of the platform by manipulating the joystick in response to a turbulence-like input-forcing function driving the platform off-horizontal. (The PEP can operate in both pitch and roll modes, but to facilitate data processing and analysis, only the pitch mode was used in this study.) Control of the PEP requires continuous attention and corrective action via a relatively sophisticated motor response. The PEP

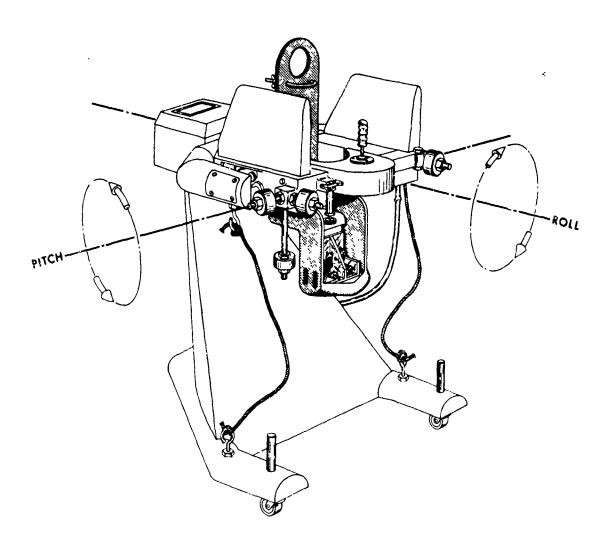


Figure 2. Drawing of the Primate Equilibrium Platform (PEP).

has proved valuable in past research designed to investigate pulsed radiation effects (2, 3, 4). Thus, its selection for this experiment was based on proven usability as well as task similarity to aircraft manual flight controls.

A block diagram of the PEP adapted from Jaeger (8) is depicted in Figure 3. Note that the input-forcing function drives the PEP. The subject senses PEP motion and compensates by moving the joystick. Therefore, the actual displacement of the PEP is due to both input-driving function and joystick displacement.

PRIMATE EQUILIBRIUM PLATFORM (PEP)

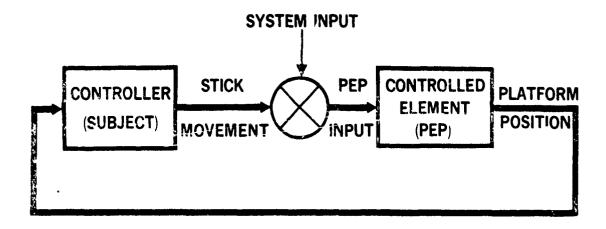


Figure 3. Block diagram of the Primate Equilibrium Platform.

The input-forcing function consisted of a random-appearing signal composed of a sum of sine functions similar to that used by Bachman et al. (1). This signal was recorded on an analog magnetic tape, and the same tape was used for each baseline and exposure run.

Four naive male rhesus monkeys (Macaca mulatta) weighing between 4.3 and 5.7 kg were randomly selected and paired as "crews." Standard operant conditioning techniques were used in training the animals in the PEP. They were first restrained in a couch with a neck bracket, a lap bar, and foot and ankle straps which allowed unrestricted use of the hands and arms. The subjects enjoyed limited freedom to readjust their positions to minimize body chaffing and to maintain local circulation. The subjects

were then trained by successive approximations to maintain the PEP in a horizontal position in the face of an externally introduced forcing function. Initially, allowable angles from horizontal were set at ± 25 degrees. Mild electrical shock (3 to 5 ma for 1 to 3 ms) was administered through conductive footplates at a rate of one shock per second when the PEP exceeded and remained outside the allowable limits. As the subjects' proficiencies improved, the allowable limits were gradually decreased to ± 10 degrees. Training was rapid, with all subjects performing at the ± 10 -degree level within eight 1-hour training sessions. After 20 sessions, the subjects were considered trained sufficiently to begin statistical definition of their preexposure performance.

At the time of exposure the subjects' performances were in the ± 3 - to 6-degree range. It would probably have been possible to establish even more stringent shock limits; however, the ± 10 -degree limits minimized the number of shocks received by the subjects and hence reduced the possibility of contaminating the data with shock-induced artifacts.

The identification and quantification of performance change deals, with comparison of the subjects' performance in a radiation environment with preexposure, or baseline performance. Training-curve trends and intrasubject variability tend to confound baseline data and to subsequently bias comparisons of radiation and baseline performance, particularly in experiments where only relatively subtle changes are expected. Therefore, to maximize the probability of detecting performance change, extensive baseline data were obtained to quantify a subject's "normal" performance. Six baselines were obtained for each animal, i.e., six 72-hour runs with all experimental parameters (except radiation exposure) identical to the exposure run.

The procedure followed for each baseline and exposure run was as follows: The animals were fed at 0730 on the initial day of the 72-hour run. At 0800, they were positioned in front of the large cobalt-60 radiation source for 10 minutes (Fig. 4). They were then transported two miles to the Low-Dose Facility (17) where 2 animals (crew A) were placed in PEPs, and the other 2 subjects (crew B) were placed in cages. This configuration is shown in Figure 5. The Low-Dose Facility consists of two buildings, an exposure building and a control building, located about 100 m apart.

The second of the second second

After the subjects were positioned in the exposure building, visual observations of the animals were made via closed circuit television from the central building. Subject performance was monitored using analog (MINIAC) and digital (PDP-12) computers connected to the PEPs by data transmission lines. At 4-hour intervals throughout the 72-hour run, the animals were exchanged and the subjects being relieved from performance tasks were fed. Water was continuously available to the caged animals. Room lights remained on during the entire 72-hour period.

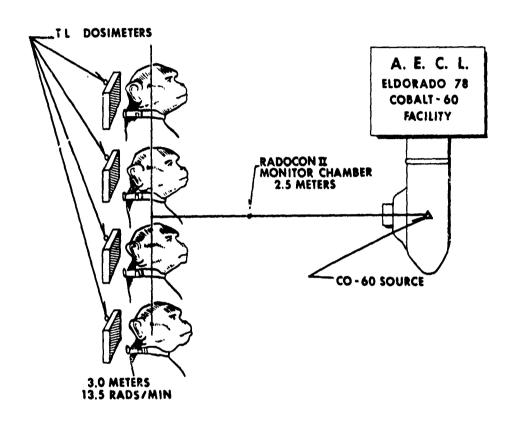


Figure 4. Exposure configuration in the AECL facility.

Standard dosimetry techniques were utilized during radiation exposure. In addition, extensive preexposure calibration was conducted using monkey phantoms, i.e., monkey-shaped figures constructed of material with characteristics similar to monkey tissue.

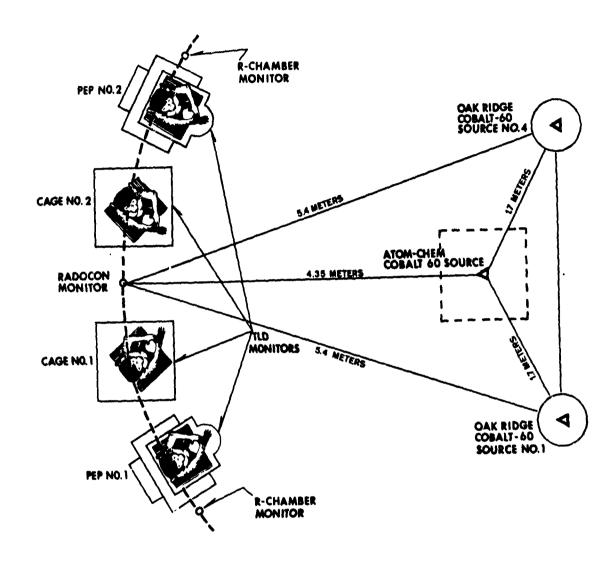


Figure 5. Exposure configuration in the Low-Dose Facility (LDF).

DATA COLLECTION, PREPROCESSING, AND ANALYSIS

On-Line Data Collection

Five variables related to the platform position (Fig. 3) were measured on-line for each subject. They were Ptime 5, Ptime 10, Ptime 15, RMS (ψ), and Static (μ). Ptime 5, Ptime 10, and Ptime 15, respectively, represent the percent time the animal maintained the platform within 5 degrees, 10 degrees, and 15 degrees of the horizontal. RMS is the root mean square value of platform position. Static is the mean platform position over a given time interval.

By definition:

$$\psi^2 = \frac{1}{T} \int_0^T P(t)^2 dt \tag{1}$$

$$\mu = \frac{1}{T} \int_{0}^{T} P(t) dt$$
 (2)

where P(t) is platform position at Time t, and T is the epoch length under observation. The root mean square of the platform position as defined is a combination of the subjects' control capability and set, or reference position with respect to the horizontal. The static, or mean platform position, is utilized as an epoch reference position which may differ from the horizontal. The static, while not necessarily indicative of performance ability, is required for subsequent off-line data reduction/manipulation.

Each of the 30-minute work sessions was divided into sixty 30-second epochs. During each of the epochs, the five basic variables were determined. These calculations were accomplished on an analog computer, Electronics Associates Incorporated MINIAC. At the end of an epoch, the digital computer, PDP-12, sampled the MINIAC's data accumulators and printed the data on the teletype for on-line review. The data were also recorded on digital magnetic tape for daily transfer to an IBM 360 for detailed analysis.

The performance data discussed above were complemented by visual observations of the animals' behavior during baseline and radiation runs using closed circuit television. In addition, during the radiation run, the video signal was taped for future study.

Off-Line Data Processing

Subsequent to transfer of the data gathered on-line to the IBM 360 computer, σ , the root mean square of the platform signal about the mean platform position, i.e., adjusted RMS, was calculated.

$$\sigma^2 = \frac{1}{T} \int_0^T \left[P(t) - \mu \right]^2 dt$$

Because σ is calculated relative to each monkey's mean platform position, it should be more representative of the animal's capability to control the PEP than ψ which is based on a horizontal reference for all animals. σ and ψ are related as follows:

$$\psi^2 = \sigma^2 + \mu^2$$

Examination of data in Appendix A revealed that the variables Ptime 10 and Ptime 15 were deterministic, i.e., they were near 100% for all cases. Ptime 5 was the only one of these percentage variables containing appreciable variation. Since one percentage score of this type is not adequately reflective of performance capability, these variables are not good performance indicators.

The variables σ , ψ , and μ were subjected to additional analysis. The consistency and the worst case score were determined for each of these variables over a 30-minute session, based on consideration of the sixty 30-second epoch scores. Consistency is defined by the standard deviation of the sixty 30-second scores about the mean and is indicative of the subjects' variability in PEP control over the session. The worst case score is the largest epoch score in a session, and if excessively large, may be indicative of momentary loss of control. In an operational environment, both these measures could be significant. A single lapse could be of concern in an unusually demanding situation, e.g., aerial refueling.

To measure rate of mean performance change and initial work period responses for each epoch, the standard least-square estimates of the slope and intercept of the regression line, y = mx + b, were computed for each variable of interest. Fatigue is suggested by a positive value of the slope, i.e., the capability to control the PEP worsens with time. The intercept is suggestive of initial performance in a session.

Comparative Analysis Techniques

The data for the six baselines were first checked for trends. If stable performance was not obtained, learning curve trends (performance improvement with time) and/or regression in performance could confuse the

analysis and make the detection of performance change with radiation more difficult. The trend test was accomplished using Page's distribution free test (13) for each subject for all of the variables.

After the trends analysis, normal performance was defined in two ways. The first method combined the data from all baselines and the range of normal performance within 95% confidence limits was computed using a simultaneous tolerance limit technique studied by Rahe (15). However, those variables which showed trends could not be legitimately treated in this manner. The presence of trends indicates that performance is not stable, i.e., learning curve effects contaminate the preexposure performance data. Therefore, a second method of defining performance utilized only the last preexposure baseline. This approach assumed that performance was asymptotically approaching a physiological limit; therefore, the last baseline would be a more reasonable standard of comparison than the average of all baselines. It is noted that for trend-free data the first approach is preferable because more subject variability is accounted for.

DISCUSS!ON

Performance

Graphical results are contained in the Appendixes. Appendixes A through C contain preexposure results. Appendix A contains the 30-minute scores for the six basic variables. Each variable is treated separately in graphs depicting all of the animal scores for each baseline. Appendix B contains the consistency, or standard deviation calculations, and the maximum epoch scores of the basic variables ψ , σ , and $|\mu|$. Appendix C contains the epoch slope and intercept calculations of the same three variables. Appendix D contains the exposure data for the six basic variables, exposure worst case and standard deviation scores, and slope and intercept calculations for exposure. Appendixes E and F depict the results of two different comparative analysis techniques. Appendix G is a detailed dosimetry report.

Significant features of the preexposure data contained in Appendix A include (1) the difference in the response characteristics of the two PEPs, (2) the clustering of the data for each subject about a unique locus, (3) anomalous data points, and (4) the lack of discrimination between subjects for the variables Ptime 10 and Ptime 15.

The PEP differences were known a priori and dictated the procedures of allocating experimental subjects to a particular PEP for the duration of the experiment. The fact that such differences were apparent in the data (subjects 1 and 2 operated PEP 1 and subjects 3 and 4 operated PEP 2) suggests that the performance metrics were reflective of actual performance. The clustering of baseline data for each subject about a unique locus also was encouraging, as change in performance would be more easily identifiable. On-line investigation of several of the anomalous data

points revealed that some experimental defect was present. For example, during the third baseline of monkey 170, the shock leads had come loose resulting in unusually high scores. This sensitivity to performance change not only pointed out the need for on-the-spot corrective action during preexposure baselines but also promised good potential for detection of postexposure performance change. The fact that the Ptime 10 and Ptime 15 measures were not sensitive to subtle performance change greatly limited their utility. Ptime 5 scores appeared to correlate with subject performance reasonably well, but a single percentage score is not definitive.

The consistency scores of σ and ψ contained in Appendix B were generally within one degree, suggesting consistent PEP control over an epoch. However, PEP and subject differences were not easily separated, limiting the credibility of this metric as a good indicator of performance. The worst case epoch scores also contained in Appendix B averaged about 5 degrees, and PEP and subject differences were more clearly pronounced.

The slope and intercept calculations for preexposure performance in Appendix C again indicated PEP and subject differences. The intercept scores generally were comparable with the epoch data, suggesting little fatigue over an epoch.

The slope data, on the average, were positive over a 30-minute session. However, the session scores remained almost constant over the 72-hour baseline, suggesting that fatigue was of little concern over this extended period. Apparently the work/rest cycle allowed excellent recuperation.

The raw exposure scores for the six variables, the consistencies and worst case scores over a session, and session slopes and intercepts are graphically displayed in Appendix D. Casual examination of these data reveal no drastic performance effects, hence the need for more sophisticated statistical techniques to quantify subtle changes.

Appendix E contains the results of the comparison of exposure scores with the averaged data from all six baselines. The results of the analysis are summarized in Table 1. The No's in the table indicate that no significant performance change ($\alpha = .05$) was found. The trend indications denote a trend in the baseline data, either increasing or decreasing, which invalidates the all-baselines comparative analysis. The times annotated in the table denote the epochs in the exposure run where significant differences were found ($\alpha = .05$). Note that no adverse effects were found in the adjusted RMS, σ , which is the variable most representative of the subjects' capability to control the PEP. This finding suggests that the experimenta! subjects maintained good PEP control capability; however, this measure is a time averaged calculation and is not very sensitive to momentary loss of control. Momentary loss of control is more likely to be reflected in the worst case calculations. In the comparisons for these measures, subject 170 exhibited significant differences between exposure and baseline performance at 20 hours into the exposure run and subject 836 at 10 hours.

TABLE 1. EXPOSURE VS. ALL BASELINE COMPARISON ($\alpha = .05$)

Monkey No.

No No No No No No No No		Monkey No.				
No T=64,66 No No No		Variable	170	836	896	902
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Max μ		Ptime15	No	No	No	No
consistency calculations $\begin{array}{cccccccccccccccccccccccccccccccccccc$		Маж 🜵	No	T=10	No	Trend ↓
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$b\sigma$ Trend † No Trend ‡ $m\psi$ No Trend ‡ No No No $m\mu$ No Trend † No No	slope	bμ	No	Trend	No	No
m _μ No Trend † No No		bσ	Trend †	No	Trend ↓	Trend
		mψ	No	Trend ↓	No	No
mσ Trend↓ No No Trend↓		m μ	No	Trend †	No	No
		Bσ	Trend ↓	No	No	Trend ↓

Trend \uparrow = Page's test detected an increasing trend with $\alpha = 0.05$.

Trend \downarrow = Page's test detected a decreasing trend with $\alpha = 0.05$.

No = No radiation effect detected by 95% tolerance limits.

T = XX:Time in hours at which radiation effects were detected by 95% tolerance limits.

* = This animal performed better than past performance.

These differences suggest momentary problems in PEP control which may be operationally significant during particularly critical mission phases. On the other hand, subject 836 exhibited an improvement in PEP control at 26 hours as reflected by the adjusted RMS, o. At 44 hours into the run the consistency of subject 170 was significantly different from normal, possibly suggesting erratic control.

Appendix F contains the results of the comparative analysis utilizing the last baseline to define normal performance summarized in Table 2. There were no performance changes in the major basic performance metrics of interest, σ ; however, the changes in the consistencies and worst case epoch scores of monkeys 170 and 836 were again evident. Note also that the improvement by monkey 836 at 26 hours into the mission using the all baselines comparison was not reflected in this analysis.

The changes in the mean platform position observed in both comparative analyses are interesting but cannot be related to performance decrement. Therefore, the operational significance of such changes is not apparent.

As a rule of thumb, those performance changes which are statistically significant in both types of comparative analyses are highly credible. On the other hand, those differences which are statistically significant only in one or other of the analyses are more questionable in their operational significance.

Emesis

The task used in this experiment is relatively simple in comparison with the duties of an actual crewmember, although some degree of similarity is evident. For this reason the performance data alone could be misleading when attempting to estimate crewmember response to nuclear radiation. Visual observations of the subjects during baseline and exposure runs provided valuable supplemental information to be considered in any extrapolation of these performance data to human operators.

During the exposure run, all 4 subjects demonstrated mouthing, retching¹, and productive emesis (vomiting). They also exhibited anorexia, refusing food over the 72-hour period as well as unusual listlessness suggestive of fatigue.

Retching is difficult to quantitatively define without relatively extensive physiological monitoring techniques. Retchings assumed precursor, nausea, is even more subjective and not amenable to direct measurement with nonhuman subjects. Even so, mouthing and retching are suggestive of nausea. We defined retching as those responses which seem to be involuntary and which involve contractions of the abdominal muscles with or without open-mouthed (gagging) responses.

TABLE 2. EXPOSURE VS. LAST BASELINE COMPARISON (α = .05) Monkey No.

			monkey, No.		
	Variable	170	836	896	902
Basic	ψ	No	No	No	No
measurements	μ	No	T=48,50,56, 58,64,66	No	No
	σ	No	No	No	No
	Ptime5	No	No	No	T=60
	Ptime10	No	No	No	No
	Ptime15	No	No	No	No
Worst case	Max ∳	T=20	T=10	No	No
and consistency calculations	Max μ	No	No	No	No
	Max o	T=20	T=10	No	No
	SD ♥	T=44	No	No	No
	SD µ	T=44	No	No	No
	SD · σ	T=44	No	No	No
Initial	b∳	No	T=8,10	No	T≃60
and trend calculations	bμ	No	No	No	No
	bσ	No	T=48,50,56, 58,64,66	No	No
	mψ	T=-14	No	No	T=68*
	m _p	No	No	No	No
	mσ	No	No	No	No

^{#6 =} No radiation effect detected by 95% tolerance limits.

 $T=X\mathcal{R}; Time in hours at which radiation effects were detected by 95% tolerance limits.$

^{* =} This animal performed better than his last biseline performance.

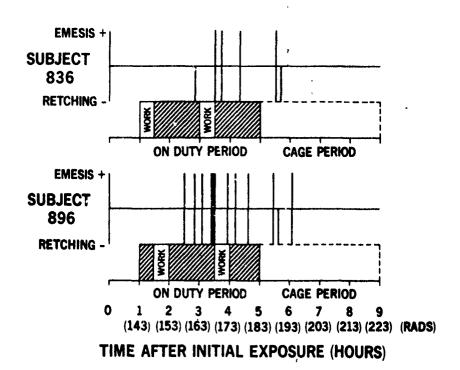
The retching and emesis data gathered in this experiment are not as definitive as had been anticipated because of poor illumination. In most experiments the animals are restrained so that retching and emesis are readily observed. However, in this experiment, 2 animals were in cages at all times and tended to lie on the cage floor or to huddle in a corner of the cage so that only productive emesis was readily apparent.

The retching-emesis data are shown in Figure 6. Three of the 4 subjects began showing signs of emesis just after the second hour following the onset of the initial radiation. The fourth subject, the largest and most robust of the group, showed less prodromal symptomology throughout the entire experiment, vomiting only once approximately 3 1/2 hours after the initial onset of radiation. It is interesting to note that the dose delivered to the animals up to the demonstration of significant emetic responses was between 145 and 165 rads for all subjects—a somewhat lower dose than might have been predicted prior to this experiment.

The number of productive episodes and their severity, as noted by the observer, varied significantly among the subjects, ranging from 1 to 9 productive episodes. The subject demonstrating 9 episodes often retched for several minutes during each period and appeared much weaker and generally more disabled during subsequent couching and working periods even though the behavioral measures did not reflect a significant degree of performance decrement.

Additionally, only 1 subject vomited while working and demonstrated only a relatively weak response just 2 minutes prior to the end of a working period. (Note that this subject had several episodes immediately prior to starting work.) It is interesting to speculate on the degree to which performing may actually ameliorate the prodromal symptoms occasioned by radiation.

The 100% rate of emesis noted in this experiment contrasts with the results of Brown et al. (5) where only 1 of 8 negatively reinforced animals performing a lever-pressing task over a 12-hour, 300-rad profile experienced emesis. In both experiments, the animals were fed immediately prior to mission start. The total dose profiles were similar, but the initial dose was higher and dose rate lower in the present experiment. Tasks and workload differed in that lever-pressing is a discrete task while PEP control is continuous. Also, the animals worked about 12% of the time in this experiment and about 92% of the time in Brown's experiment. Another difference, perhaps of even greater import, is related to movement of the subject and the contiguity of that movement with the receipt of radiation. In a recent pilot study at USAFSAM, Mattsson (11) exposed naive monkeys to cobalt-60 radiation in order to establish an ED_{50} for productive emesis. The subjects couched in a stationary apparatus vomited at an ED $_{50}$ dose of 450 rads, while those subjects placed in the PEP and subjected to random motion vomited much more readily, establishing an ED50 dose of 258 rads.



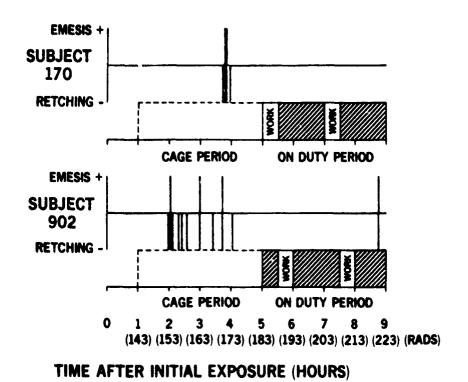


Figure 6. Record of retching and emesis for the four subjects.

The present findings certainly lend credence to the hypothesis that motion and the absence of performance combine to yield an ideal environment for initiation of productive emesis by gamma irradiation.

CONCLUSIONS

Analysis of the data obtained in the experiment indicates that minor changes in subject performance resulted from exposure to 300 rads. These changes suggest possible momentary lapses in PEP control for 2 of 4 subjects.

Such changes may be of concern in an operational situation during critical mission phases; however, the relatively mild effects seen here would probably only result in some increase in the time required for the performance of any given task. Of more concern than the minor performance changes were the physiological changes of the animals observed during the exposure run. All of the animals exhibited classic prodromal symptoms, i.e., ancrexia, asthenia, and nausea, and all experienced productive emesis. Since it is difficult to predict human reactions to such discomfort, extrapolation of the performance data alone to the more heavily burdened and stressed crewmember must be done with great care.

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APPENDIX A

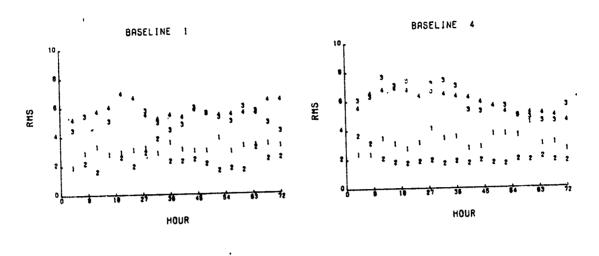
BASIC MEASUREMENTS

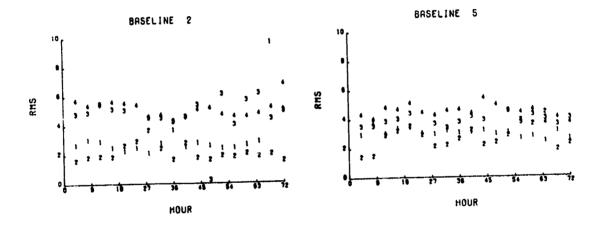
This appendix contains the eighteen 30-minute baseline scores for each subject for the variable RMS (ψ_K), adjusted RMS (σ_K), static (μ_K), Ptime σ_K , Ptime σ_K , and Ptime σ_K , where σ_K in these figures

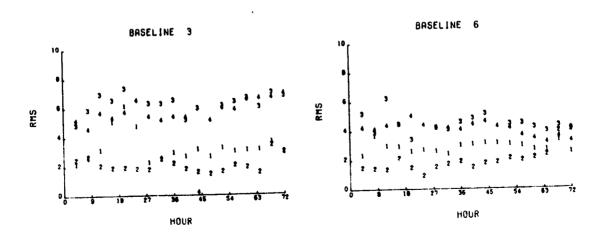
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- 3 = Subject No. 896
- 4 = Subject No. 902

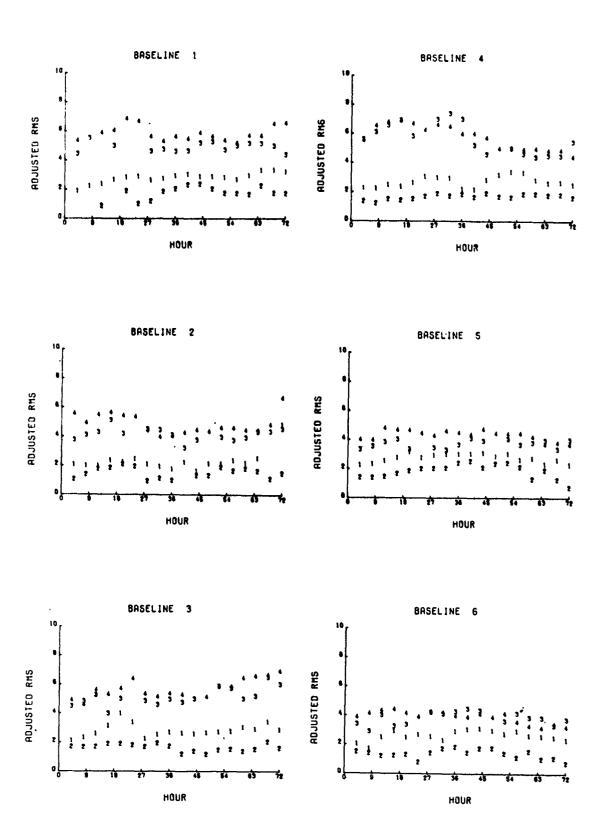
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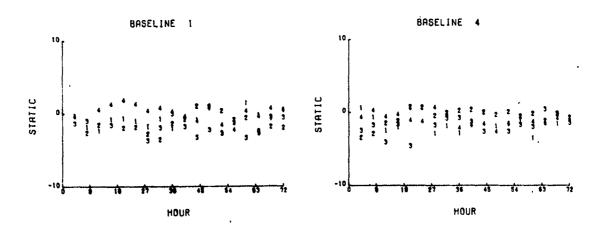
Page	Variable
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25	Adjustec RMS
26	Static
27	Percent Time 5
28	Percent Time 10
29	Percent Time 15

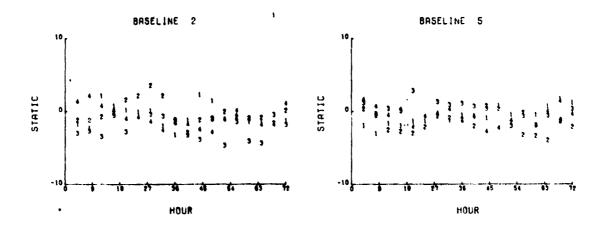


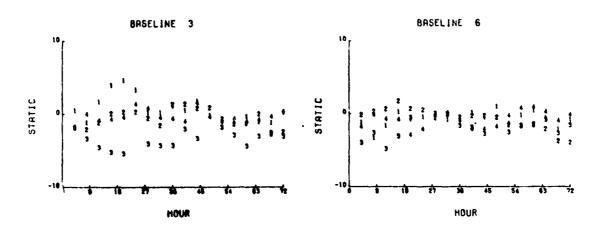


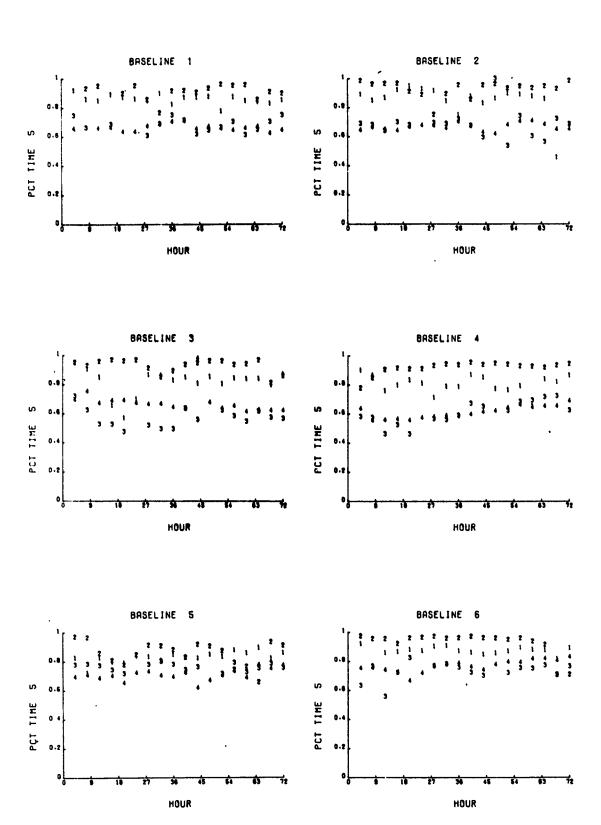


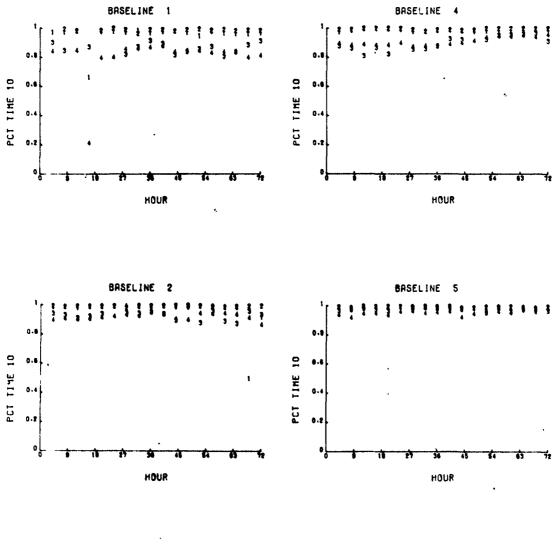




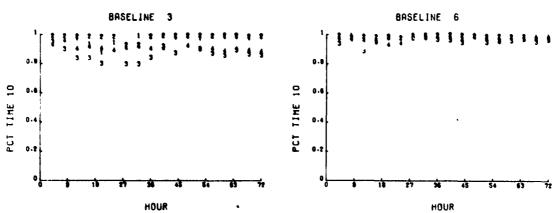




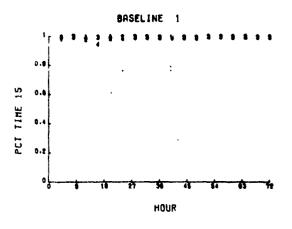


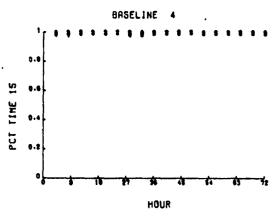


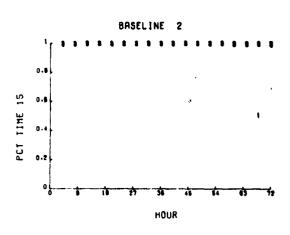
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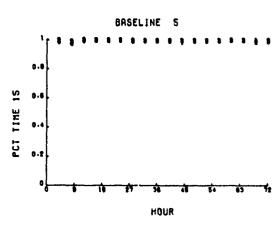


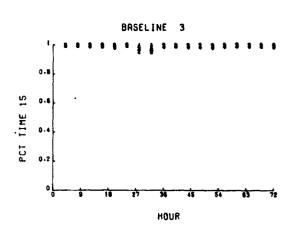
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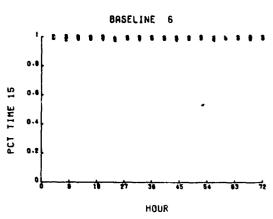












APPENDIX B

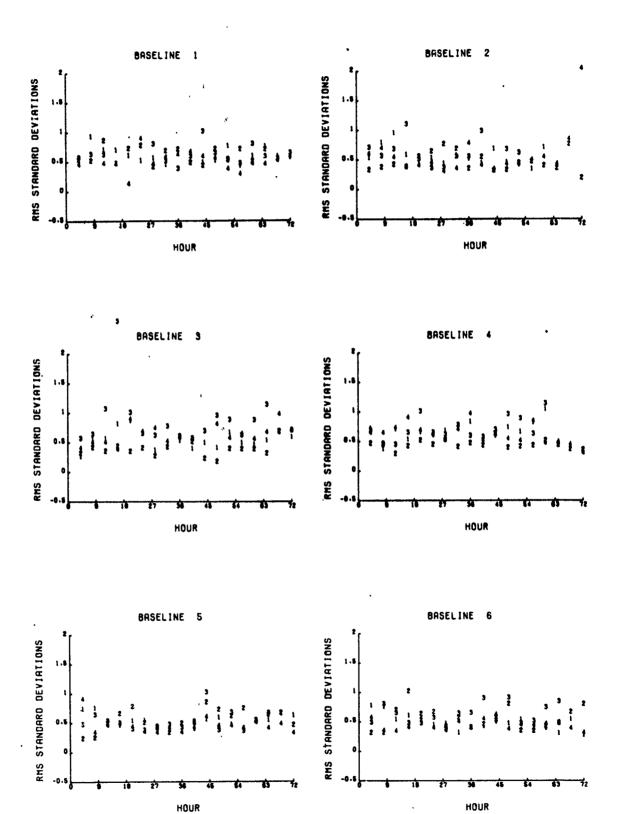
WORST CASE AND CONSISTENCY MEASUREMENTS

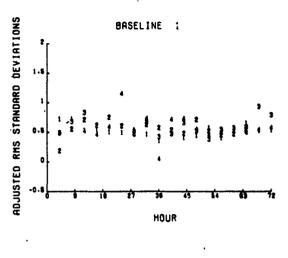
This appendix summarizes consistency of response by means of RMS standard deviations (SD ϕ_K), adjusted RMS standard deviations (SD σ_K), and static standard deviations (SD μ_K). It also gives worst case maximum RMS and adjusted RMS scores Max ψ_K and Max σ_K as well as the maximum absolute static deviation Max μ_K where K = 1,...18. We continue the convention that

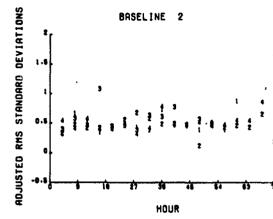
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- 3 = Subject No. 896
- 4 = Subject No. 902

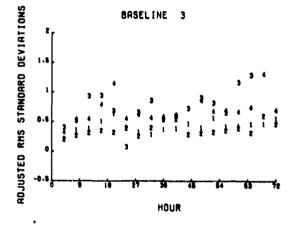
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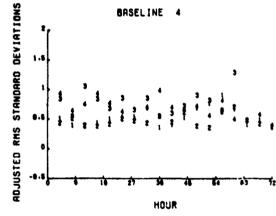
Page	<u>Variable</u>
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32	Adjusted RMS Standard Deviations
33	Static Standard Deviations
34	RMS Maximums
35	Adjusted RMS Maximums
36	Absolute Static Deviations

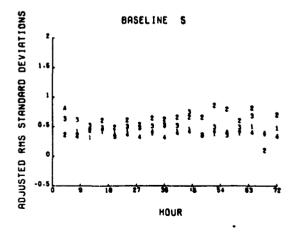




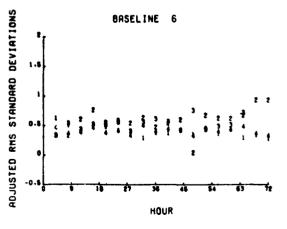


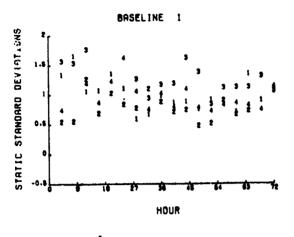


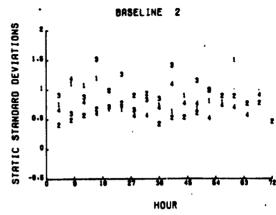


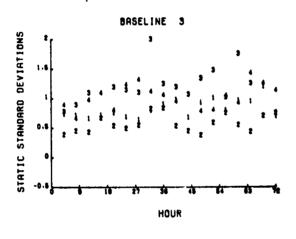


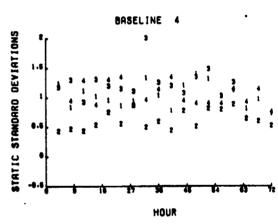
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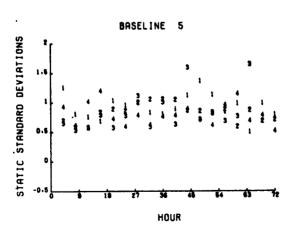


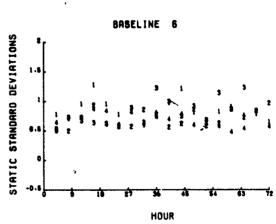


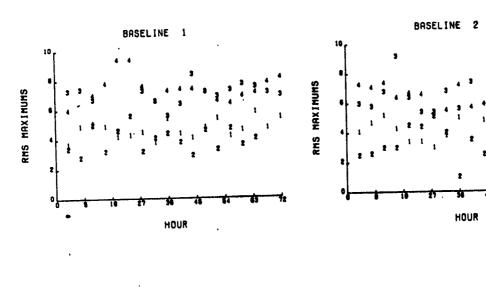


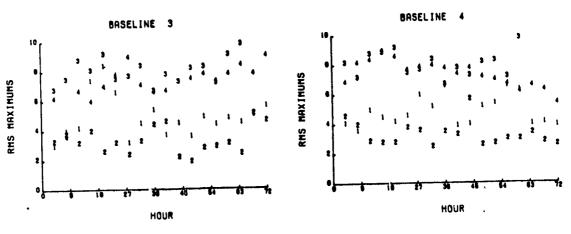




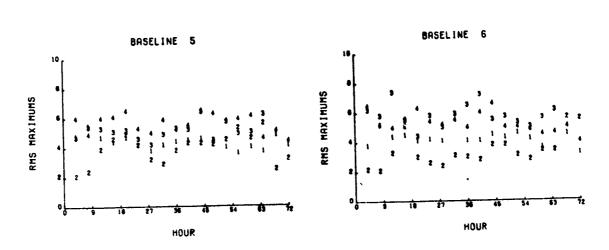


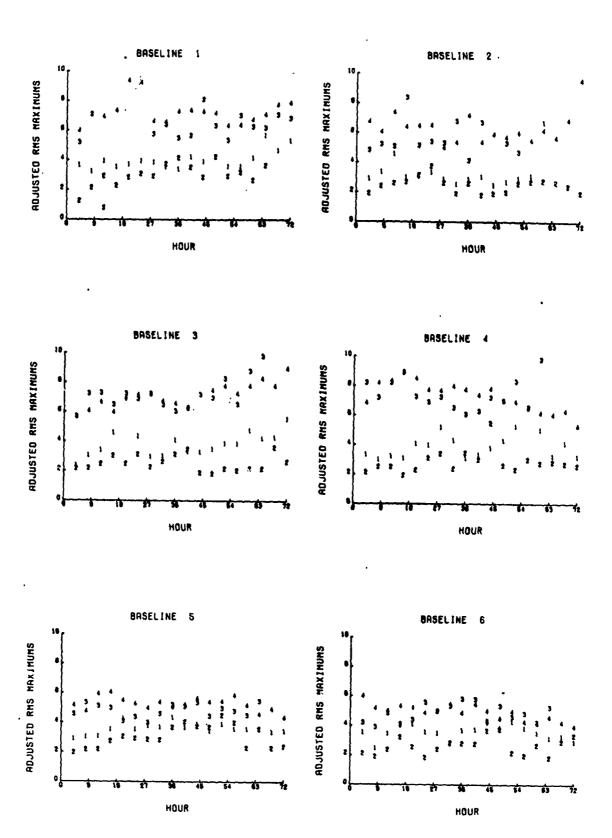




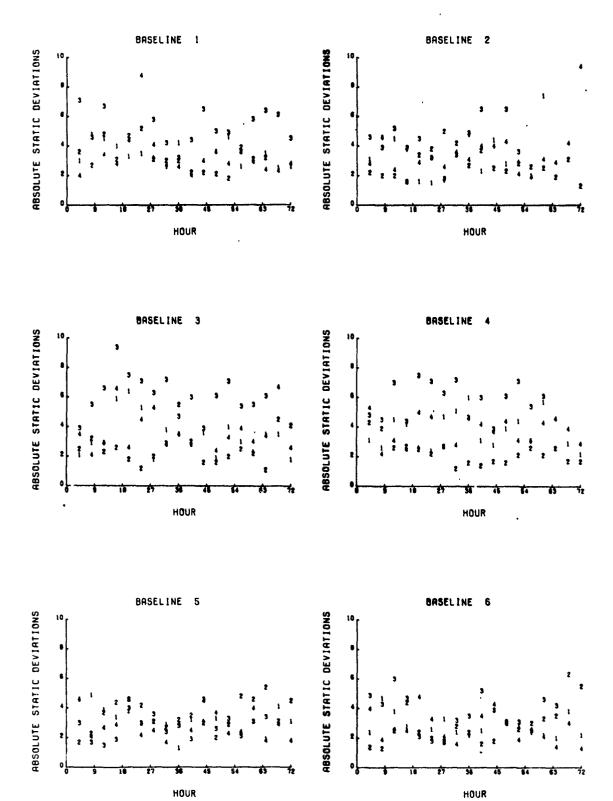


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APPENDIX C

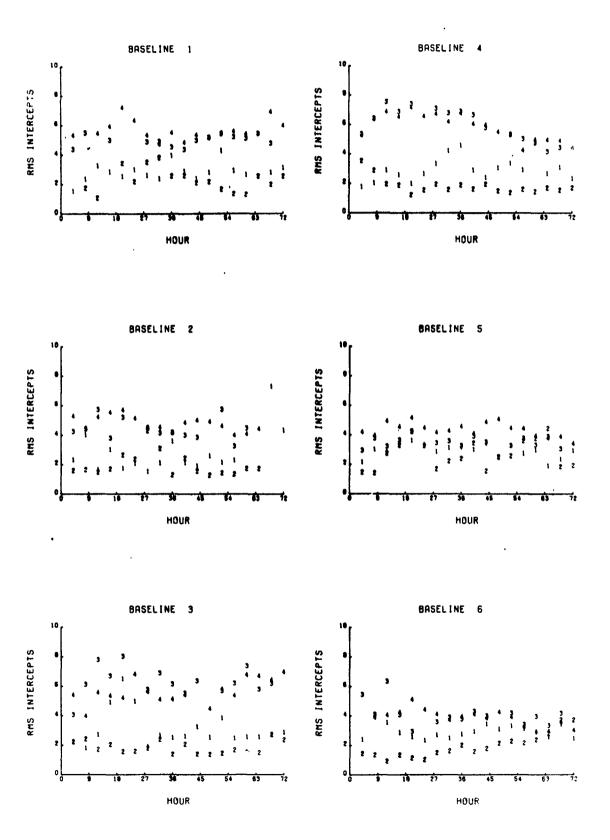
INITIAL AND TREND MEASUREMENTS

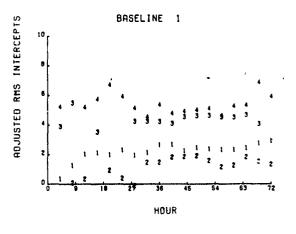
This appendix contains the eighteen 30-minute baseline scores for each subject for the variables RMS intercept (b ψ_K), adjusted RMS intercept (b σ_K), static (b μ_K), RMS slope (m ψ_K), adjusted RMS slope (m σ_K), and static slope (m μ_K) where K = 1,...,18. In these figures

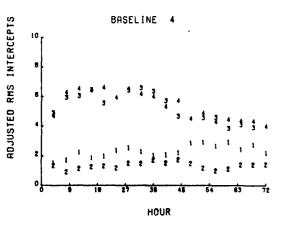
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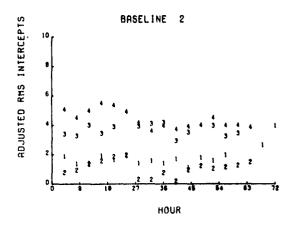
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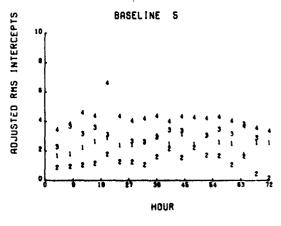
Page	Variables
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39	Adjusted RMS Intercepts
40	Static Intercepts
41	RMS Slopes
42	Adjusted RMS Slopes
43	Static Slopes

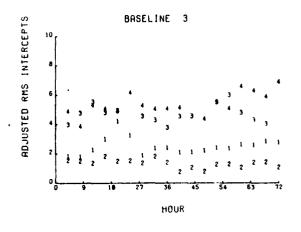


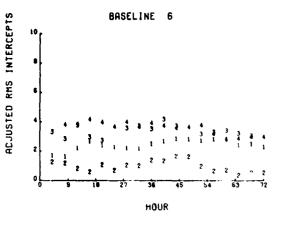


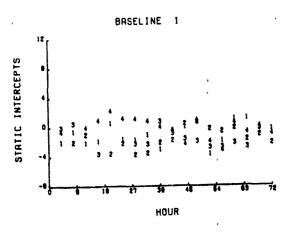


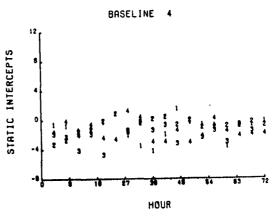


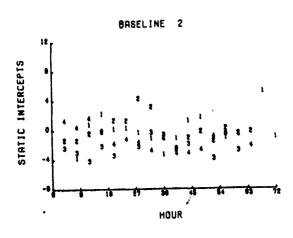


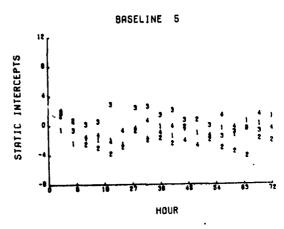


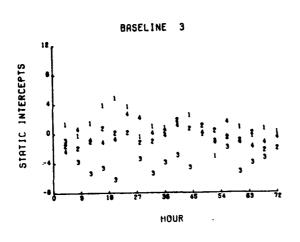


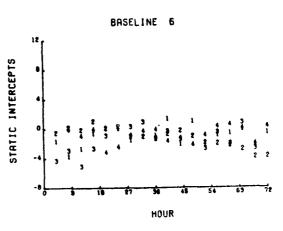


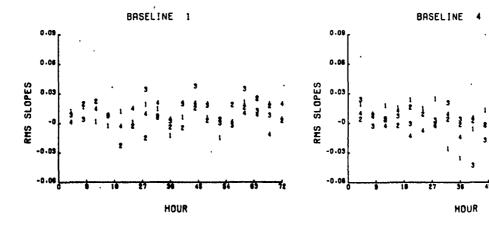


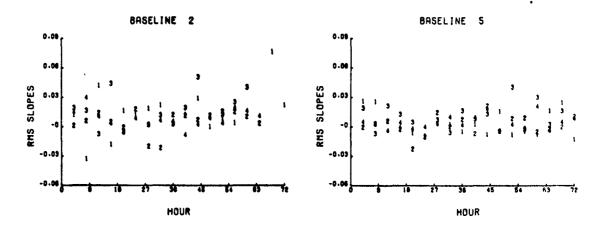


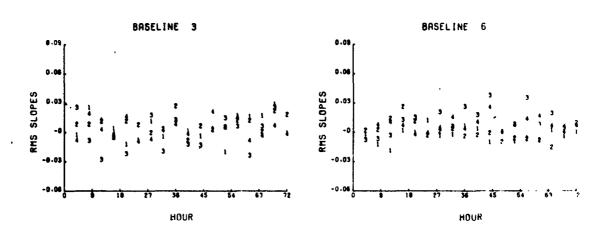


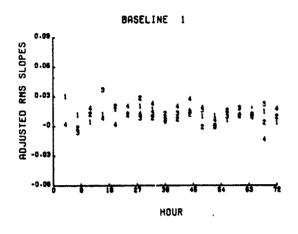


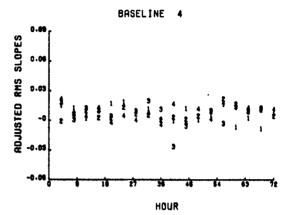


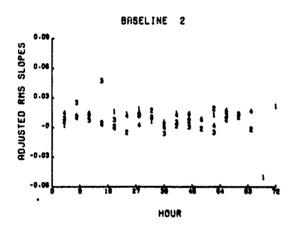


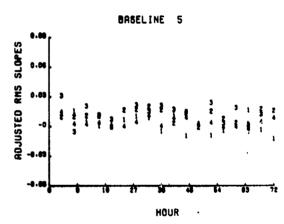


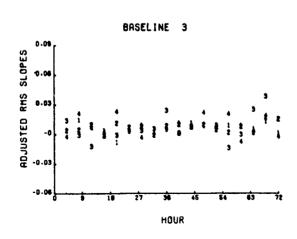


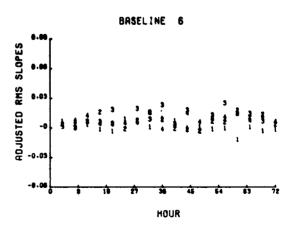


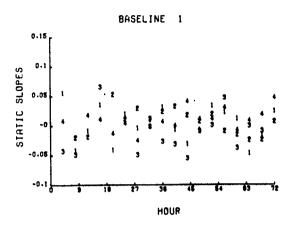


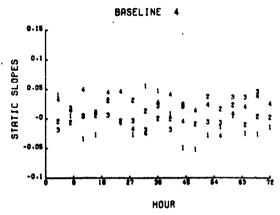


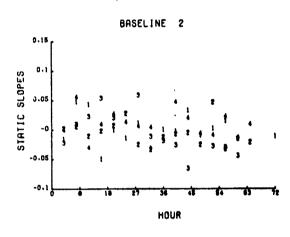


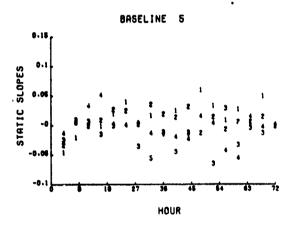


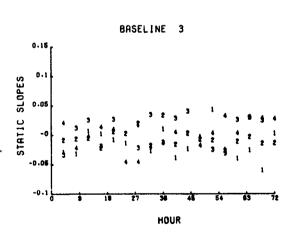


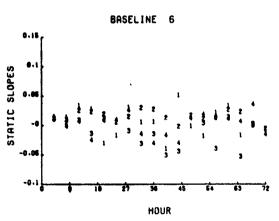












APPENDIX D

EXPOSURE SCORES

This appendix contains the eighteen 30-minute exposure scores arranged in the following format:

Page 45 -- Basic Measurement

RMS (V_K)

Ptime 5_K

Adjusted RMS (σ_{ν})

Ptime 10K

Static (μ_K)

Ptime 15_{K}

Page 46 -- Worst Cases and Consistency

RMS Maximums (Max /)

RMS Standard Deviations (SDVK)

Adjusted RMS Maximums ($Max\sigma_K$)

Adjusted RMS Standard Deviations (SD σ_{K})

Absolute Static Deviations ($Max\mu_K$)

Static Standard Deviations (SD μ_K)

Page 47 -- Initial Positions and Trends

RMS Intercepts (by)

RMS Slopes (m/_V)

Static Intercepts (b#K)

Static Slopes $(m\mu_K)$

Adjusted RMS Intercepts (b_{σ_K})

Adjusted RMS Slopes (mog) .

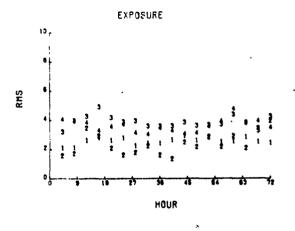
In these figures

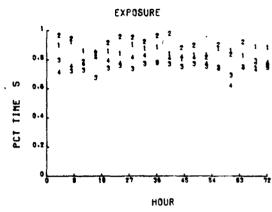
1 = Subject No. 170

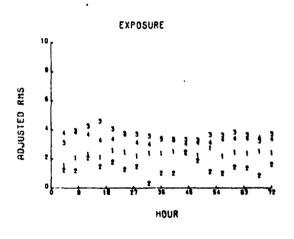
2 = Subject No. 836

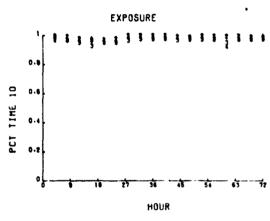
3 = Subject No. 896

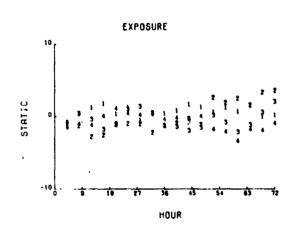
4 = Subject No. 902

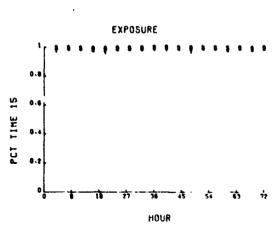


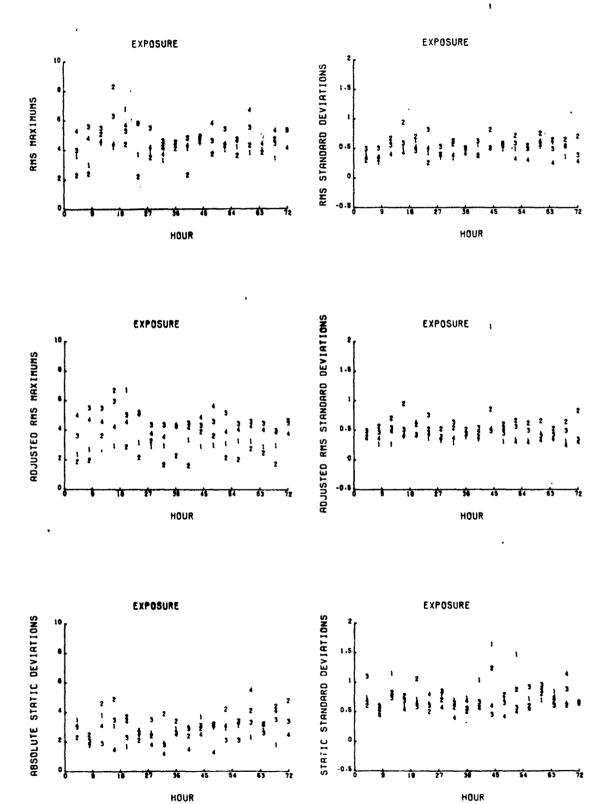


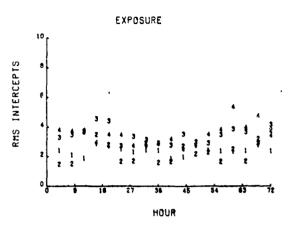


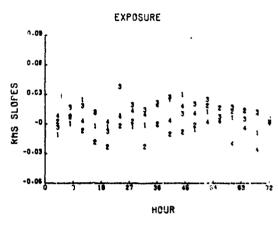




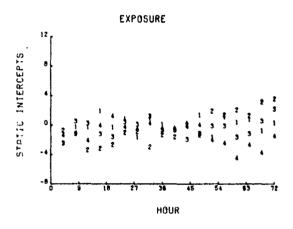


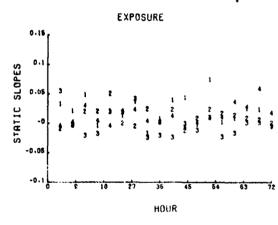


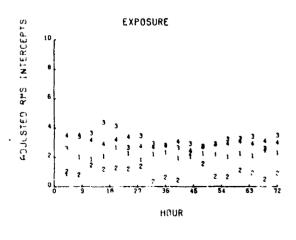


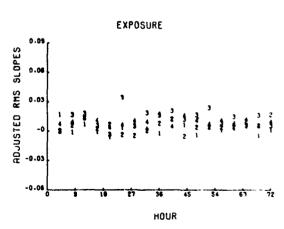


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APPENDIX E

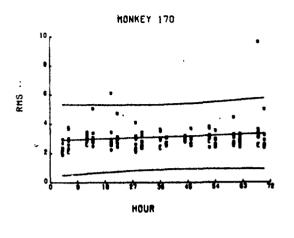
TOLERANCE LIMITS FOR EXPOSURE VS. ALL BASELINE COMPARISONS

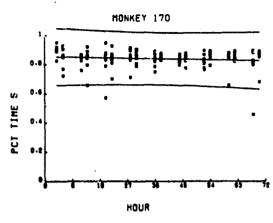
Simultaneous tolerance limits studied by Rahe (15) were used to define bands of normal for baseline scores; that is, linear regression models were used to fit the six preexposure baselines and ($\alpha = .05$, P = .95) simultaneous tolerance intervals were constructed for this model. A ($\alpha = .05$, P = .95) simultaneous tolerance interval will contain 95% of the population of all baseline scores over the entire 72-hour period with ($1-\alpha$) percent confidence. In contrast, the "usual" 95% confidence intervals are narrower because they represent the probability of a single point lying within the interval as 95%. If one were to draw inferences about more than 1 point, the probability of committing a type I error with the "usual" 95% confidence interval will exceed 5%.

This appendix is arranged as follows:

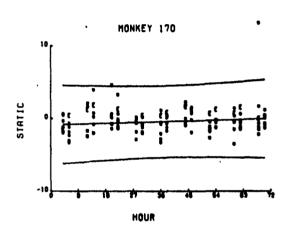
Pages Variables

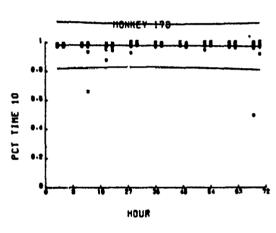
- 49 through 52 Basic Measurements*
- 53 through 56 Worst Case and Consistency Measurements*
- 57 through 60 Initial and Trend Measurements*
- *Arranged in ascending order of subject ID number.

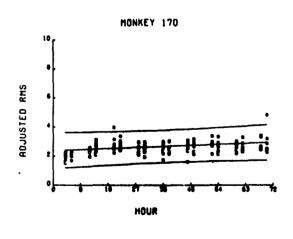


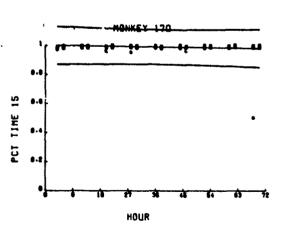


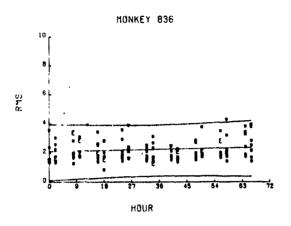
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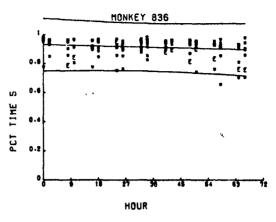


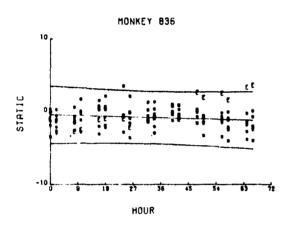


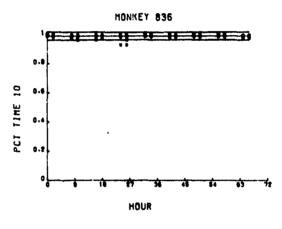


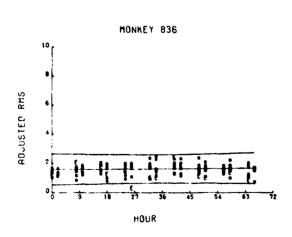


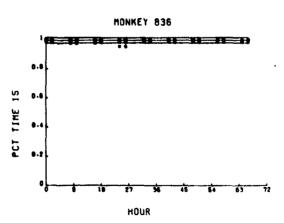


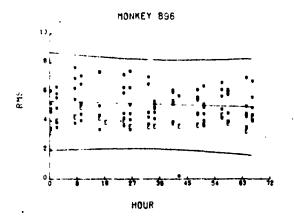


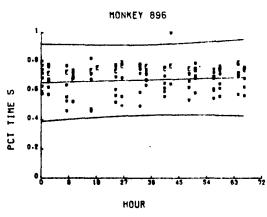


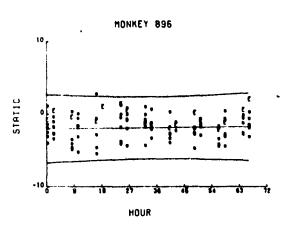


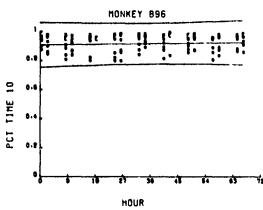


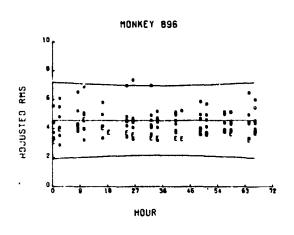


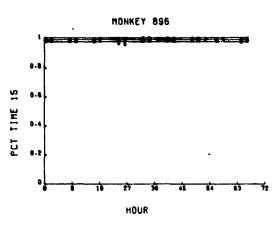




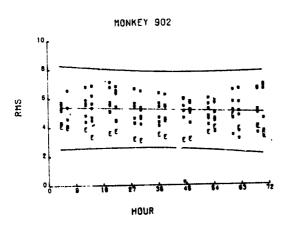


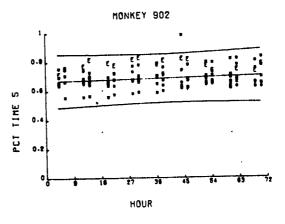


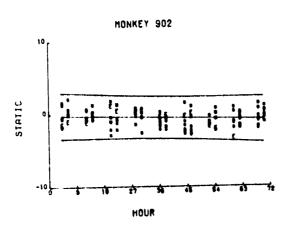


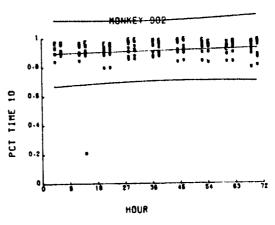


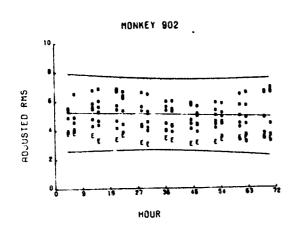
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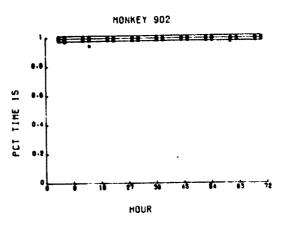


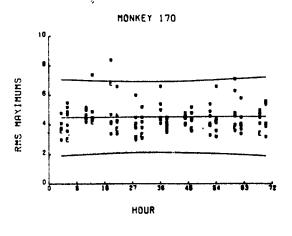


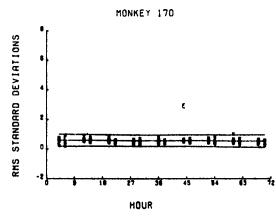


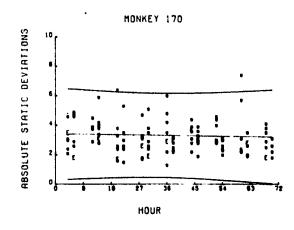


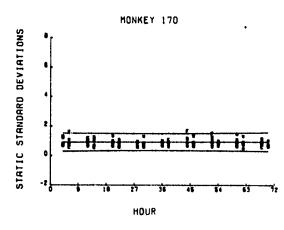


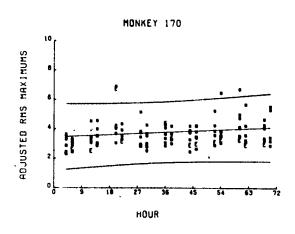


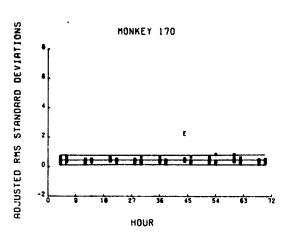


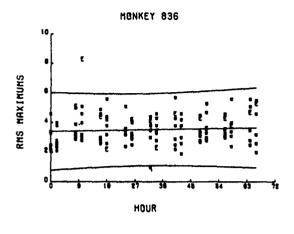


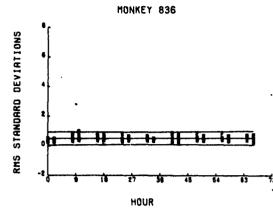


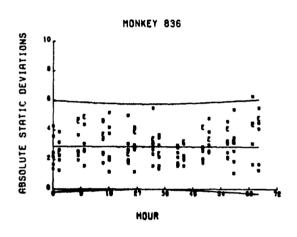


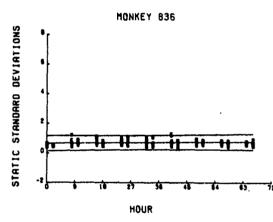


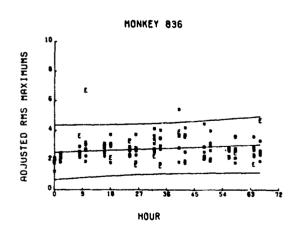


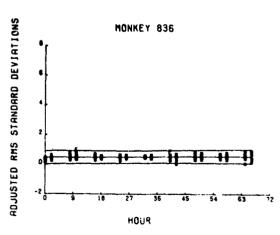


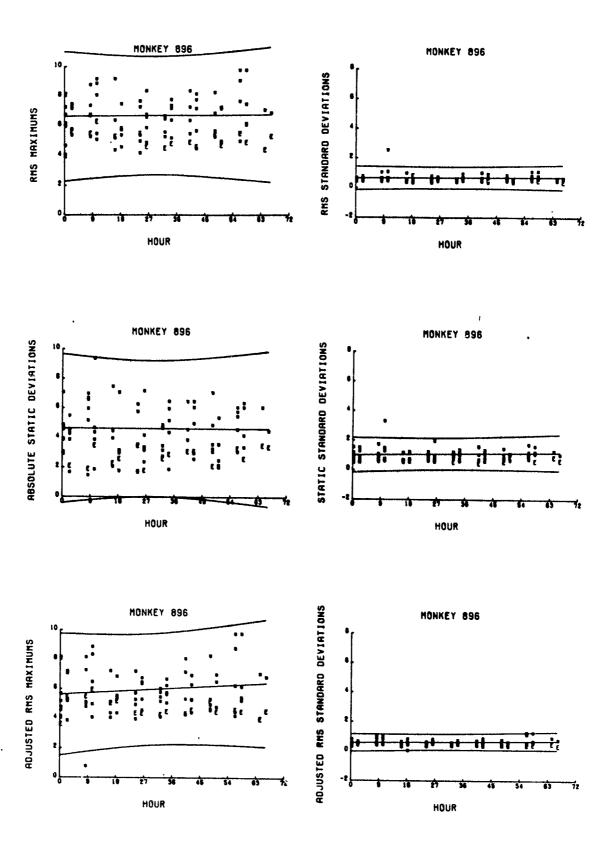


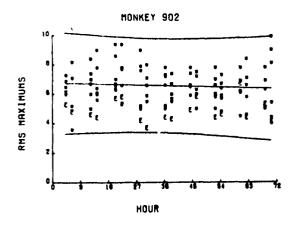


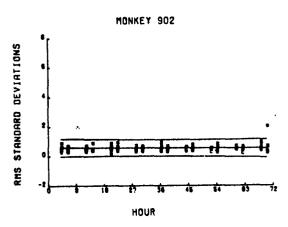


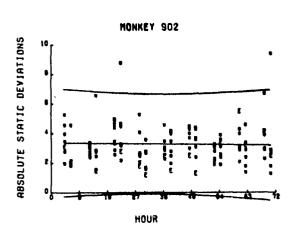


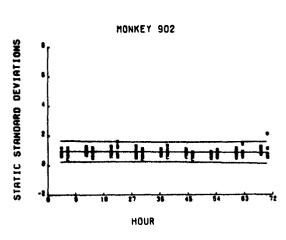


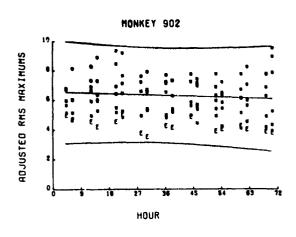


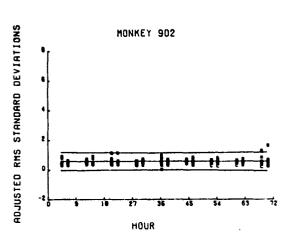


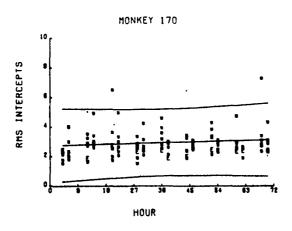


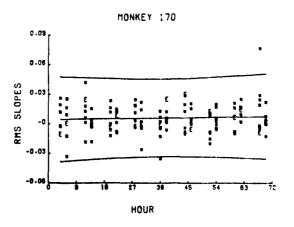


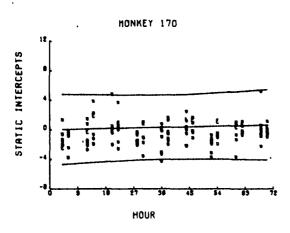


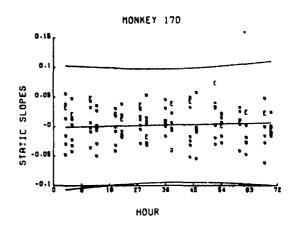


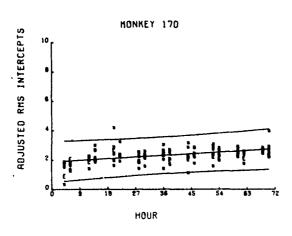


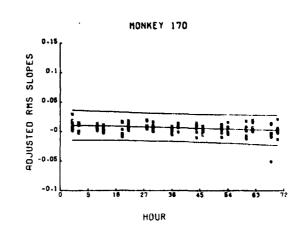


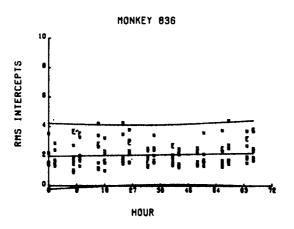


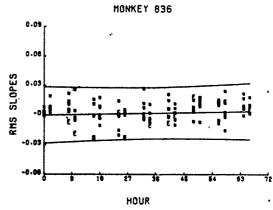


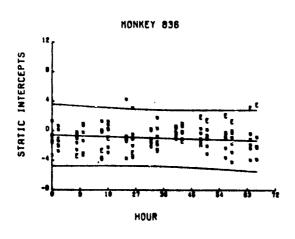


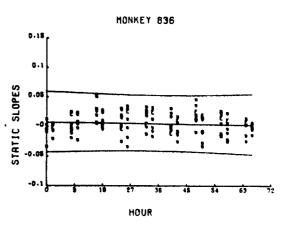


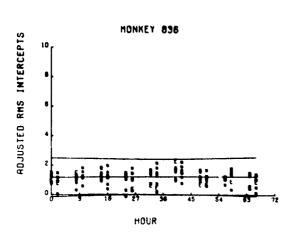


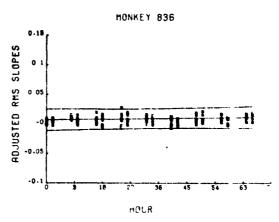


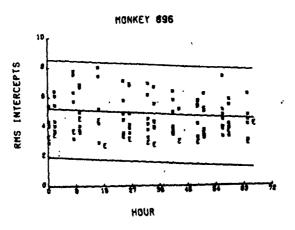


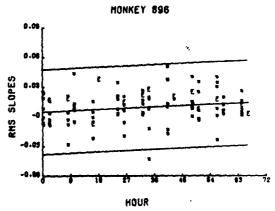


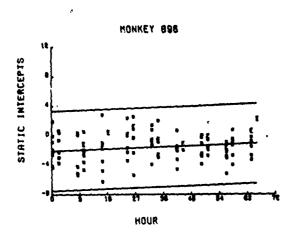


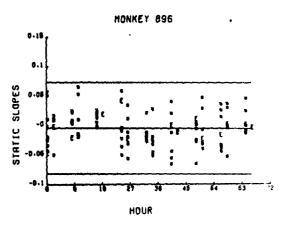


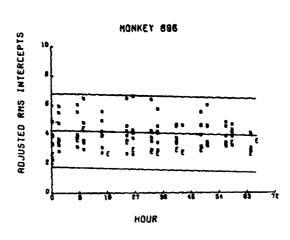


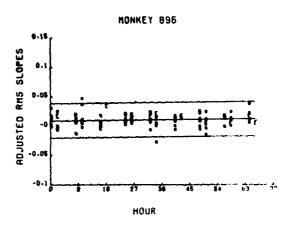


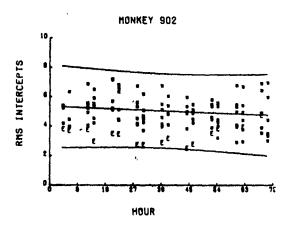


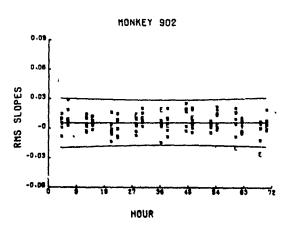


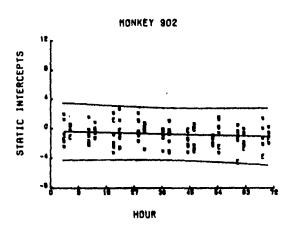


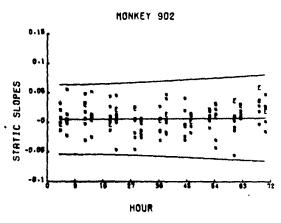


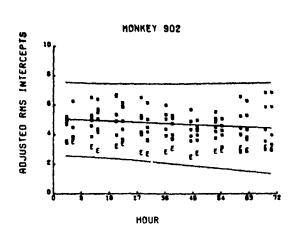


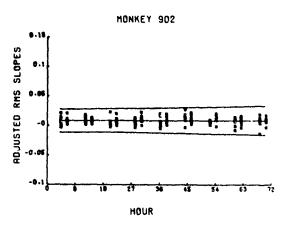












APPENDIX F

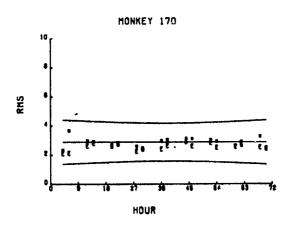
TOLERANCE LIMITS FOR EXPOSURE VS. LAST BASELINE COMPARISONS

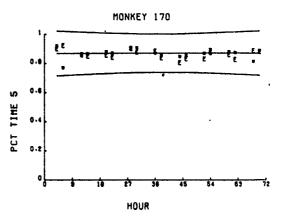
This appendix uses ($\alpha=.05$, P=.95) tolerance limits for the last baseline in order to define a region of preexposure behavior for each subject. The interpretation of these limits is the same as described in Appendix E with the exception that all inferences are made relative to the last baseline.

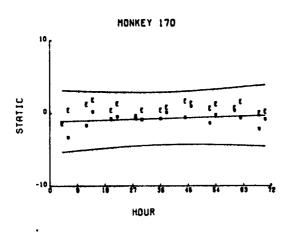
This appendix is arranged as follows:

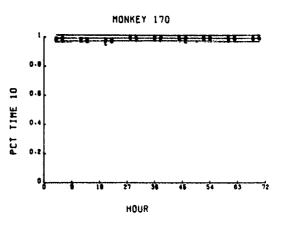
Pages	Pages <u>Variables</u>	
62 through 65	Basic Measurements*	
66 through 69	Worst Case and Consistency Measurements*	
70 through 73	Initial and Trend Measurements*	

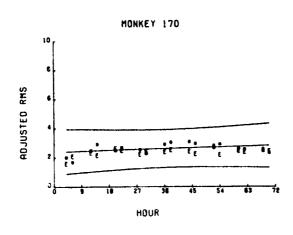
^{*}Arranged in ascending order of subject ID numbers.

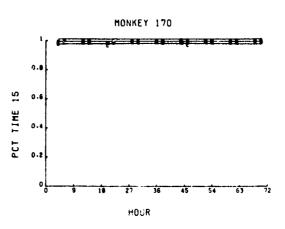


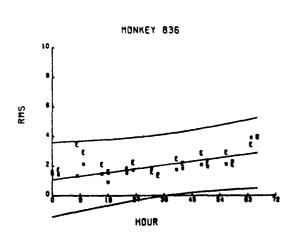


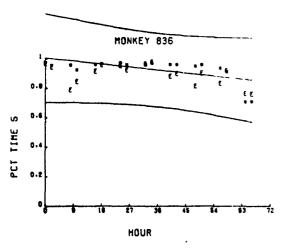




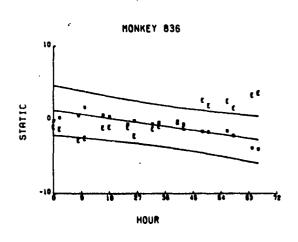


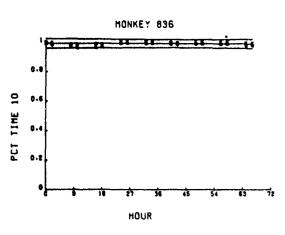


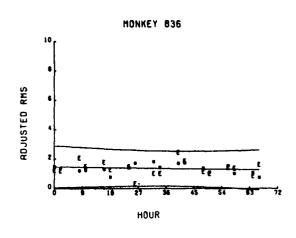


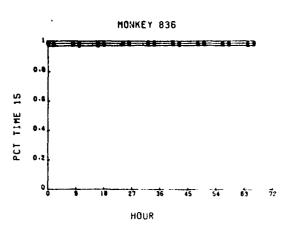


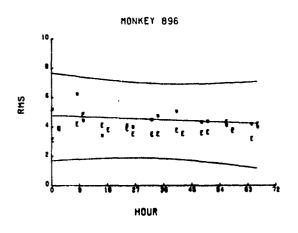
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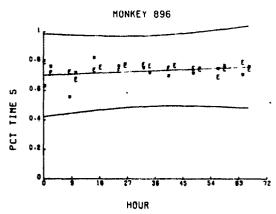


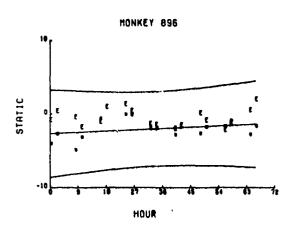


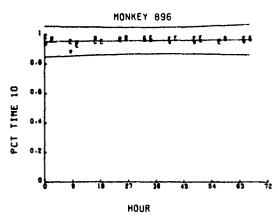


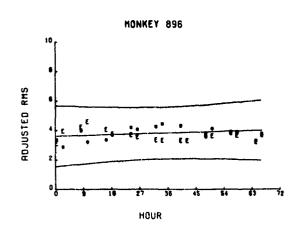


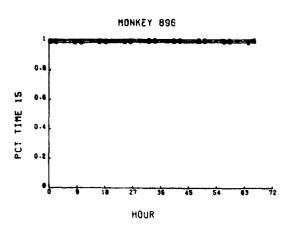


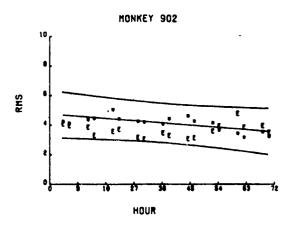


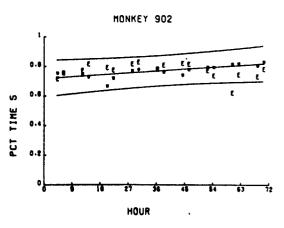


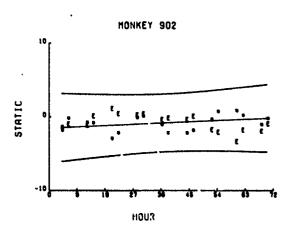


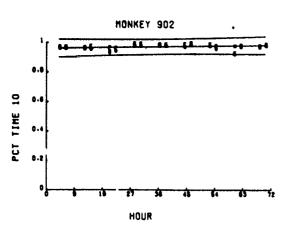


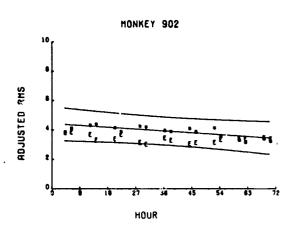


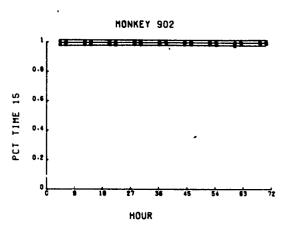


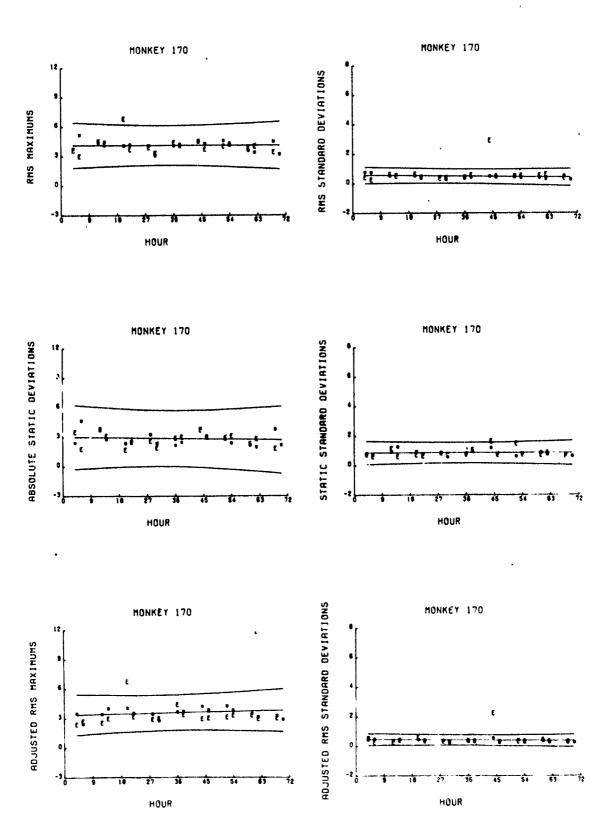


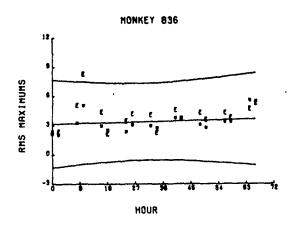


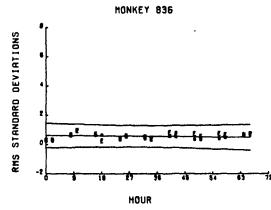


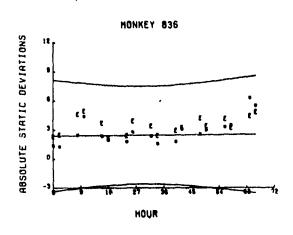


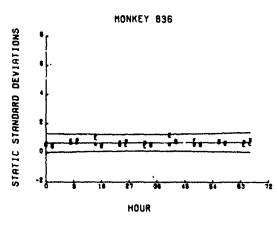


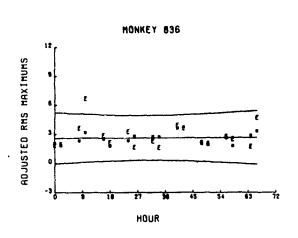


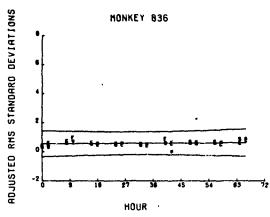


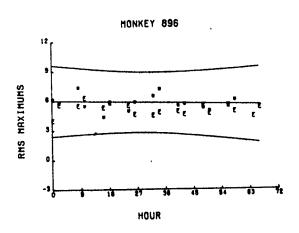


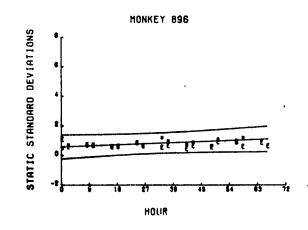


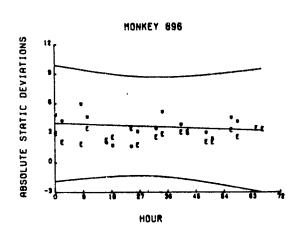


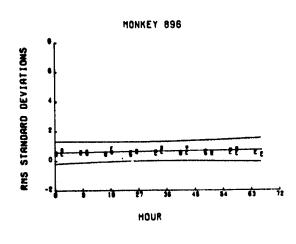


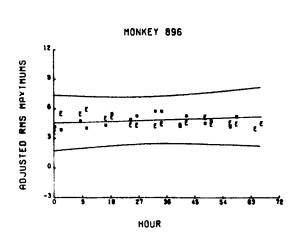


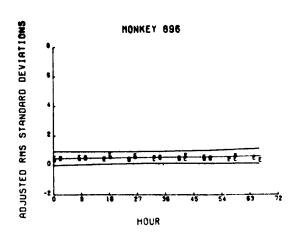


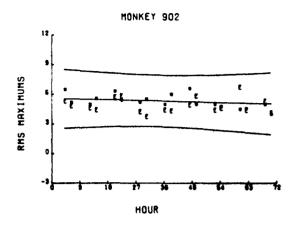


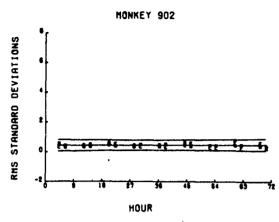


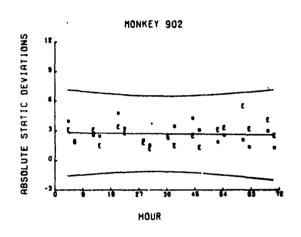


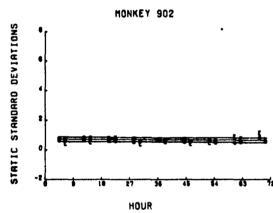


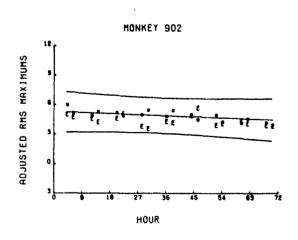


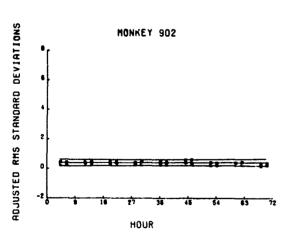


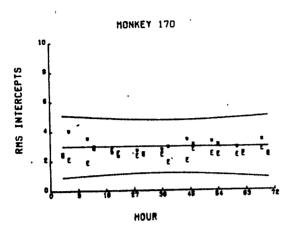


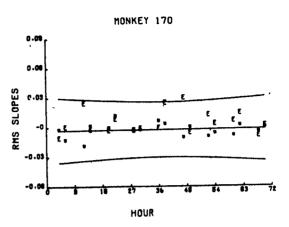


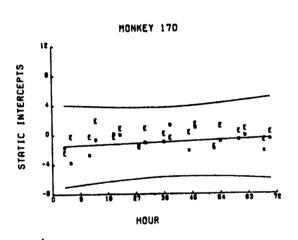


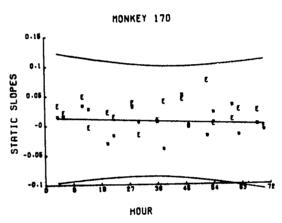


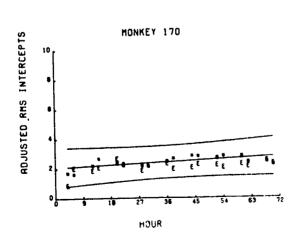


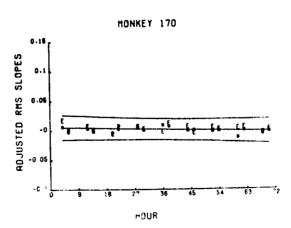


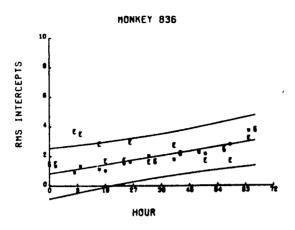


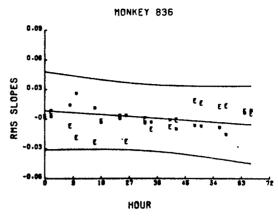




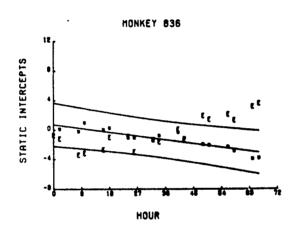


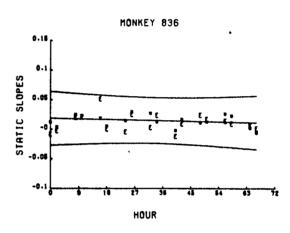


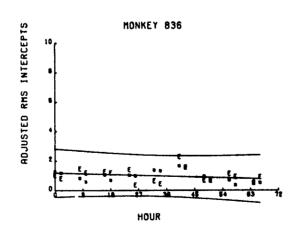


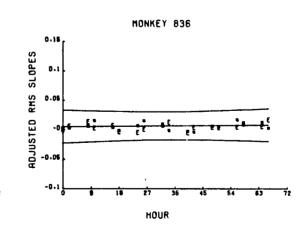


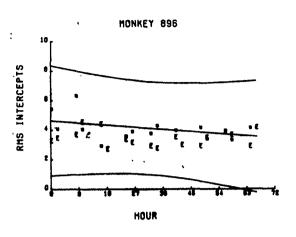
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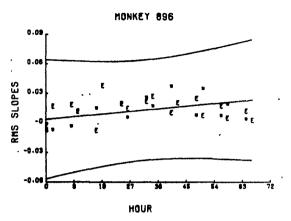


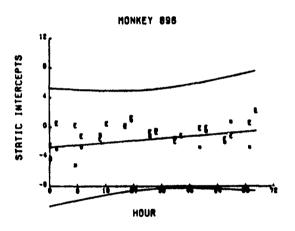


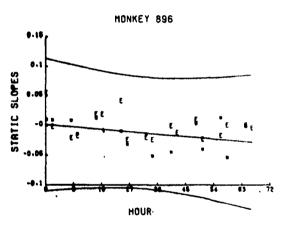




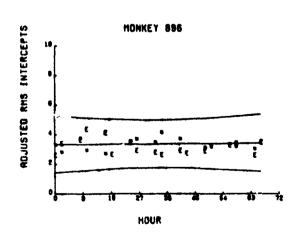


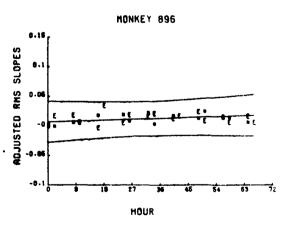




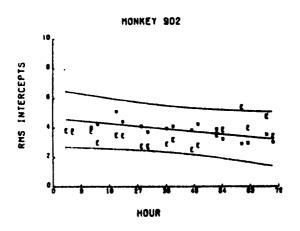


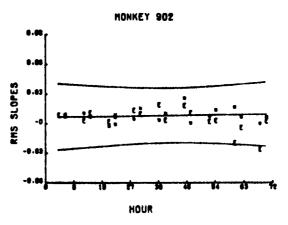
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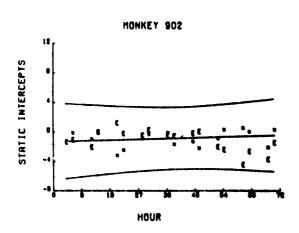


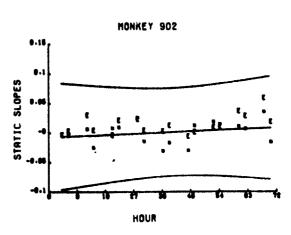


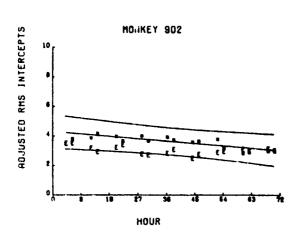
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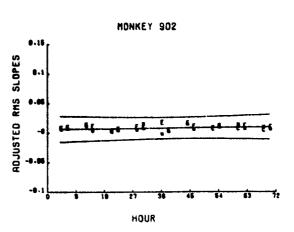












APPENDIX G

DOSIMETRY

The target radiation exposure profile consisted of (1) an initial dose of 135 rads delivered over a 10-minute period prior to the start of the 72-hour experimental run, (2) a 10-hour exposure at a dose rate of 10 rads/hr, and (3) approximately 1 rad/hr for the remaining 61 hours. The total dose desired over the run was 300 rads. All 4 of the animals were to be simultaneously exposed, i.e., the 2 in the cages and the 2 in the PEP. During the change-over period every 4 hours (which required about 15 minutes), the radiation sources were retracted and sealed. Therefore, compensation in the exposure dose rate during the remaining part of the 4 hours was necessary to achieve the desired 4-hour dose.

The approach to obtaining accurate and reliable animal exposure was threefold. First, calculations were made to determine the geometric and source strength arrangements required to realize the desired dose/dose rates. Then, instrumented monkey simulacra, or phantoms, were used under actual exposure conditions to verify the calculations. Finally, during the actual exposure run, radiation monitors were used as a double-check of the predetermined exposure conditions.

The initial dosimetry effort involved determining those free air exposure rates in roentgens per unit time necessary to deliver the required midline dose rates in rads per unit time. On the AECL source, the closest distance possible for the simultaneous exposure of all 4 primates was 3 m. The exposure rate at this distance was 15.8 roentgens/min. Using a roentgen to rad conversion factor of 0.95 and an attenuation factor of 0.90 for the midline dose, the midline dose rate was estimated to be 13.5 rads/min. Figure 4 illustrates the exposure configuration used on the AECL facility. Field maps indicate that the exposure field was uniform to within 95% of the beam centerline value.

Using the same roentgen to rad conversion factor and attenuation factor plus an added factor of 1.06 for source shutdown time for animal changeover, it was calculated that exposure rates of 12.4 and 1.24 roentgens/hr were required to deliver 10 and 1 rads per hour, respectively, in the Low-Dose Facility. The Low-Dose Facility housed a 185-curie Atomchem and four 15-curie Oak Ridge cobalt-60 sources. Based on source calibration data it was determined that the initial rate of 12.4 R/hr could be achieved at an approximate distance of 4.4 m using the 185-curie Atomchem source. Source calibration data indicated that the 1.24 R/hr exposure rate could be achieved by using a combination of two of the nominal 15curie Oak Ridge cobalt-60 sources at approximately 5.4 m. Because the larger portion of the dose was to be delivered by the Atomchem source, it was decided to place the PEP platforms and cages in a circular arc about the Atomchem source at 4.4 m, with the two Oak Ridge cobalt-60 sources situated symmetrically on either side of the Atomchem source. Field maps made with dosimeters indicated that the exposure fields in this configuration were uniform to approximately 90% of the midfield value. The

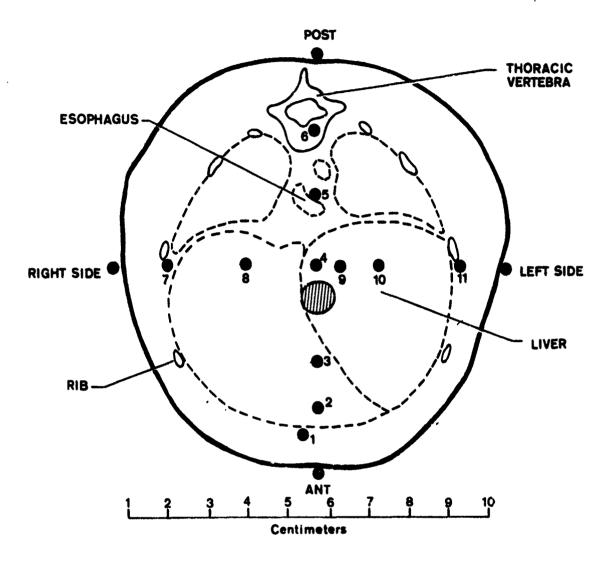
exposure dose rates at midcage were observed to be approximately 4% and 7% lower than the PEP chair exposure rate for the Atomchem and Oak Ridge sources, respectively, due to attenuation by the cages. As the animals were to be equally exposed in both the PEP platforms and the cages, the final configurational distances were chosen so that the average exposure dose rate between the PEPs and the cages equaled the desired exposure rate.

The next phase involved performing dosimetric measurements in Alderson tissue-equivalent primate phantoms to confirm the estimated midline dose rates. The phantoms were constructed about an actual primate skeleton of plastic (Alderson RANDO plastic) which is tissue equivalent to X- and gamma rays (7, Fig. 4). The physical size of the phantoms corresponded closely to the primates used in this experiment. The phantoms were cross-sectioned into 8 segments with holes drilled into each segment for insertion of dosimeters. Figure G-1 shows a typical cross section corresponding to the midepigastric region. The dosimeter sites are indicated by the numbered spots on the figure. Dosimetric measurements were made in the cross sections corresponding to the head, midepigastric, and lower abdominal regions of the animal for each of the required exposure configurations. The overall midline dose rate was determined at each configuration from the average of the midline doses obtained in all three sections.

In the AECL facility configuration the phantoms were exposed anterior-posterior (A-P) while sitting in aluminum training couches. A measured midline dose rate of 13.5 rads/min was obtained, in excellent agreement with the calculated value.

In the Low-Dose Facility, the phantoms were exposed simultaneously in a PEP and in a cage. In the PEP, the phantom was exposed (A-P) just as was the actual animal. In order to better simulate a freer moving animal in the cage, the phantoms in the cage were exposed while seated on a rotating platform, turning at about 2 RPM. Table G-1 summarizes the dosimetric results obtained. These rate values were the final values used to calculate the final midline dose. It should be noted that the actual midline dose rates were slightly higher than the programmed rates of 10 rads/hr and 1 rad/hr in order to compensate for the 15-minute downtime every 4 hours. If the data is corrected to a 4-hour exposure, the midline dose rates become 10.5 and 1.02 rads/hr in good agreement with the desired values.

Type 700 LiF thermoluminescent dosimeter (TLD) powder encapsulated in polyethylene tubing was used in the phantom measurements. The dose response of this material was determined by comparison of its response to known cobalt-60 doses delivered on the AECL source. This source has been calibrated with National Bureau of Standards (NBS)-calibrated 3-terminal guard-ring chambers and Victoreen condenser R-Chambers. The LiF powder was analyzed on a Harshaw model 2000 TLD system. Approximately 5 readings were obtained at each dosimeter site. Based on the results of these measurements, the midline dose rates at each exposure configuration were established as shown in Table G-1.



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Figure G-1. Typical cross section of monkey midepigastric region.

Thermoluminescent dosimeters and R-Chambers were also exposed simultaneously with the phantoms in each configuration for the purpose of obtaining correlation factors with the measured midline doses to be used in monitoring the subsequent animal exposures. The results obtained from the monitor dosimeters converted to midline dose are listed in Table G-2.

Based on the measured midline dose rates and recorded exposure times, the animals received a total midline dose of 299 rads. Monitor dosimeters exposed with the animals indicated that a midline dose of 294 rads had been delivered, which is well within the limits of the accuracies of the dosimetry systems.

TABLE G-1. MIDLINE DOSE RATES MEASURED IN ALDERSON PRIMATE PHANTOM

Rate norm to 4-hour exposure	13.5 rads/min	10.2 rads/hr	1.02 rads/hr
Average of cage and PEP		11.2 rads/hr	1.08 rads/hr
Cage		11.0 rads/hr	1.02 rads/hr
PEP	13.5 rads/min ^a	11.4 rads/hr	1.14 rads/hr
Configuration	AECL source	Atomchem source	Oak Ridge source

a In aluminum couch only.

TABLE G-2. MIDLINE TOTAL DOSES DELIVERED TO THE ANIMALS BASED ON MEASURED DOSE RATES AND MONITOR DOSIMETER RESULTS

R-chamber TLD monitors (rads)	No: used 134	104.1 160ª	61.1	294
Radocon monitor (rads)	129.4	105.0	59.7	294.1
Programmed dose (rads)	135	101.9	61.9	298.8
Configuration	AECL source	Atomchem source	Oak Ridge source	Total

^aTotal dose from Atomchem and Oak Ridge sources.