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TEMPORAL STABILITY AND PRECISION OF VENTRICULAR DEFIBRILLATION THRESHOLD DATA*

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INDEX TERMS

ventricular defibrillation
heart ventricle
cardiac arrhythmias
resuscitation
sudden death

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ABSTRACT

Over two-hundred measurements of the minimum damped sinusoidal current and energy for transchest electrical ventricular defibrillation (ventricular defibrillation threshold) were made to determine the stability and precision of threshold data in 15 pentobarbital-anesthetized dogs. Threshold was determined by repeated trials of fibrillation and defibrillation with successive shocks of diminishing current, each 10% less than that of the preceeding shock. The lowest shock intensity that defibrillated was defined as threshold. In three groups of five dogs each, threshold was measured at intervals of 60, 15, and 5 min. over periods of 8, 5, and 1 hr. respectively. Similar results were obtained for all groups. There was no significant change in mean threshold current with time. Due to a decrease in transchest impedance, threshold delivered energy decreased by 10% during the first hour of testing. The standard deviations for threshold peak current and delivered energy in a given animal were 11 and 22 percent of their respective mean values. Arterial blood pH, pCO_2, and pO_2 averaged 7.38, 34 mmHg, and 72 mmHg respectively. The rates of change of pH, pCO_2 and pO_2 were not significantly different from zero. The data demonstrate that ventricular defibrillation threshold is a stable physiologic parameter which may be measured with reasonable precision.

Introduction

An electric shock applied across the chest or directly to the heart is the only practical and effective means for terminating ventricular fibrillation, an otherwise lethal cardiac arrhythmia. During the past five years the electrical dose concept for ventricular defibrillation has been developed in the animal laboratory (6,7) and extended to man(13,11). The electrical dose concept holds that a predictable peak current or delivered energy per kilogram of body weight is required to defibrillate the ventricles. Defibrillating current or energy can therefore be administered like a drug; heavier subjects requiring a larger dose. The minimum electrical dose necessary for defibrillation, in terms of either current or energy, is defined as the defibrillation threshold.

In addition to body weight and heart weight, other factors influence the ventricular defibrillation threshold. These include hardware-dependent factors, such as the amplitude, duration, and waveform of the electrical stimulus (8, 12, 3), electrode size (5) and electrode placement (9); as well as subject-dependent factors such as chest conformation, body temperature, electrolyte and acid-base balance, drug effects, and the presence of disease states such as myocardial infarction (1, 14). In a typical investigation of such factors an experimental animal is subjected to repeated trials of fibrillation and defibrillation to establish a "baseline" or control defibrillation threshold. Then a drug is given or a pathologic change is produced, and the effect upon the defibrillation threshold is observed and compared to the control value. However, to date no systematic studies have been reported which establish under what circumstances and to what extent the control defibrillation threshold is stable. Such information is needed to interpret correctly experiments in which hardware or subject dependent factors appear to alter the defibrillation threshold.

The question of the stability and reproducibility of control data is especially pertinent because of the intrinsic nature of defibrillation studies in which the experimental animal literally is rescued from impending death on repeated occasions. Each fibrillation -- defibrillation sequence represents a stress to the animal subject, including transient circulatory arrest, possible tissue hypoxia and acidosis, and the electric shock itself, any of which might effect the measured defibrillation threshold.

Accordingly, the studies reported in this paper were undertaken to determine (1) to what extent defibrillation threshold is stable and reproducible with time in pentobarbital anesthetized dogs and (2) to what extent the stability of the baseline threshold level is dependent upon the recovery interval between threshold measurements.

Methods

Fifteen mongrel dogs of both sexes, weighing 4 to 16 kg and anesthetized with pentobarbital sodium (30 mg/kg, i.v.), served as subjects. No other drugs except 0.9% saline were administered at any time. The trachea of each dog was intubated and the animal placed in dorsal recumbency for the duration of the study. The urinary bladder was catheterized with a #8 French fillform catheter connected to a closed volumetric drainage bottle. Aortic blood pressure was recorded using a P23DB Statham transducer. Respiratory minute volume was measured with a Wright respirometer. Arterial blood pH, pCO_2, and pO_2 were monitored using an Instrumentation Laboratories Model 213 blood-gas analyzer. Disk electrodes 8, 10, or 12 cm in diameter were applied to the shaved skin of the right and left hemithoraces with electrolytic jelly and sutured in place. The diameter of the electrodes was standardized to 20 percent of the chest circumference, measured at the mid-sternal level. One electrode was centered over the apex beat area and the other was located at a corresponding position on the right chest wall, 3 cm cephalad of the left electrode.

Mean aortic blood pressure, respiratory minute volume, urine output, arterial blood gases, and esophageal temperature were recorded at half-hour intervals. A stable level of surgical anesthesia was maintained in each animal by the intravenous doses of pentobarbital sodium, 2-5 mg/kg each hour. Saline solution, 0.9 percent, was given at a rate of 1-2 ml/kg/hr by vein to maintain hydration. Esophageal temperature was maintained in the range of 36-39°C with the aid of warm overhead lights.

Ventricular fibrillation was initiated by 2-10 volt, 60-Hz electrical stimulation of the right ventricle delivered via a bipolar electrode catheter inserted through the right jugular vein. The position of the electrode catheter in the right ventricle had been previously verified by recording the cardiac electrogram from the catheter electrodes. Ventricular fibrillation was confirmed by replacement of the QRS-T complexes of the electrocardiogram with random waves and the fall of aortic blood pressure toward zero.

The output circuit of the damped sine wave defibrillator employed contained a capacitance of 16 microfarads, an inductance of 44 millihenrys and an internal resistance of 7 ohms, as determined by the method of Babbs and Whistler (2). The voltage on the capacitor could be varied continuously from 0 to 8000 volts. The maximum stored energy available was 512 Joules. A 1.00-ohm, 100-watt resistor in series with one electrode was used for measuring the current.

In a typical trial a defibrillator shock calculated to be adequate for defibrillation on the basis of the dog's body weight was delivered at the time of end-expiration, less than 15 sec after the onset of fibrillation. The voltage across the electrodes and current passing through the subject were recorded on a Tektronix model D-11 dual-channel storage oscilloscope. Defibrillation was confirmed by return of pulsatile blood pressure and QRS complexes in the electrocardiogram. After restoration of aortic blood pressure to a stable

level, the animal was refibrillated and defibrillation was attempted with a voltage setting approximately 10 percent less than that of the previous trial. This procedure was repeated until defibrillation was not achieved, whereupon a stronger shock was applied immediately to restore cardiac pumping action. At no time did fibrillation persist for more than 30 seconds.

Threshold voltage and current were defined as the lowest values able to defibrillate the ventricles. In this study threshold values were considered adequately precise if peak current differed no more than 10 percent from a value unable to defibrillate the ventricles. Only data from the first shock delivered after the onset of fibrillation were used in calculations of threshold. Delivered energy was calculated as described previously (2).

Three series of five dogs each were studied. In Series 1, threshold was measured every hour for 8 hours. In Series 2, threshold was measured every 15 min. for 5 hours. In Series 3, threshold was measured every 5 min. for 1 hour. This last series represents the closest spacing of threshold measurements consistently possible when only first-shock data are acceptable.

Results

The stability of ventricular defibrillation threshold is demonstrated by Figures 1 and 2, which present mean threshold current and energy ratios as a function of time, for animals in all three series. The threshold current and energy ratios were calculated by dividing the individual threshold values by the average of the first three "baseline" threshold values obtained for each animal. Hence the threshold energy and current ratios may be interpreted as the relative values obtained in experiments in which each animal served as its own control.

Threshold peak current remained stable in all three series. Decreasing the recovery interval between threshold measurements from 60 to 15 to 5 minutes did not cause a discernible upward or downward drift of threshold current. Threshold current stability was further assessed by computing the linear regression function relating the threshold current dose to time for each animal. The slopes of the regression lines so obtained give sensitive estimates of the overall rate of change of threshold current with time. The slopes were positive for 7 of 15 dogs, negative for 8 of 15 dogs, and not significantly different from zero (mean slope -0.008 amp/kg/hr, n=15, Student's t=0.69, p=0.50).

Threshold delivered energy data were more variable than the current data and appeared to drift slightly downward during the first hour. In all three series, defibrillation threshold energy after one hour was about 10 percent less than the initial threshold energy. The observed decrease in threshold energy was associated with a corresponding decrease in transchest electrical impedance, calculated by dividing peak voltage by peak current (Figure 3).

Arterial blood pH, pCO_2, and pO_2 remained stable in all control series, averaging 7.38, 34 mmHg, and 72 mmHg respectively. To evaluate subtle changes in blood-gas values during the course of experimentation, linear regression functions relating pH, pCO_2, and pO_2 values to time were computed for each animal. The mean regression coefficients for each series are presented in the Table. One-way analyses of variance reveal no significant differences in the regression coefficients for the three experimental groups, indicating that increasing the frequency of threshold measurements from 1 to 12 per hour did not cause a deterioration in arterial blood gas status. The observed rates of change in arterial blood pH, pCO_2, and pO_2, indicated by the slopes of the linear regression functions, were not statistically different from zero.

The precision of defibrillation threshold data may be appreciated with reference to Figure 4, which illustrates the frequency distributions of the 209 threshold energy and current ratios obtained in all three series. The distributions of the three series were pooled since all have means of 0.97 - 0.99 and variances which are not significantly different (Bartlett's $\chi^2 = 0.20$, $p = 0.90$ for current; Bartlett's $\chi^2 = 2.84$, $p = 0.24$ for energy). These histograms illustrate the relative dispersion of threshold data about the baseline established for each animal at the beginning of each experiment. The standard deviations of the distributions are a measure of the reproducibility of the threshold data. Under control conditions the precision of threshold current data is greater than the precision of threshold energy data.

Discussion

In the absence of pharmacologic or pathologic intervention, the threshold current for ventricular defibrillation remains stable in pentobarbital-anesthetized dogs. Even though the animal is repeatedly rescued from impending death, there appears to be no cumulative influence of repeated trials of fibrillation and defibrillation upon the threshold current, provided no more than 30 seconds of fibrillation are permitted on any trial. This conclusion is valid even if threshold is measured as frequently as every five min., under which circumstances there is loss of pulsatile blood pressure for 10-20 percent of the elapsed time. This stability in threshold current is associated with comparable stability in the arterial blood pH, pCO_2, and pO_2.

The approximate 10 percent decrease in threshold delivered energy during the first hour of testing is explained by a corresponding decrease of the apparent impedance between the defibrillating electrodes. Geddes (10) and Chambers (4) have reported similar decreases in transthoracic impedance during successive ventricular defibrillation trials in animals and in man. These reports imply that the critical variable associated with decreasing impedance is the number of fibrillation-defibrillation trials. In our studies, however, time appears to

be a better predictor of subject impedance than trial number. The decrease in transchest impedance during the first hour of testing averaged 4.64 Ω/hr for the dogs of Series 1 and 5.21 Ω/hr for the dogs of Series 3. These values are not statistically different (Student's $t = -0.28$, $p = 0.79$) even though threshold was obtained 12 times in Series 3 and only 2 times in Series 1. Accordingly factors other than the number of fibrillation-- defibrillation trials, such as impregnation of high resistivity skin with electrolytic jelly, may be responsible for the slight initial fall in transchest impedance and threshold energy.

Using the method described in this paper, defibrillation threshold current may be measured with a precision of $\pm$ 10.9 percent of the mean, as indicated by the standard deviation of a large population of repeated threshold measurements in stable animal preparations. The comparable precision of threshold energy measurements is $\pm$ 21.8 percent of the mean. The two-fold greater uncertainty in threshold energy is a direct result of the fact that delivered energy is proportional to the square of the peak current. As reported in detail elsewhere (2), the energy, W, delivered by a damped sine wave defibrillator may be calculated from the peak current, I, by an expression of the form $W = aI^2$, where the factor, a, contains terms relating to the internal resistance, inductance, and capacitance of the defibrillator and the transchest impedance of the subject. However, if a is taken as a simple constant, all of the observed variance in threshold energy, W, may be explained. Consider Gaussian random variable, I, with mean value, m_I, and standard deviation σ_I. If $W = aI^2$ for any constant, a, then

$$\frac{\sigma_W}{m_W} = \frac{\frac{\sigma_I}{m_I}\sqrt{2\,\frac{\sigma_I^2}{m_I^2} + 4}}{\frac{\sigma_I^2}{m_I^2} + 1} .$$

For the special case $\sigma_I^2/m_I^2 << 1$, indicating relatively small variations in I, $\frac{\sigma_W}{m_W} \approx 2 \frac{\sigma_I}{m_I}$. If I is taken as the threshold current ratio in our experiments one would therefore expect

$$\frac{\sigma_W}{m_W} \approx 2 \frac{0.107}{0.984} = 0.217$$

The observed uncertainity, σ_W/m_W, in the threshold energy ratio was 0.218. Thus the greater uncertainty of threshold energy, compared to threshold current, may be explained entirely by the necessary mathematical relationship between energy and current. The slight decrease in the observed transchest impedance does not contribute significantly to the variability in threshold energy data.

One additional factor which may be quantitated at this time contributes to the variability in defibrillation threshold data. Some of the variability in measured threshold values is due to the method of threshold determination in which discrete current values differing by approximately 10 percent are tested, rather than due to variation in the animal's true threshold. In a discussion of the precision of defibrillation threshold data, it is worthwhile to identify the magnitude of this sampling variance in order to assess how much of the observed variance in threshold data is due to the experimental animal and how much of the observed variance is due to the experimental protocol.

Suppose the true, physiologic value of the defibrillation threshold current remained absolutely constant at a value I_o and that the distribution of measured thresholds is uniform within the interval I_o - 1.1 I_o as indicated in Figure 5. This distribution of measured thresholds would occur if the first suprathreshold shock tested were selected "blindly" with no fixed

relation to the true threshold, a situation which exists in practice. In this case, the mean measured threshold would overestimate the true threshold by 5 percent, and the variance of the distribution of measured thresholds may be calculated analytically as:

$$\sigma^2_{sampling} = \frac{10}{I_o} \int_{I_o}^{1.1\, I_o} I^2\, dI - (1.05\, I_o)^2 = 0.00083\, I_o^2 .$$

Since the mean of the measured values overestimates true threshold by 5 percent ($M_I = 1.05\, I_o$), one may express the sampling variance in terms of the mean measured threshold as

$$\sigma^2_{sampling} = 0.00076\, M_I^2 \quad \text{or} \quad \sigma_{sampling} = 0.027\, M_I .$$

Further, since sampling variance and physiologic variance are independent phenomena*; one may estimate the physiologic variance in defibrillation threshold current to be

$$\sigma^2_{physiologic} = \sigma^2_{observed} - \sigma^2_{sampling} = 0.01188\, M_I^2 - 0.00076\, M_I^2 = 0.01112\, M_I^2,$$

and

$$\sigma_{physiologic} = 0.105\, M_I .$$

* That is, the variability of the experimenter and the variability of the animal are not correlated.

That is, if only physiologic variation were present the standard deviation of measured threshold currents would be 10.5 percent of the mean. This figure is hardly different from the 10.9 percent standard deviation observed using the m method described in this paper. The algebraic variance introduced by testing discrete defibrillator currents differing by 10 percent in amplitude is negligible compared to the physiologic variance. Therefore there appears to be little justification for testing defibrillator currents differing by less than 10 percent in the routine measurement of defibrillation threshold.

In conclusion, these studies show that repeated fibrillation and defibrillation are well tolerated by pentobarbital-anesthetized dogs which fibrillate for less than 30 seconds. The experimental manipulations inherent in defibrillation studies as described in this paper do not in themselves alter the phenomena under investigation. The precision of threshold data obtained by the method here reported is limited only by physiologic variability of the animal subject and, in the case of threshold energy, by the mathematical relationship of energy to current.

FIGURE LEGENDS

Figure 1. Stability of defibrillation threshold current. Data points represent mean values of the threshold current ratio for the 5 dogs in each series at various times after the first fibrillation--defibrillation trial. Average baseline values of threshold current (1.00 on the vertical axis) were 1.40 amp/kg for Series 1, threshold interval = 60 min ■; 1.10 amp/kg for Series 2, threshold interval = 15 min ▲; and 1.13 amp/kg for Series 3, threshold interval = 5 min ● . The baseline values are not statistically different ($F = 2.49$, $p = 0.12$). The time scale is logarithmic.

Figure 2. Stability of defibrillation threshold energy. Data points indicate mean values of the threshold energy ratio for the 5 dogs in each series at various times after the first fibrillation - defibrillation trial. Average baseline values of threshold energy (1.00 on the vertical axis) were 1.23 j/kg for Series 1, threshold interval = 60 min ■; 0.87 j./kg for Series 2 threshold interval = 15 min ▲; and 1.06 /kg for Series 3, threshold interval = 5 min ●. The values are not statistically different ($F = 2.34$, $p = 0.14$). The time scale is logarithmic.

Figure 3. Stability of transchest electrical impedance. Data points represent mean values of the ratio Z/Z_0 of transchest impedance, Z, at various times after the first fibrillation - defibrillation trial to the initial impedance value, Z_0, at time zero. The apparent impedance Z, in ohms between the defibrillating electrodes was calculated as peak voltage/peak current for shocks delivered at the time of end expiration. Absolute values of Z_0 for the three series of dogs were 57Ω for Series 1, ; 60Ω for Series 2, ; and 52Ω for Series 3, ● . These values are not statistically different ($F = 0.72$, $p = 0.51$).

Figure 4. Histograms of threshold current and energy ratios obtained in 15 control dogs. The width of each class interval is 0.05. The value 1.00 on the horizontal axes represents the average of the first three threshold values obtained for each animal. Variance represented by the histograms therefore reflects only variability of individual subjects. The standard deviation of the threshold current distribution is 11 percent of the mean. The standard deviation of the threshold energy distribution is 22 percent of the mean.

Figure 5. Uniform distribution of measured threshold currents expected if physiologic variance were zero. Probability density is scaled such that the total area under the distribution function is unity. For a given experiment of n observations., the expected number of observations in class interval,

$$I \pm (\Delta I)/2, \text{ would be } n\, f(I)\, \Delta I.$$

TABLE

Linear regression analysis of the stability of arterial blood gas data. Regression coefficients a_0 and a_1 of equations of best fit of the form $y = a_0 + a_1 t$ are presented as "initial" values and "rate of change" for blood gas variables $y = pH$, pCO_2, or pO_2 as a function of time, t. Coefficients a_0 and a_1 were computed for each animal. Table entries represent the mean values of the coefficients for the animals in each series.

The F ratios for one-way analyses of variance and associated p values test the null hypotheses that the coefficients for the three series are the same. The Student's t statistics and associated p values test the null hypotheses that the mean values of the regression coefficients a_1 are zero for the population of all 15 animals. The regression coefficients for the three series are not significantly different, and the coefficients, a_1, are not significantly different from zero.

TABLE

SERIES	THRESHOLD INTERVAL (Min)	pH		pCO_2		pO_2	
		INITIAL	RATE OF CHANGE (hr^{-1})	INITIAL (mmHg)	RATE OF CHANGE (mmHg/hr)	INITIAL (mmHg)	RATE OF CHANGE (mmHg/hr)
		a_o	a_1	a_o	a_1	a_o	a_1
1	60	7.37	-0.003	35	-0.5	71	-0.2
2	15	7.38	0.006	34	-1.4	71	0.1
3	5	7.39	-0.03	34	1.7	79	-6.3
grand mean		7.38	-0.007	34	-0.07	73	-1.8
F		0.31	3.27	0.04	1.16	0.67	2.40
P		0.74	0.09	0.96	0.36	0.54	0.15
Student's t			-1.29		0.03		-1.26
p			0.22		0.98		0.24

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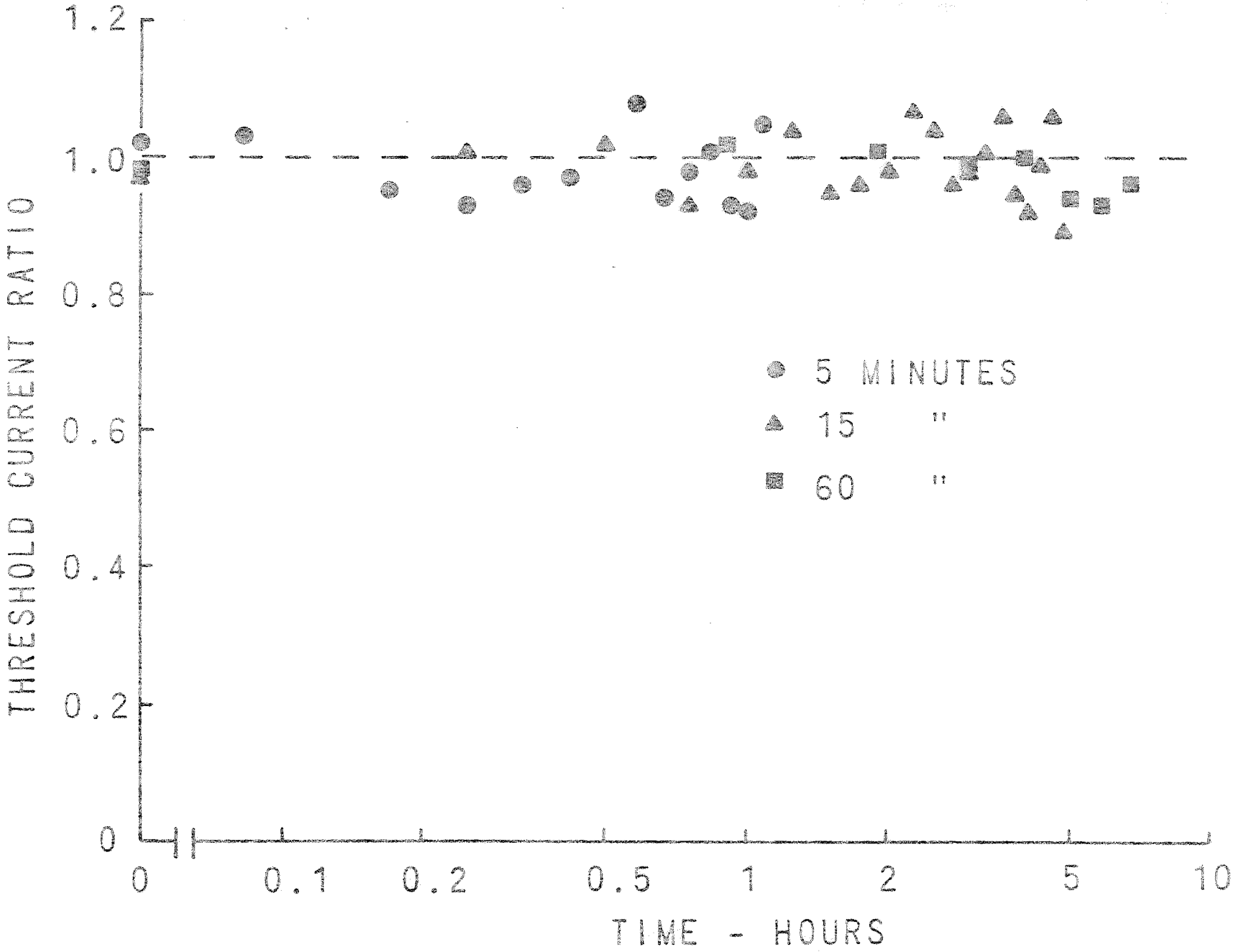
FIGURE 1


1.2
1.0
0.8
0.6
0.4
0.2
0
THRESHOLD CURRENT RATIO
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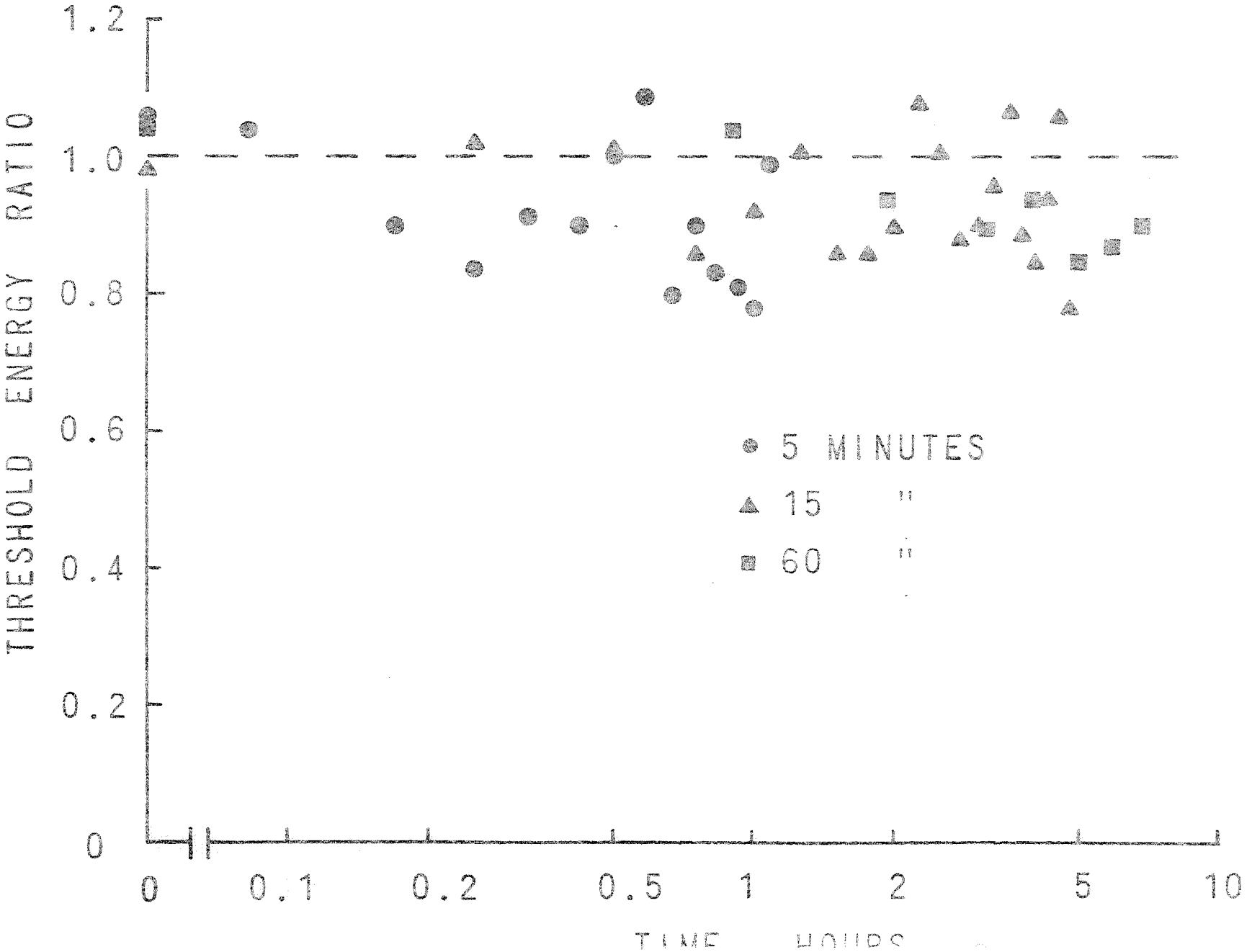
60 "
0
0.1
0.2
0.5
1
2
5
10
TIME - HOURS

FIGURE 2


THRESHOLD ENERGY RATIO
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1.0
0.8
0.6
0.4
0.2
0
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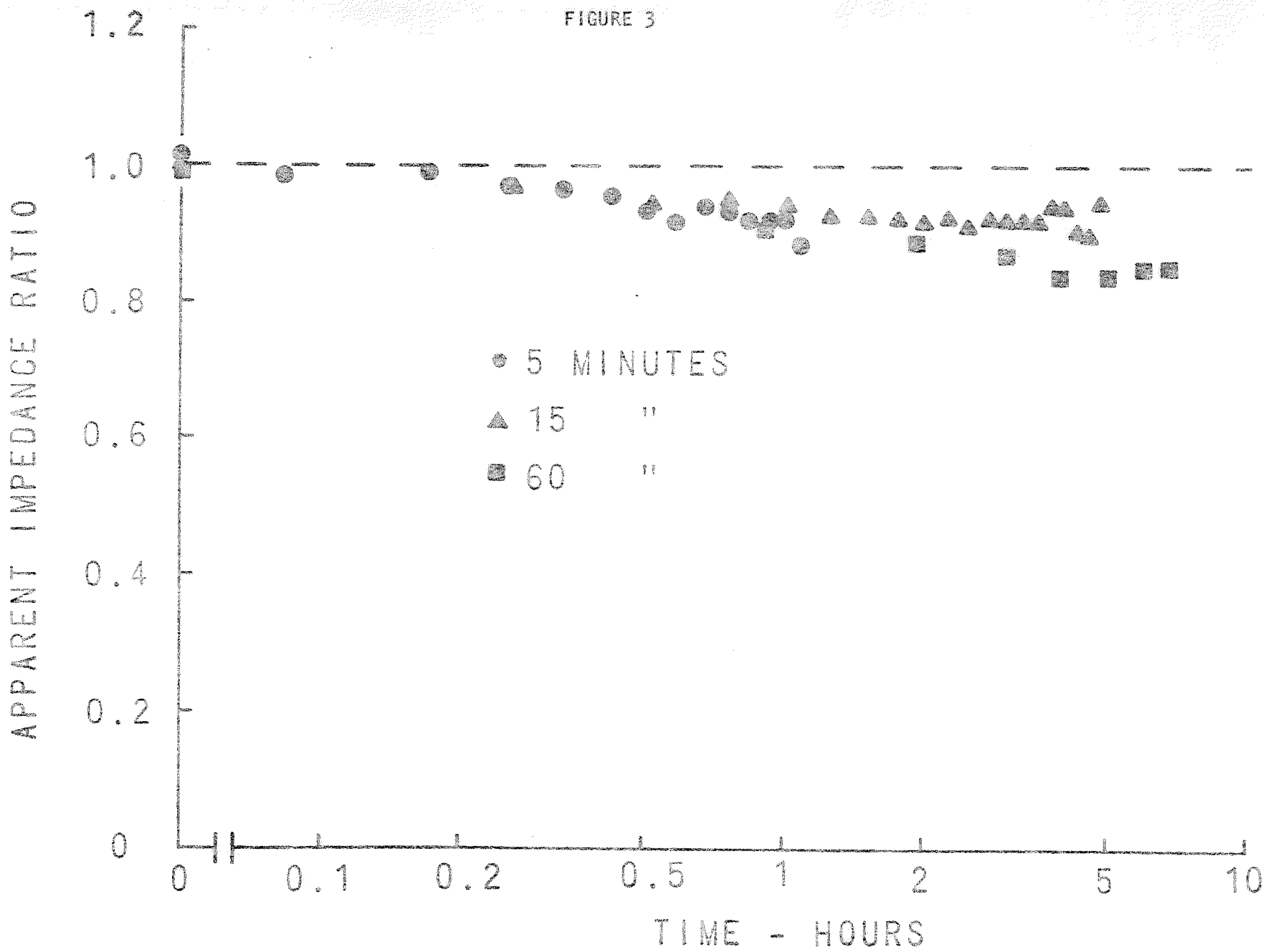
0.1
0.2
0.5
1
2
5
10
TIME HOURS
5 MINUTES
15 "
60 "

FIGURE 3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1.0
0.8
0.6
0.4
0.2
0
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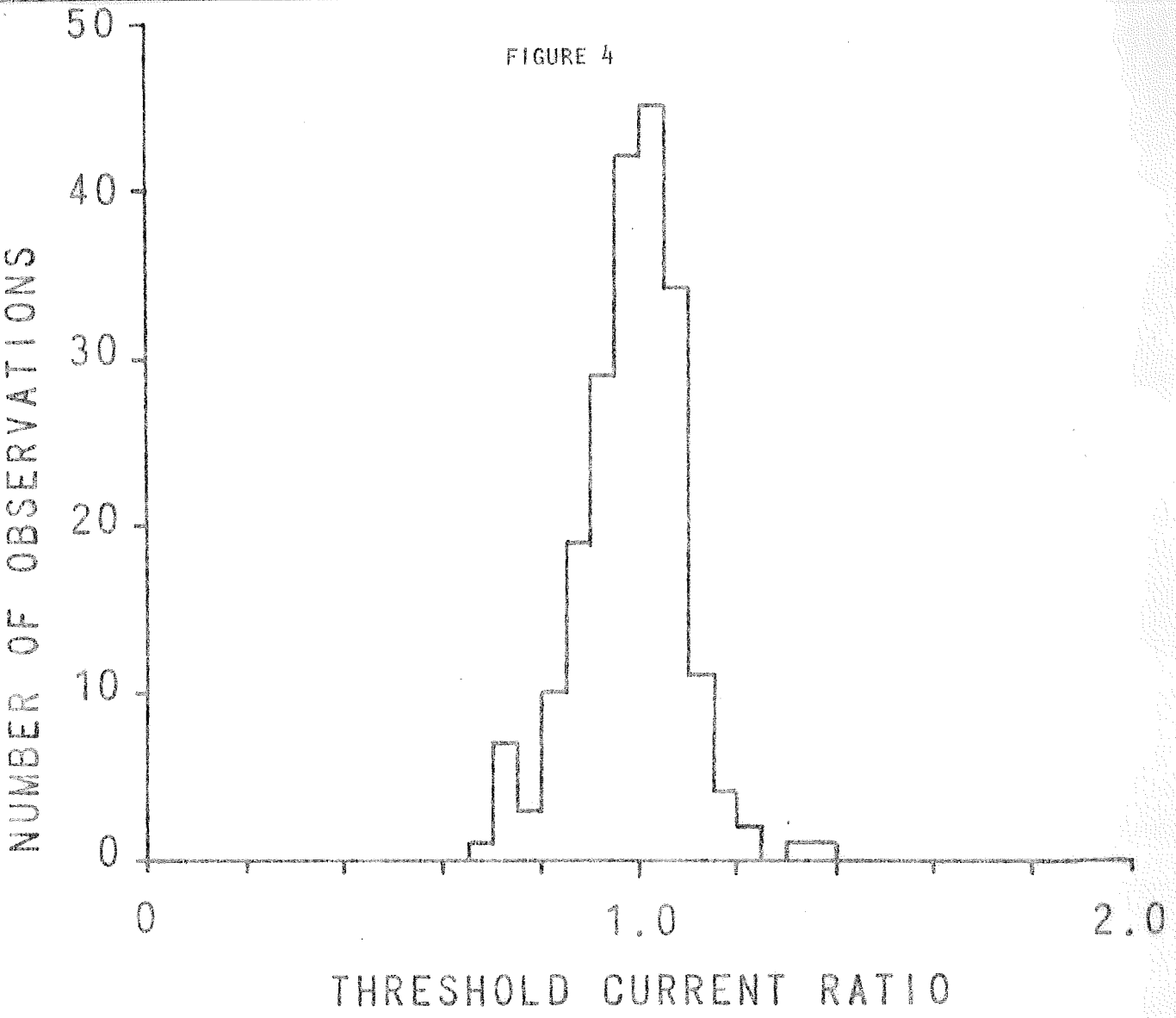
15 "
60 "
0
0.1
0.2
0.5
1
2
5
10
TIME - HOURS

FIGURE 4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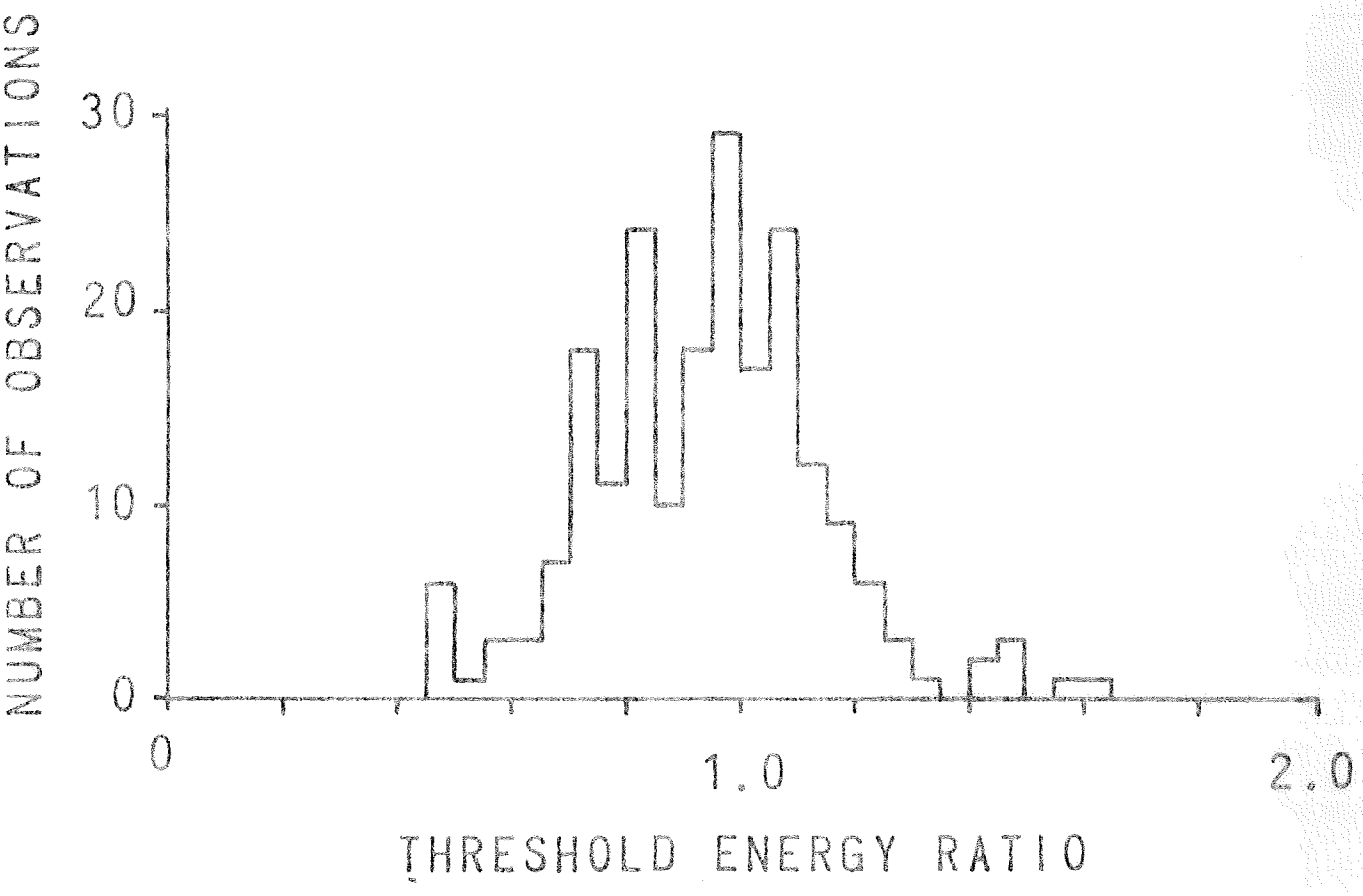
THRESHOLD CURRENT RATIO


NUMBER OF OBSERVATIONS
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20
10
0
0
1.0
2.0
THRESHOLD ENERGY RATIO

FIGURE 5