Article abstract

A method for rapid, accurate measurement of saccade amplitude, duration, and velocity (average and maximum) was developed as a functional test of the extraocular motor system. Recordings were made with a direct-current electro-oculographic system, and data analysis was performed on a laboratory digital computer. Saccade amplitude and duration were found to be linearly correlated in 25 normal subjects, with a mean slope of 2.7 msec per degree over a large amplitude range. In the same subjects, saccade amplitude and velocity (maximum or average) had a nonlinear relationship that was best fit by an exponential equation. The two constants of this equation adequately characterized the relationship between saccade amplitude and velocity and permitted rapid statistical comparison between normal and abnormal subjects.

Quantitative measurement of saccade amplitude, duration, and velocity

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Identification of an eye movement disorder that is not apparent on routine clinical examination would be helpful in the diagnosis of several neurologic diseases. Obvious examples are documentation of a second lesion in multiple sclerosis, demonstration of early third or sixth nerve involvement in a patient complaining of diplopia, and documentation of eye muscle weakness in a patient with an ill-defined neuromuscular disease. Since the high velocity attained by saccadic eye movements (as high as 700 degrees per second) requires a high rate of synchronized motor neuron firing, accurate assessment of saccade velocity should be a sensitive functional test of the extraocular motor system. Because of the high velocity of saccades, however, simple observation cannot detect slowing until the velocity has decreased several-fold. Even paper recording of saccadic eye movements (with routine electronystagmography equipment) does not detect early saccade slowing.

Technology exists for accurate measurement of saccade amplitude, velocity, and duration, and preliminary reports[1-4] suggest that a decrease or asymmetry in saccade velocity is a sensitive indication of extraocular motor dysfunction. Normal subjects have not been systematically studied, however, and a workable method for dealing with the nonlinear relationship between saccade amplitude and velocity has not been developed. It seemed apparent that a rapid clinical test for accurate measurement of saccade velocity would require averaging and correlation techniques if consistent results were to be obtained. With a laboratory digital computer, such techniques are readily available and results can be instantaneously evaluated. This report describes a test for routine clinical assessment of saccade velocity using a laboratory digital computer. A following report presents findings in normal subjects and selected patients to demonstrate reliability and usefulness of the test.

Materials and methods. *Generation of a moving target.* The subject is seated in a chair with the head mechanically fixed and is asked to follow a dot displayed on a modified 24-in. television screen as it moves through a standard

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tracking sequence. The sequence is played from a Tandberg (TIR) FM tape recorder at 7½ IPS (for maximum bandwidth). The standard sequence consists of a calibration step in which the dot is displaced 15 degrees to the right and left of center for 5 seconds, a series of random stepwise jumps (3 to 36 degrees in each direction for a total of 66 jumps; time between jumps is also randomly varied between ½ and 2½ seconds), five fixed-cycle constant velocity ramps (0.1 Hz, 0.3 Hz, 0.5 Hz, 0.7 Hz, 0.9 Hz), and recalibration. For special studies, larger saccades (up to 90 degrees) were generated by moving the subject closer to the screen.

Recording of eye movements. Electro-oculograms of horizontal eye movements are differentially recorded with electrodes fixed either lateral to both outer canthi (for binocular recording) or near the inner and outer canthi (for monocular recording) and to the forehead for reference ground. The electrodes are small (6.5 mm in diameter by 4.5 mm thick) to allow for placement close to the eyes. The sensing element is a hybrid composition of silver, silver chloride, and platinum blacking, which minimizes direct-current (DC) drift and impedance due to low alternating-current (AC) polarization. The skin is cleansed thoroughly at the contact points before electrodes are applied.

A high-impedance DC amplifier ($> 100\ \mu\Omega$) with a gain of 100 is strapped to the patient's arm, and the electrodes are connected via short leads to minimize stray capacitance and noise interference. The signal then goes into a low-gain amplifier adjusted to cancel any DC bias before a last amplification for a total gain of 1,000. The bandwidth of these amplifiers is from 0 to 100 Hz (−3dB), but the signal is then passed through a 35 Hz (−6dB) low pass filter to eliminate high frequency noise. This filter was chosen by starting with larger bandwidths and then reducing the bandwidth to a point where noise was minimized while saccade peak velocity was not significantly altered. The amplified signal is recorded simultaneously by a polygraph (Grass model 7 curvilinear pen recorder) for quick visual reference and by a Tandberg (TIR) FM tape recorder operating at 3¾ IPS. The overall signal-to-noise ratio varies with recording conditions (individual's corneal-retinal potential, one or both eyes), but is in the range of 40 dB.

Data analysis. Analog-to-digital conversion is made at a rate of 200 sampling points per second using a PDP-11/20 digital computer. The signal is calibrated by measuring the voltage corresponding to a known displacement of the eye (15 degrees horizontal angular deviation). As the data are read through the saccade-identifying routine, they are treated by a simple harmonic digital filter of the form $Y_i = Y_{i-1}(0.25) + Y_i(0.5) + Y_{i+1}(0.25)$. The velocity is calculated for every interval between two smoothed samples. Saccades are identified by setting a minimum velocity and duration (usually 40 degrees per second and 0.03 second). When the eye speed exceeds the minimum velocity for longer than the minimum duration, a saccade is identified. The saccade ends when the velocity drops back below the minimum velocity. The following parameters are obtained for each saccade: (1) starting and ending time, (2) amplitude, (3) average velocity (amplitude/duration), (4) maximum velocity, and (5) time of maximum velocity. The sequence is then visually displayed with a mark at the end of each identified saccade (figure 1). Artifacts such as eye blinks (arrows in figure 1) or electric interference are deleted either by the rejection parameters (i.e., minimum velocity and duration) or by the computer terminal operator, who can erase segments of the data containing artifacts.

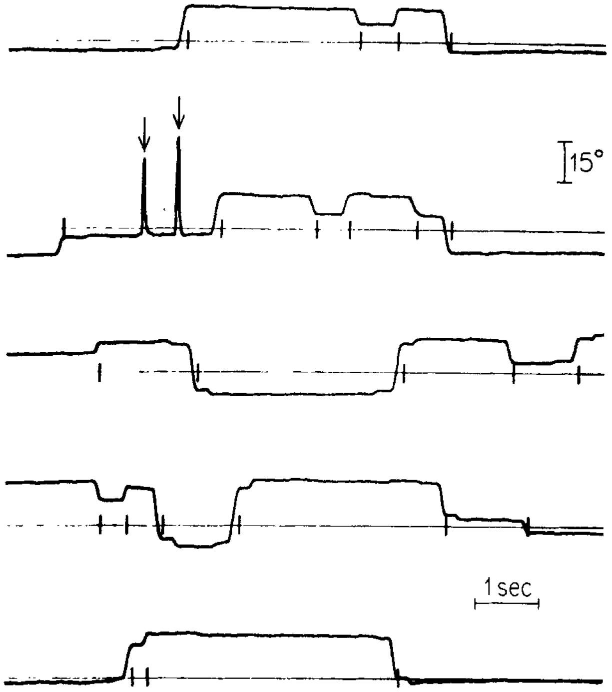

Figure 1. Digitized (200 samples per second) saccade sequence as displayed on the computer monitor. Vertical lines indicate the ending of each saccade identified by the computer program, and arrows indicate two unusually prominent eye blinks. Several of the smaller saccades are not identified because they did not meet the minimum duration requirement (0.04 second in this instance).

Results. The velocity time course of different amplitude saccades had a characteristic appearance (figure 2). Smaller saccades were approximately symmetrical, whereas larger saccades were significantly skewed. The relationship between saccade amplitude and duration was linear in normal subjects (figure 3a and b), although a few normal subjects demonstrated a mild curvature to the amplitude-duration relationship (figure 3c). When a straight line was fit to similar saccade amplitude-duration plots in 25 normal subjects, the average slope was 2.7 msec per degree with a Y-intercept of 37 msec. In other words, for every 10-degree increase in amplitude, the saccade duration increased 27 msec. In normal subjects tested with large-angle saccades, linearity remained over an amplitude range of 6 to 90 degrees (figure 4a). In the same subjects, plotting amplitude against velocity fall

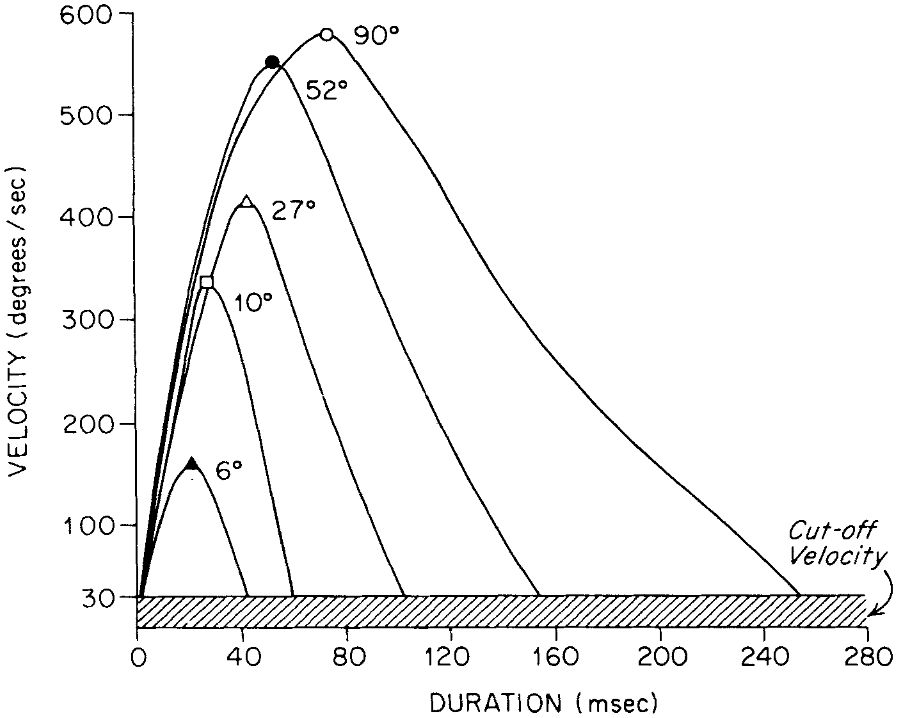

Figure 2. Velocity profiles of five different amplitude saccades in a normal subject. The cut-off velocity was 30 degrees per second, and minimum duration was 0.03 second.

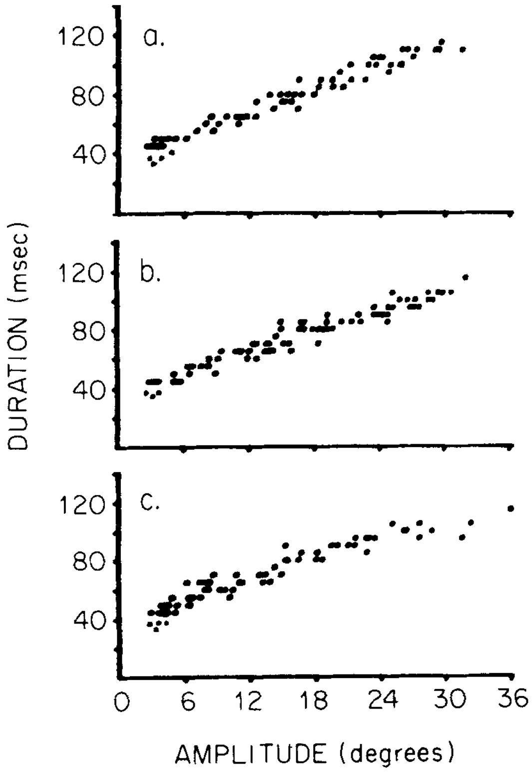

Figure 3. Saccade amplitude-duration plots in three normal subjects using standard saccade sequence (3 to 36 degrees).

time (i.e., time from maximum velocity to end of saccade) gave a linear relationship over the same amplitude range (figure 4b).

When either saccade maximum velocity or average velocity was plotted against amplitude, a distinct nonlinear relationship was observed. Figure 5 shows three typical plots from normal subjects of maximum velocity versus amplitude (binocular recording) for the standard series of saccades. In order to do statistical analysis on these nonlinear plots, it was necessary to summarize each plot with a small number of coefficients and then compare the values of these coefficients. The method chosen to summarize each plot was nonlinear regression analysis, which means that a theoretical curve would be fit to the data in such a way that the mean square error between the theoretical line and the actual data points was minimized. The program would return the "best-fit" coefficients that described the theoretical curve, along with an estimate of the standard deviation of these coefficients. In the absence of a definite model to explain the data, two types of curves were tried. One was a power-law curve of the form $EV = K(A)^L$ and the other, an exponential curve of the form $EV = K(1-\exp.[-A/L]$ where EV = eye velocity, A = saccade amplitude, and K and L = constants returned by the curve-fitting program expressed in degrees per second and degrees, respectively.

When these two curves were fit to amplitude-velocity plots in normal subjects, several factors suggested that the exponential curve was best suited for the data. First, the sum of squares, which is a measure of the error between

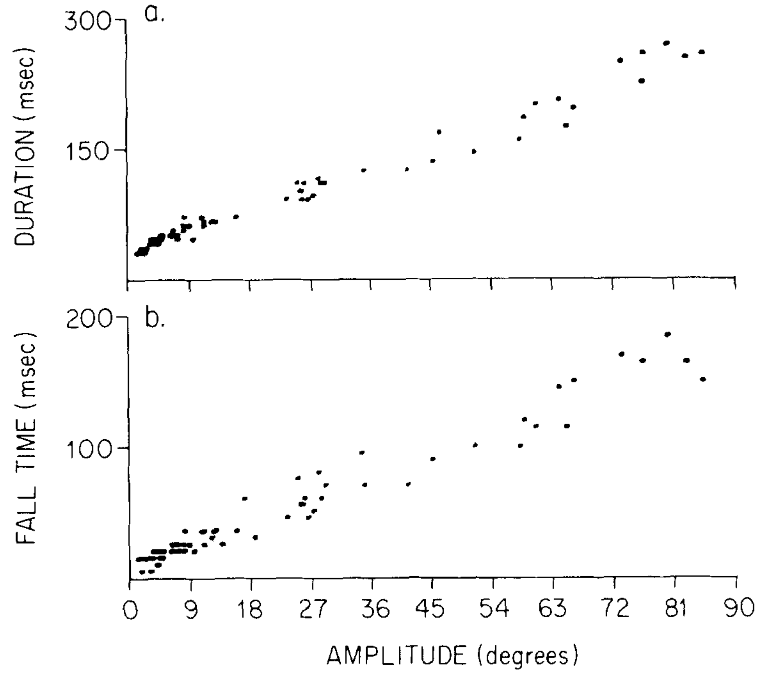

Figure 4. The relationship between duration and large-amplitude saccades (a) and between velocity fall time (time from peak velocity to ending) and same large-amplitude saccades (b) in a normal subject.

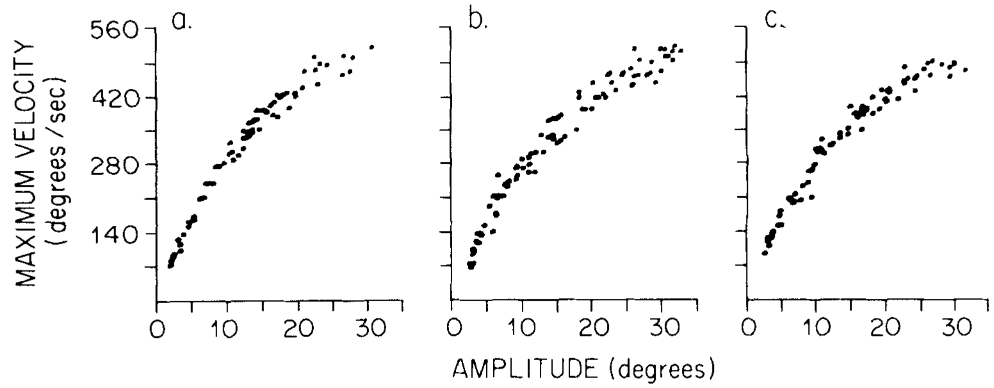

Figure 5. Saccade amplitude-maximum velocity plots in three normal subjects using standard saccade sequence.

the actual data points and the curve, was less than half that for the power-law model. Second, it appeared on visual inspection of the data that the experimental points had an asymptotic behavior at the higher amplitudes of saccades, something that the exponential model clearly displays but is not possible for the power-law model. To check this, a few experiments were done using very large-angle saccades (up to 90 degrees). Figure 6 shows the fit of the two models. It is apparent that the power curve (6a) does not follow the curvature of the experimental points as well as the exponential curve (6b). A more complex argument for choosing the exponential model and its theoretical implications is being prepared for publication.

When the exponential curve was fit to amplitude-maximum velocity plots (as shown in figure 5) from 25 normal subjects (binocular recordings), the mean K value was 551 ± 65 degrees per second and the mean L value was 14.0 ± 1.7 degrees, giving a normal range of 421 to 681 and 11.6 to 17.4 for K and L, respectively. Of particular importance, the exponential curve also fit amplitude-velocity plots from patients with a variety of diseases affecting the extraocular motor system. The earliest change in the amplitude-maximum velocity plots was slowing of the larger-amplitude saccades, resulting in lower K values. For example, the mean K value in a group of five patients with olivopontocerebellar degeneration was 303 ± 56.9 degrees per second.

Discussion. Concepts of saccade generation have changed as recording techniques have improved. Early investigators[5,6] described saccadic eye movements as ballistic in nature, based on the assumption that they were started and stopped by sudden bursts of the agonists and antagonists, respectively. Beginning with the careful measurements of Westheimer,[7] followed by those of Hyde,[8] Robinson,[9] and subsequently Cook and Stark,[10] this hypothesis became untenable. Westheimer's recording system consisted of photographing the horizontal deflection of a vertical light slit incident on the cornea.[7] The recorded saccade velocity profiles were symmetrical, with equal acceleration and deceleration phases. Westheimer introduced the concept of a step or pulse change in innervation to agonist muscles, with the eyes assuming a new position in the orbit determined by

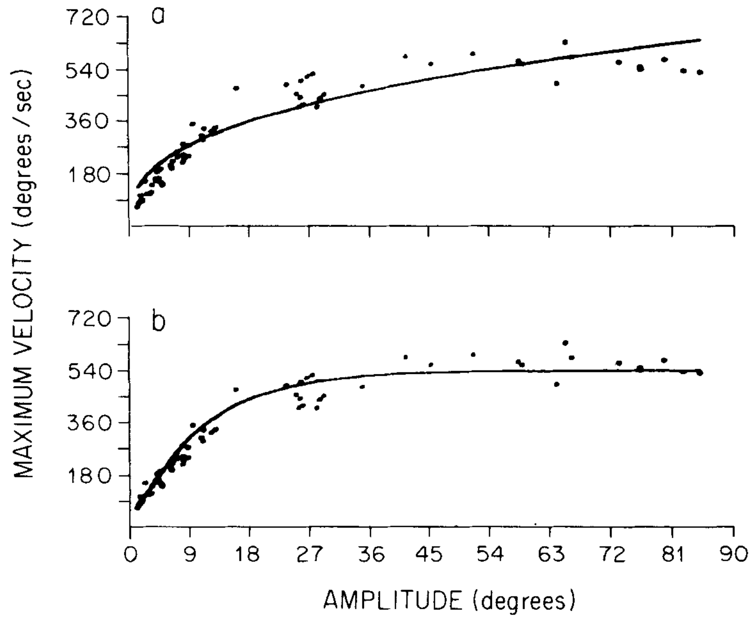

Figure 6. Goodness of fit of power-law model (a) and exponential model (b) to saccade amplitude-maximum velocity plots from a normal subject.

the net torque produced by muscle contraction balanced by orbital opposing forces: friction, inertia, and elasticity. Hyde[8] photographed the entire eye using the pupil as a landmark for pupil position. She found that the acceleration time remained relatively constant as saccade amplitude increased, but the deceleration time progressively increased, with prolonged deceleration tails for very large-amplitude saccades (60-90 degrees). A large portion of these large-amplitude saccades were apparently accurate, since they did not require a corrective movement. Careful analysis of the 90 degree saccades revealed a "creeping up" to the target phenomenon, suggesting the presence of corrective forces before the eyes came to a stop.

Robinson[9] recorded eye movements with a scleral search coil in a magnetic field attached to the globe by a suction scleral contact lens. With this recording system, he was able to record all three degrees of eye motion with a sensitivity of 15 seconds of arc. Recording in three normal adults revealed that during a saccade, the eye was driven by a brief burst of force much larger than was needed to maintain the eye in the new position. Deceleration appeared to be entirely due to the viscous nature of the orbital supporting structures without any active checking. Finally, Cook and Stark,[10] using a recording system that depended on the difference of reflected infrared light from the border of the iris and sclera, confirmed most of Robinson's findings and constructed a mathematical model that closely approximated recorded saccades.

This report describes a DC electro-oculographic recording system designed to conveniently and accurately record saccadic eye movements and allowing a rapid clinical assessment of the extraocular muscles and their control system. A laboratory digital computer identifies saccades, measures important parameters, plots these parameters, and performs statistical analyses. The large number of saccades (more than 66) recorded in each subject are rapidly analyzed, permitting averaging techniques that would be impossible with manual methods. With this technique, most previous findings on the mechanical properties of saccadic eye movements were confirmed and additional quantitative observations were made.

Saccade duration and amplitude were linearly correlated in normal subjects for amplitudes as high as 90 degrees. Further, the time from the maximum velocity to the saccade ending was linearly related to amplitude. The prolonged deceleration tails observed by Hyde were not seen. Average and maximum saccade velocities increased nonlinearly as amplitude increased, with maximum velocity showing the most prominent divergence from linearity. An exponential equation, eye velocity = K(1−exp.[−amplitude/L]), best fit these nonlinear relationships in normal subjects and a variety of patients. This equation predicts a nearly linear relationship for small-amplitude saccades but prominently deviates from linearity for large-amplitude saccades.

Because of the difficulty in clearly identifying the beginning and ending of a saccade, measurement of saccade duration was less precise than measurement of saccade velocity (particularly maximum velocity). Therefore, it was decided to concentrate on velocity measurements in future studies. This permits comparison with earlier reports, since previously used analog techniques could measure only amplitude and maximum velocity accurately. Figure 7 demonstrates the normal range of saccade maximum velocity versus amplitude (both directions) measured with electro-oculography in the present study compared with the photographic methods of Westheimer[7] and Hyde[8] and the infrared technique of Cook and Stark.[10] The data of Westheimer and of Cook and Stark are from a single normal subject, while Hyde's data represent the average of 10 normal subjects. With this limited comparison, the different

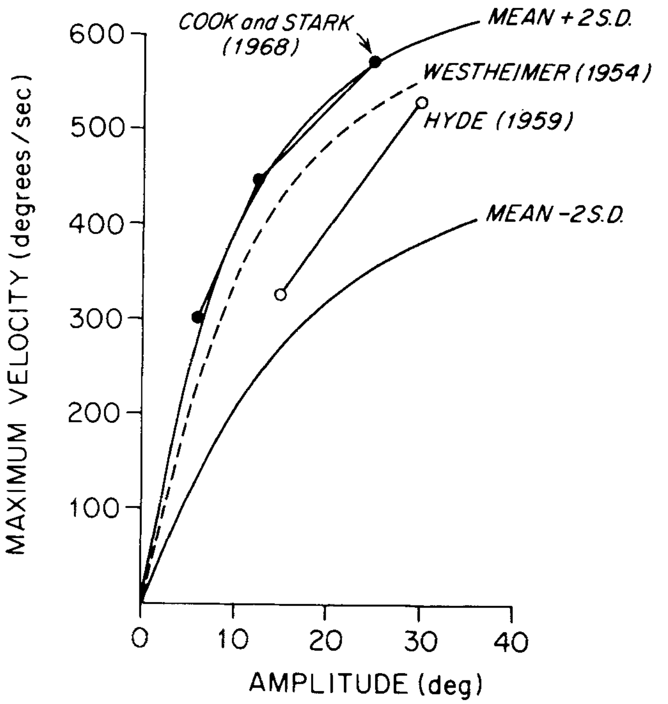

Figure 7. Normal range for maximum saccade velocity as determined by electro-oculography in the present report compared with previous reports using different recording techniques.

methods compare favorably.

The techniques used in this report, however, differ from previously reported techniques in several ways. The system was designed as a clinical tool that could be used on a large number and variety of patients, requiring only a brief testing period but providing quantifiable results. The testing sequence lasts only 10 minutes (including the slow-pursuit tests, which will be described elsewhere) and includes 66 jumps spread equally over a large amplitude range. Because of several unique features in the electro-oculographic recording system, the signal-to-noise ratio permits accurate assessment of the high velocities attained by saccades. Processing of this large amount of data is rapidly and accurately performed by a laboratory digital computer.

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