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DYNAMIC MECHANICAL PROPERTIES OF HUMAN BRAIN TISSUE*†

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Abstract—Investigators have been studying the mechanical phenomena associated with impact to the head for many years. Several theories on the behavior of the brain during head impact have come from these studies but there has been a notable lack of information on the bulk mechanical properties of the brain which are necessary for the evaluation of these theories. This paper represents an initial attempt at providing such information.

The dynamic complex shear modulus of *in vitro* samples of human brain have been measured. Specimens from eight brains have been subjected to a sinusoidal shear stress input under resonant conditions in an electro-mechanical test device. Tests were conducted to determine the effects of time after death, refrigeration of material and shear strain dependence. A device to measure the dynamic properties of brain *in vivo* is described and preliminary data on *in vivo* tests on Rhesus monkeys is presented.

The results of the dynamic shear testing on *in vitro* human brain indicate that the storage modulus G' lies between $6–11 \times 10^3$ dyn/cm^2, the loss modulus G'' lies between $3{\cdot}5–6{\cdot}0 \times 10^3$ dyn/cm^2 and the loss tangent tan δ is in the range 0·40–0·55.

INTRODUCTION

THE MECHANICAL phenomena associated with accelerations and impacts to the head have been studied by a number of investigators over the years. The prime interest in these studies has been the motions of the brain and its subsequent damage or malfunction. Holbourn (1943) proposed on theoretical grounds that injury to the brain is caused by shear strains. These shear strains can be produced in the brain at the point of impact due to severe deformation or fracture of the skull resulting in contact of the brain, or they can be produced remotely from the impact point due to the rotations of the brain within the skull. Holbourn also proposed that concussion is uniquely the result of rotation. Pudenz and Sheldon (1946) and Ommaya (1966) reported on experiments in which Rhesus monkeys were fitted with transparent plastic calvaria and subjected to head impact. The motions of the brain during impact were easily visible and tended to confirm Holbourn's predictions of brain rotational movement. Martinez (1963) has shown that brain injury in rabbits can be produced by the rotational motions of severe whiplash alone without impact to the head.

Other theories of brain injury being proposed at the present time are based on the idea of a hydrostatic tension being produced in regions of the brain during impact. Goldsmith (1966) discussed the concept of a compressive wave in the brain caused by an impact being reflected from the inner surface of the skull back into the brain as a tensile wave which could result in damaging cavitation phenomena. Unterharnscheidt

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(1966) also proposed a cavitation phenomenon but attributes its formation to an inertia process wherein the brain tries to separate from the skull as the skull accelerates upon impact.

The final correlation of head injury theories with head injury experiments has not been forthcoming because of the almost complete lack of knowledge of the mechanical properties of brain tissue. Goldsmith (1966) has pointed out this problem and has suggested some of the pertinent properties to be determined. Ommaya (1968) has reviewed the scientific literature pertaining to the mechanical properties of the tissues of the nervous system. In the case of brain tissue, only three papers on the mechanical properties of brain were found. Franke (1954) determined the coefficient of shear viscosity from calculations made on data from driving point impedance measurements of a glass sphere vibrating within whole, fresh pig brain and pig brain homogenates at frequencies of 150–500 Hz. The viscosity was reported to be similar to that of room temperature glycerin. Creep experiments were performed by Dodgson (1962) on fresh mouse brain in an attempt to determine the Mises–Hencky flow condition under static compression. Koeneman (1966) studied creep and dynamic cyclic properties from rabbits, rats and pigs. Again, the loading condition was compression. All of the above methods have been *in vitro* tests on species other than primates. Ommaya emphasized the importance of future studies including *in vivo* experiments to check the validity of the *in vitro* work and the use of animals suitable for scaling the data for extrapolation to human brain.

The purpose of this paper is to report the results of the initial phase of a program to provide information on the mechanical properties of human brain pertinent to the problem of head injury. Both *in vitro* and *in vivo* techniques were used. In accordance with the concepts of shear strain mechanisms of brain injury, the dynamic shear properties of *in vitro* human brain have been determined. An *in vivo* test has been developed to provide correlation between the living state and the *in vitro* condition using Rhesus monkeys.

One of the reasons that there have been few studies of the mechanical properties of the brain is that it is a complex and difficult material to work with. From the standpoint of engineering materials it can best be likened to a soft gel. The tissues of the brain are quite heterogeneous both on the macroscale and on the microscale. In addition, the brain has a complex geometric arrangement of these tissues. The outer covering of the brain is a combination of tissues known as the pia-arachnoid which appears to be much tougher than the interior brain tissue. There are a large number of blood vessels in the brain, which under pressure help to lend rigidity to the soft brain structure. A good analogy might be to consider the brain in its entirety as an inflated or pressurized structure with a tough covering and filled with a gel-like material.

The apparatus used in the *in vitro* testing of human brain was an electro-mechanical device that subjects a specimen to a sinusoidal shear strain. This device, described later in this paper, is normally used for routine evaluation of the dynamic shear properties of elastomers. The *in vivo* test device was developed especially for this project. It is a small driving point impedance probe which is placed in direct contact with the pia-arachnoid through a hole in the skull. *In vivo* tests such as this have been performed on the surfaces of the human body, such as the thigh and the upper arm, by Franke (1951) and von Gierke *et al.* (1952). The effects of blood pressure on dynamic behavior and postmortem changes in properties can be studied with the probe.

MATERIALS AND METHODS

A. *In vitro testing*

The complex dynamic shear modulus (G^*) of a viscoelastic material is defined as the vector sum of G' and iG'', with G'' normal to G'. G' is the dynamic elastic modulus and is a

measure of the spring stiffness of the test material under shear stress. G'', the dynamic loss modulus, is a measure of the damping ability of the material and represents viscous losses in the material. The relative damping ability of the material, tan δ, is defined as G''/G'.

G^* is determined by applying a dynamic shear stress to the viscoelastic test material and measuring the resulting strain. The Dynamic Mechanical Apparatus (DMA) consists of a sinusoidally actuated mechanism for shearing the sample and electronic equipment to monitor input force, strain level (output) and the phase angle between them. See Fig. 1. The sample shear mechanism is centrally located on a magnesium–aluminum alloy rod which connects twin electromechanical transducers. The driving signal, from a function generator operating in the sine mode, is connected to one transducer. The input force is determined by the current to the driving transducer and is adjustable by means of the function generator signal level control. An auxiliary amplifier is provided for increased signal strength, if needed. The other transducer provides an output signal, operating as a velocity transducer. Strain and strain rate are measured by output voltage and amplitude. The driving current and output voltage are measured on a vacuum tube voltmeter. (The current is measured as a voltage across a shunt resistor on the driving transducer.) The input and output signals are displayed as an x–y (Lissajous) plot on an oscilloscope to aid the operator in placing the system in resonance. The input frequency at resonance is read directly from the function generator control.

The sample shearing mechanism consists of a horizontal aluminum base plate rigidly attached to the magnesium–aluminum rod and a clear plastic plate which is positioned above, and parallel to, the aluminum base plate. This plastic plate is rigidly attached to the main structure of the DMA and is vertically

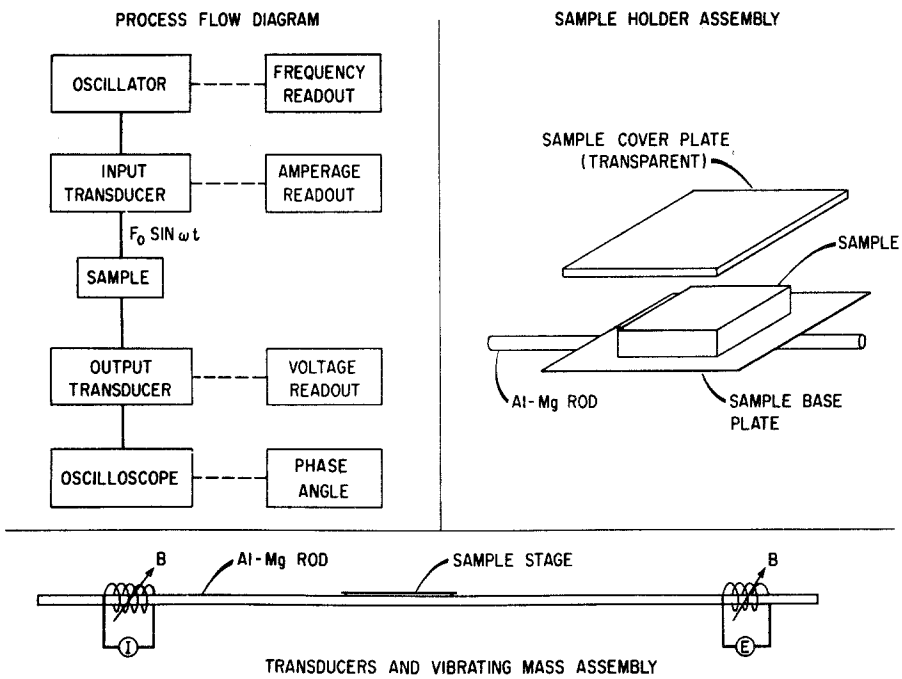

Fig. 1. Schematic views of the Dynamic Mechanical Apparatus.

adjustable. The test sample is sandwiched between these two plates. The sample section, between the twin transducers, is enclosed in a chamber heated by a small electrical heater-fan system. The temperature is controlled by means of a temperature potentiometer which utilizes an iron-constantan thermocouple placed adjacent to the sample.

The DMA operates as a subtractive impedance device, i.e. the impedance of the unloaded system must be subtracted from that of the system with the sample in place. This is accomplished by obtaining a master curve of input amperage (I_0) and resonant frequency (f_0) as functions of test amplitude and then subtracting these values from the raw test data for corresponding amplitudes. All measurements are obtained with the system in resonance. Briefly stated, the data reduction consists of the following equations:

$$G' = q(\omega^2 M - \omega_0^2 M) \tag{1}$$

$$G'' = \omega q C\left(\frac{I - I_0}{E}\right) \tag{2}$$

$$|G^*| = [(G')^2 + (G'')^2]^{1/2} \tag{3}$$

$$\tan\delta = G''/G'$$

where:

q = Sample shape factor, height/area,
$\omega = 2\pi f$,
M = vibrating mass of DMA, 243 g,
C_2 = force constant of DMA, $1{\cdot}53 \times 10^6$ g · Ω · sec^{-1},
I = driving amperage,
E = output voltage,

subscript zero indicates values for the DMA without sample and at corresponding amplitude. The apparatus and data reduction are based on the work of Fitzgerald and Ferry (1953). The dynamic viscosity (η_0) and spring (k) constants are obtained from the relations

$$\eta_0 = G''/\omega \tag{4}$$

$$k = G'/q. \tag{5}$$

The test procedure includes the following operations:

(1) The sinusoidal input amperage and frequency are adjusted to yield resonance at the desired strain level.

(2) The resonant frequency (f), input amperage (I), and output voltage (E) are recorded.

(3) Steps (1) and (2) are repeated for each desired strain level.

(4) A photograph of the sample is taken vertically from the overhead position. The sample area (A) is determined by using a planimeter.

(5) The sample height (h) is determined by a vernier micrometer.

(6) Steps (1) and (2) are repeated without a sample (i.e. unloaded), in order to obtain master curves of (f_0) and (I_0) vs. strain level.

Human brain sections, taken at autopsy, were obtained from the Veterans Administration and University of Michigan Hospitals in Ann Arbor. The sections were packed in polyethylene bags and placed on ice and water within 10 min after removal from the skull. They were then transferred to Dow Corning within 2·5 hr. Initial tests were run immediately upon receipt. Subsequent storage was at 3°C, since early tests on Rhesus brain confirmed that gross change occurs in the modulus upon freezing the tissue. Freezing lowered the storage modulus approximately an order of magnitude and the loss modulus by a factor of three.

Rectangular solid test specimens with the approximate dimensions of 2 cm × 3 cm and 0·4–0·7 cm in height were used. Both of the sample-holder plates contacting the specimen were scored with a cross-hatch pattern to reduce slippage. An aerosol adhesive was sprayed on both plates to further reduce slippage. The test specimen was placed on the base plate and the cover plate was then allowed to rest in light contact with the upper specimen surface before being rigidly secured to the DMA frame. A plastic cover was placed over the sample section to form

the test chamber and the temperature was adjusted to test specifications. Testing was begun after a 15-min equilibration period.

A total of 13 samples of human brain tissue from eight individuals has been tested *in vitro* utilizing the DMA. All of the samples were cerebral white matter and were tested at 37°C. The tests were conducted at 9–10 Hz.

In order to describe the specific test procedure for each sample, two terms are employed. A *scan* consists of approximately six individual measurements conducted in rapid sequence, generally moving from low to high strain levels. Strains approaching 0·37 were achieved during the testing, though not for all samples. A *series* consists of a number of scans conducted in rapid sequence. Each test was numbered to identify it as to type of brain, specific brain, and specific scan.

B. *In vivo testing*

The Dynamic Mechanical Apparatus, though suitable for *in vitro* testing, can not be used in *in vivo* testing. To meet the need of an *in vivo* test, a small driving point impedance device was constructed. Termed the Dynamic Probe Apparatus (DPA), it consists of a sinusoidally-driven probe attached to an impedance head, and associated electronic equipment for signal conditioning and display.

The output shaft of a small electrodynamic shaker is connected to the impedance head. A flat-ended, cylindrical probe of 0·1 cm^2 cross-sectional area, mounted on the impedance head, transmits the sinusoidal motion of the shaker output to the test material and measures the transmitted force. An accelerometer mounted on the impedance head measures the acceleration of the probe. See Fig. 2.

The apparatus functions as a driving point impedance device. The output consists of the force transferred from the probe to the test material and the dynamic displacement of the probe. The force transducer measures a composite signal consisting of the force transferred to the test material and the force caused by the acceleration of the probe mass. This latter force component is subtracted from the composite signal in order to obtain the desired transfer force function. This is accomplished with the acceleration transducer by electronically subtracting an

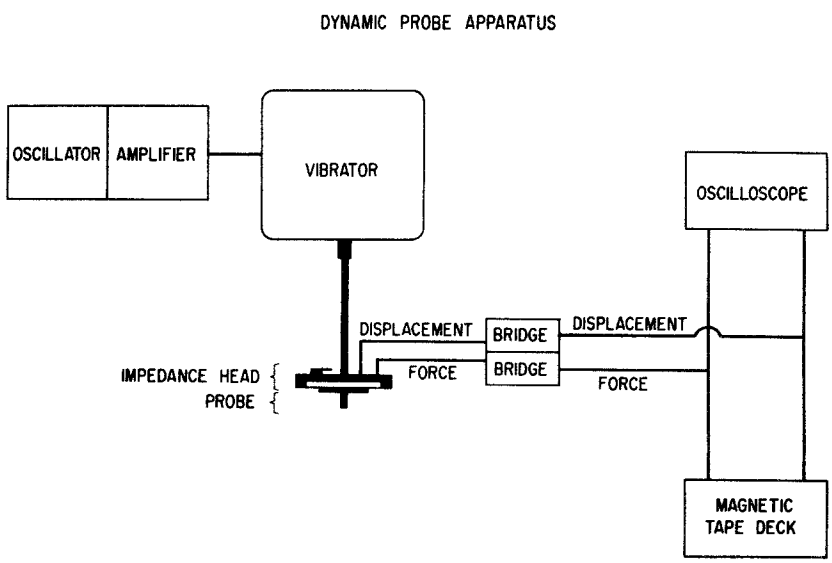

Fig. 2. Dynamic Probe Apparatus.

acceleration signal, equal in magnitude to the mass acceleration of the probe, from the composite signal. The accelerometer output is also utilized to measure dynamic displacement by electronically shifting it 180° out of phase (i.e. inverting it). The resultant signal is proportional to displacement, at a given frequency.

The transferred force and dynamic displacement signals are displayed on a dual-beam oscilloscope. Both linear and *x-y* (Lissajous) plots are possible. The Lissajous figures are recorded with a Polaroid camera mounted on the oscilloscope. A complete test record is recorded on magnetic tape.

Subjects tested in initial experiments using the DPA were young adult Rhesus monkeys (*Macaca mulatta*) ranging from 4·5 to 5·5 kg and anesthetized with phencyclidine hydrochloride and sodium pentobarbital. The right internal carotid artery was cannulated for blood pressure monitoring and the right internal jugular vein was cannulated for saline infusion and drug administration. Subjects were mounted in a primate chair and the head secured with a surgical head holder through an intra-orbital to dental clamp. The cranial test sites were prepared after a midsagittal incision in the scalp and separation of the overlying skin and the galea aponeurotica. At a point located according to coarse stereotaxic position over the medial area of the precentral gyrus, a burr hole was made in the calvarium and enlarged with a $\frac{3}{8}$ in. trephine. Upon attaining hemostasis the dura mater under the test site was removed. Either one test site or two contralateral sites were prepared.

The DPA was then positioned over the monkey's head so that the probe tip would be able to contact the exposed cerebral cortex. After positioning, the probe could be pressed into the brain surface through a screw drive mechanism on its crosslide mount and the static brain deformation measured with an attached dial indicator. The pia-arachnoid was not punctured during the tests.

While at a specified static deformation the probe was driven with a small sinusoidal amplitude and the force and acceleration signals from the probe recorded. These signals were displayed on an oscilloscope and also recorded on magnetic tape. The oscilloscope display permits a simple analysis of $\tan\delta$ and the recorded data can be digitized and used to solve a model of the brain-probe system.

In tests where the dynamic mechanical properties were measured as a function of blood pressure, the arterial pressure was controlled by intravenous infusion of a 0·1 per cent solution of trimethaphan camphorsulfonate in Ringer–Locke solution. The infusion rate was adjusted to get the desired blood pressure depression, which could be restored to normal values by stopping the administration.

RESULTS

A. *In vitro tests*

Initial tests yielded modulus values which increased with time as the test series progressed. This increase has been attributed to sample drying. Subsequent tests were conducted in a high-humidity environment and generally with a very thin coating of a silicone adhesive on the sample surface. Values of G' and G'' for a typical test (HBM-6-20) are shown in Figs. 3 and 4. The first scan of a series yields a strain-dependent modulus whereas the second and third scans do not show descernible strain dependence. Repeated series following a period with the specimen at rest yield similar results, with the modulus returning to the same level as in the previous series during the first scan and remaining so through subsequent scans. This repeatability indicates that there is no rapid irreversible change occurring as a result of the test environment. It is concluded that the change in modulus during the first scan shows not a strain dependence, but a conditioning caused by shear. Stiffening of the specimen edge while at rest is likely, relieved by shear

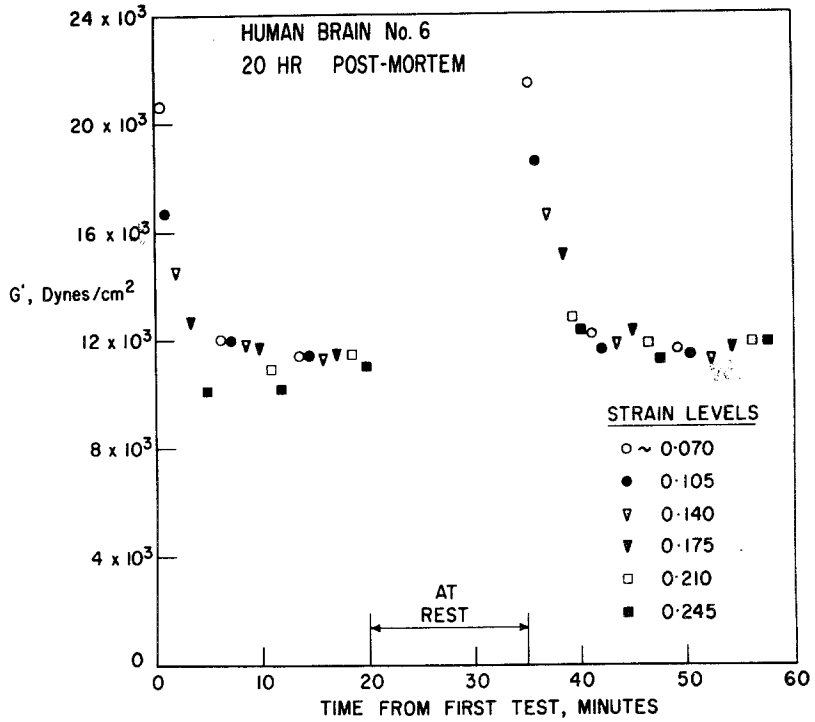

Fig. 3. Dynamic elastic modulus of human brain No. 6, 20 hr post-mortem.

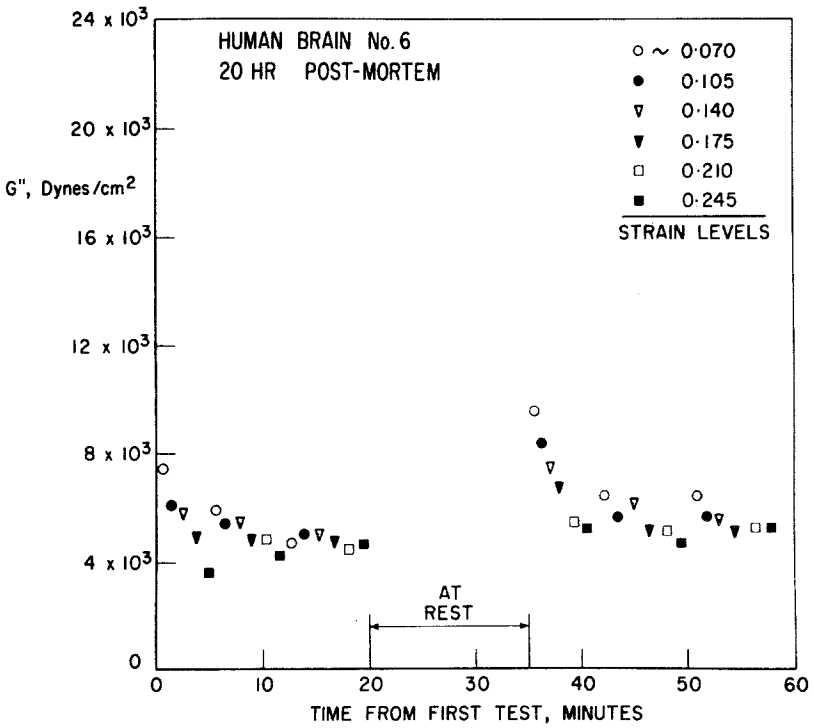

Fig. 4. Dynamic loss modulus of human brain No. 6, 20 hr post-mortem.

or redistribution of moisture under shear. Thixotropy has not been ruled out, however.

Table 1 summarizes the modulus values obtained from all tests conducted on the eight brains, listing the steady-state values from shear-conditioned samples. Based on the above interpretation, these tests indicate that G' lies between $6–11 \times 10^3$ dyn/cm^2, G'' lies between $3{\cdot}5–6{\cdot}0 \times 10^3$ dyn/cm^2, and tan δ is in the range 0·40–0·55.

B. *In vivo tests*

Using the DPA and the experimental procedure discussed above, Lissajous figures of force vs. deformation have been obtained on eight Rhesus monkeys. The experiments were designed to examine the effects of static probe deformation, dynamic amplitude, frequency and systemic blood pressure on the *in vivo* dynamic behavior of the brain. The animals were sacrificed during the experiments and postmortem effects were studied. *In vitro* tests on Rhesus monkey brain were also performed.

Figure 5(A) shows a typical high amplitude (30×10^{-3} cm) test result demonstrating a highly asymmetric Lissajous figure. This type of figure can not be analyzed by present techniques. The symmetric Lissajous plot in Fig. 5(B) is typical of the lower amplitude tests ($2{\cdot}5 \times 10^{-3}$ cm). The symmetry of this type of sinusoidal force Lissajous pattern allows certain dynamic constants to be calculated (Gehman, 1957) after suitable analysis but allows the loss tangent tan δ to be calculated directly as indicated in Fig. 5(B).

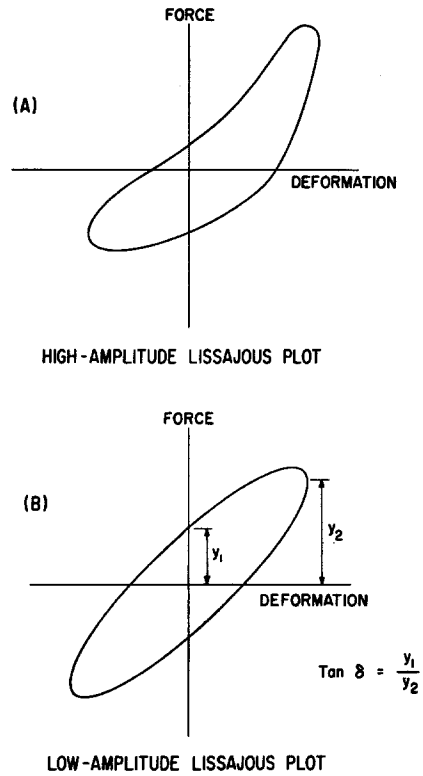

Fig. 5. DPA Lissajous plots.

A complete analysis of the test results in

Table 1. Summary of *in vitro* dynamic mechanical properties of human brains

Brain	Age	Hours post-mortem	G' (dyn/cm^2)	G'' (dyn/cm^2)	tan δ
1	48	10	$11{\cdot}1 \times 10^3$	$5{\cdot}1 \times 10^3$	0·46
		33	9·8	5·2	0·53
2	77	10	6–9	5.5–6·5	0·65–1·00
3	44	33	7·7	3·9	0·51
		51	9·0	5·0	0·55
4	92	20	14·1	6·0	0·42
5	80	28	9·7	4·8	0·50
6	50	20	10·0	4·5	0·45
7	49	47	7·5	3·0	0·35
		62	10·5	4·5	0·43
8	71	25	7·7	4·0	0·52

terms of the basic dynamic shear moduli depends on a mathematical analysis of the DPA-brain system now in progress. This analysis will allow direct comparison with the *in vitro* results of the previous section. It is possible, however, to present values of tan δ for *in vivo* Rhesus monkey cerebral cortex as a function of blood pressure as shown in Fig. 6. These results for a single amplitude test ($2{\cdot}5 \times 10^{-3}$ cm) show a decreasing tan δ with decreasing blood pressure.

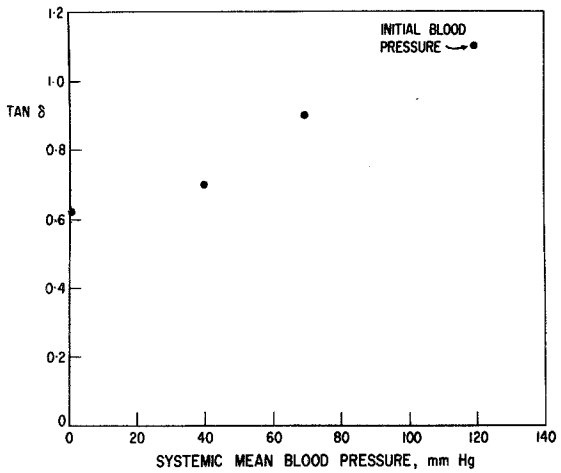

Fig. 6. Tan δ vs. systemic mean blood pressure.

DISCUSSION

In view of the very soft nature of brain tissue, the values of the *in vitro* dynamic shear moduli are not surprising. The lowness of these values is emphasized when they are compared to soft engineering materials as shown in Fig. 7.

Approximate values of the shear elasticity and shear viscosity of soft human body tissue have been calculated by von Gierke *et al.* (1952) from impedance measurements. The value of the shear elasticity was found to be $2{\cdot}5 \times 10^4$ dyn/cm² and the shear viscosity was 150 P for *in vivo* muscular tissues. Comparison of G' values from the *in vitro* brain test ($6\text{–}11 \times 10^3$ dyn/cm²) with this approximate shear elasticity coefficient places the *in vitro* human brain stiffness just below that of

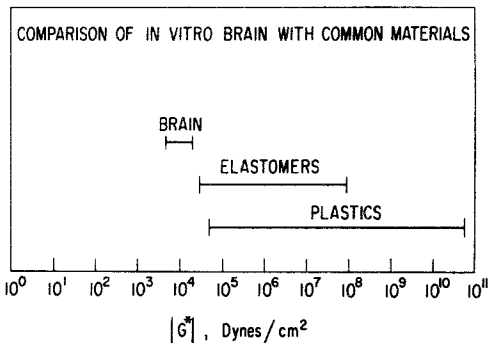

Fig. 7. Comparison of brain with common materials.

in vivo human muscular tissue. Equation (4) can be used to calculate the dynamic shear viscosity η_0 for the *in vitro* human brain giving a range of 56–96 P, which again places it just below that of *in vivo* human muscular tissue. Koeneman (1966) found the dynamic elastic compression modulus of *in vitro* brain white matter of rabbits, rats and pigs to lie in the range from 0·8 to $1{\cdot}5 \times 10^5$ dyn/cm². Assuming the compression modulus is approximately three times the shear modulus for a linear viscoelastic material of this type, Koeneman's values are equivalent to a G' range of $2{\cdot}7\text{–}5 \times 10^4$ dyn/cm², somewhat higher than von Gierke's values for muscular tissue. Koeneman reported a dynamic viscosity of 43·5 P while Franke (1954) reported a shear viscosity of 14·9 P calculated from impedance measurements on *in vitro* pig brain. Dividing Koeneman's value by three gives a dynamic shear viscosity of 14·5 P, in close agreement with Franke. Both of these values were calculated from data obtained in the frequency range of 100–500 Hz. Since the *in vitro* tests reported in this paper were performed at 9–10 Hz, the differences between the shear viscosity coefficients could very well be due to variation of the dynamic properties with frequency, a situation found in most viscoelastic materials. The possibility of differences between the mechanical properties of the brain in lower animals and those of primate brain cannot be ruled out, however. Ommaya (1966) discussed the high

impact tolerance of small animals with their compact brains which are not as deformable as larger brains.

The high values of tan δ (Table 1) obtained in the *in vitro* testing characterize the brain tissue as a material with high internal damping. These high values correlate with the *in vivo* test as shown in Fig. 6 where the tan δ for zero blood pressure approaches the range found for *in vitro* human brain. The indications from this initial *in vivo* to *in vitro* correlation are that the test will provide the means for resolving the questions of post-mortem changes, blood pressure effects and frequency effects on the dynamic properties of brain tissue. Von Gierke (1966) showed that for this type of material being tested and for the frequency range being employed, that the probe test is basically a shear test. Thus, the possibility of calculating G' and G'' from the data using the proper mathematical techniques is quite good.

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