J Neurosurg
29(9): 793-798
1962

TISSUE INTERFACE DETECTOR FOR VENTRICULOGRAPHY AND OTHER APPLICATIONS

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(Received for publication May 1, 1962.)

A simply employed instrument for determining when a penetrating cannula enters the ventricular system of the brain has been developed and put into routine use. Its use eliminates from human ventriculographic procedures the dependence on criteria now employed, i.e., the detection by hand of a change in mechanical resistance on penetrating the ventricular wall and the flow of cerebrospinal fluid from the cannula when the stylet is removed. It makes practical routine ventriculography on experimental animals such as rat, cat and monkey and therefore provides a rapid means of determining coordinates of internal landmarks of the brain for positioning electrodes, ultrasonic foci, etc. in deep structures of the brain of these animals. The method is based on the measurement of changes in electrical impedance as the penetrating cannula, enclosing a removable concentric, insulated, inner electrode, passes through interfaces separating media of different electrical conductivity and/or dielectric susceptibility.

Ventriculographic procedures in the human using the transcortical approach are, of course, in widespread use for the identification of intracranial shifts caused by tumors and other space-occupying masses, for obtaining coordinates of internal landmarks of the brain for use in stereotactic work, for reducing intracranial pressure in, for example, cases of hydrocephalus, etc. All of these applications require that the "end" of the cannula be positioned within the fluid of the ventricular system so that either a contrast medium can be inserted (gas or radio-opaque material) or so that the cerebrospinal fluid can flow freely out through the cannula. In some cases this identification of the position of the tip of the cannula presents difficulty resulting from both the absence of a detectable change in mechanical resistance as the wall is penetrated and the absence of flow of cerebrospinal fluid—the latter the result, for example, of tissue at the opening of the cannula acting as a check valve. Multiple penetration of the cannula may then be employed in an attempt to identify one of these criteria. This is an unsatisfactory procedure since each penetration increases the possibility of a vascular accident and of course brain tissue is damaged each time the cannula is inserted. Consequently, a simple method of determining unambiguously when the ventricle is penetrated and not depending upon either of the above criteria is desirable.

The difficulties, which sometimes are encountered in the human when present criteria are employed, make routine ventriculography on animals such as the cat completely impractical. Therefore, a method is essential for determining unambiguously penetration of the ventricular wall if routine ventriculography on experimental animals such as rats, cats and monkeys is to be accomplished. That such a procedure is extremely desirable is indicated by the poor accuracy of anatomic placement achieved for production of lesions and placement of electrodes when the standard ear-bar midpoint is used as the zero reference and the plane determined by it and the infraorbital ridges is used as a base plane. Extensive experimental work by the authors[2] and others (see for example Loewenfeld and Altman[3]) shows that, for example, a variation of position of several millimeters for thalamic and subthalamic structures is characteristic of cat brain using this coordinate system. Increased accuracy in the localization of these structures would be anticipated if internal landmarks of the brain are employed as has been demonstrated for the human.[5] The authors have shown that this is the case for cat (unpublished data of the Biophysical Research Laboratory‡) and, in

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‡ It appears on the basis of data now in hand that the use of ventricular landmarks—ventricular boundaries of the anterior and posterior commissures at present—for the placement of lesions in the thalamus and subthalamus of this animal reduces the average uncertainty of placement by roughly a factor of five over that characteristic of the system employing the ear bars and "infraorbital" plane as references.

fact, were led to this stage of development after extensive use of first the standard Horsley-Clarke system of reference followed by the use of the internal configuration of the brain case as a reference for the placement of brain lesions.[2] The precision achieved has required the design and construction of rigid head holders provided with roentgen-ray cassettes which fit into reproducible positions on the holder.[2] These cassettes include coordinate axes from which the locations of chosen landmarks can be determined. After achieving the necessary mechanical rigidity and precision and the experience using roentgenographic procedures to superimpose brain-case configurations for positioning lesions (employing a set of reference brains cut down *in situ*), it became obvious that ventriculography with the identification and measurement of location of the landmarks of the brain would constitute the next logical step in the development of increased accuracy of positioning in the experimental animal. As soon as this work was initiated, it was apparent that the criteria employed in the human for determining when a cannula entered the ventricular system were practically useless. The necessary use of a small cannula excludes the possibility of sensing by hand when the ventricular wall is penetrated, and the difficulty of nonrigidly supporting and maintaining a cannula with its tip at a site in a small ventricular system is apparent from the observation that the distance between adjacent walls of the lateral ventricle in a cat is only about 1 mm. when the cannula is inserted vertically at a lateral and anterior position to prevent damage to the subcallosal fornix. In addition, with the maximum size (No. 22) of ventricular cannula that the authors considered acceptable, no backflow of cerebrospinal fluid is observed normally and usually not any can be aspirated. Such flow does not occur even if the animal is supported head down. This probably is explained by the fact that the distance of spacing between opposite walls of the ventricular system at the sites of penetration is so small that if any backflow starts, the opposite wall deflects slightly to act as a check valve.

It is the primary purpose of this paper to indicate how the problem of identifying ventricular penetration was solved, to describe the procedure employed, and to illustrate the results obtained on both experimental animals and humans. Potential applications of the method other than that for which it was developed initially are also indicated.

PRINCIPLES OF OPERATION AND PROCEDURE IN USE

The operation of the detector of ventricular penetration is based on the identification of changes in the electrical impedance measured between a metal sleeve or cannula and an inner concentric slightly projecting electrode (Fig. 1). The result of the measurement is presented on a meter with the deflection from a preset value proportional to the magnitude of the measured change in the impedance. Since the impedance is determined primarily by the electrical properties of the material[6] in the immediate neighborhood of the projecting tip of the inner conductor, any change in the structure of the medium as the cannula assembly penetrates the tissue, which is characterized by a corresponding unambiguously detectable change in impedance, can be identified.[4] The deflection of the pointer of the meter which occurs in moving from subcortical white matter, corpus callosum, or other similarly dense fiber-tract region to the cerebrospinal fluid of the ventricular system is a decrease of 30 to 40 per cent for the currently employed operating frequency of 2000 c./sec. and for the size of needles and concentric configuration of electrodes that the authors employ for cat, monkey and human:

For the experimental animals a No. 22 needle is used in conjunction with a 0.010″-diameter nichrome or stainless-steel electrode (insulated with Formvar or Teflon)

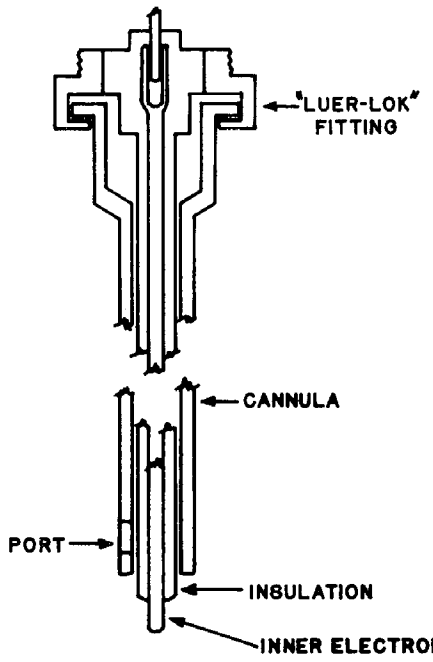

FIG. 1. Cannula and concentric electrode assembly including quick-disconnect fitting for removing stylet-inner electrode and connecting concentric cable. Threads on the fitting are provided for the cable connection and a side port provides a second orifice in addition to the end of the cannula if such is desired. The assemblies currently employed by the authors both for experimental animal and for human work do not include a side port.

which projects approximately 1.25 mm. beyond the end of the needle (the insulation on the electrode projects 0.5 mm. beyond the end of the needle, leaving exposed part of the electrode 0.75 mm. in length). A similar reduction is observed in the human when a No. 14 needle and 0.038″-diameter (0.050″ with insulating Teflon sleeve) stainless-steel electrode projecting 2.5 mm. beyond the end of the needle (1 mm. of projecting insulation) is employed. The observed differences in impedance are reduced considerably (No. 22 needle assembly) when the exposed length of uninsulated electrode is, for example, 0.33 mm. and interpretation of results is not always obvious as it is when longer unnsulated projecting electrodes are employed. The use of assemblies with the dimensions indicated makes possible the identification of ventricular penetration every time.

The electrical part of the system is designed in compact fashion so that the entire instrument can be readily supported in one's hand (weight 3 lb.) and it is operated by battery. A small-diameter, flexible, Teflon-insulated concentric cable connects the cannula assembly to the electrical circuitry. This cable may be sterilized by autoclave and is fastened readily to the instrument case at one end and the center electrode of the cannula assembly at the other. A standard "Luer-Lok" connection to the cannula provides for rapid extraction of the inner electrode as it remains attached to the connecting cable thus permitting it to serve as an ordinary stylet. The coaxial-electrode arrangement provides the necessary electrical shielding so that the deflections on the meter are entirely independent of the presence and configuration of electrical conductors and operators in the immediate neighborhood and in contact with the patient. That is, once the tip of the assembly is inserted into the tissue the deflection is independent of events and configurations of media not in the immediate neighborhood of the tip of the electrode.

The preparation for ventriculography is carried out in the usual manner: either a burr hole or single drill hole is made in the skull, the cannula assembly with flexible cable attached then is inserted partially, and penetration to a depth immediately below the cortex is accomplished before observing the instrument. Then the indicating needle on the meter is brought to a convenient location on the scale by adjusting the single control knob on the instrument. This procedure results in an electrical "balancing" and is not done previous to this stage since large variations in impedance occur as one passes the cannula through the incision in the scalp, bone opening, subarachnoid space, and cortex. After the tip of the electrode is within the dense subcortical white matter, the impedance does not change to any marked extent until the tip either penetrates the ventricular wall or passes into a mass of deep gray matter. In passing the cannula through the tissue a continuous slow steady movement is employed and the indicating pointer is observed simultaneously for deflection. If a stepwise procedure is used, that is, the cannula moved a fixed amount, stopped, the position of the pointer noted and this process repeated, one observes, when the assembly of the small-diameter needle is employed, a sequence of alternating variations in impedance. These apparently are the result of changes in the configuration of the contact between the electrode and the tissue, that is, in the thickness, and consequently the conductivity of the interposed liquid layer. When the indicating meter shows that the tip of the cannula has penetrated the ventricular wall the center electrode, which also serves as the stylet, is removed and air or radio-opaque medium can be introduced as desired.

It has proved advantageous in ventriculographic work on the human, when stereotactic procedures are the objective, to provide some support for the cannula so that the angular orientation of the assembly can be preset and maintained. For experimental work on animals such a supporting assembly is essential, since it is not feasible to maintain the tip of the electrode of the cannula system in the ventricle with the cannula unsupported. Of course, both in the experimental animal and in stereotactic work on the human a support is provided readily from the stereotactic apparatus. In nonstereotactic work on the human if support is indicated or desired, a simple headband arrangement supporting a guide provides one method of accomplishing this.

Using the deflection of the meter as the indicator the accuracy in setting the position of the assembly along the line of the axis of the cannula is ± 0.1 to 0.2 mm. in the experimental work on animals so that, for example, the lateral ventricle can be pierced from above without touching or penetrating the opposite or ventral wall. Since the passage of the tip of the electrode pair through border zones of adjacent white and gray masses results in variations in deflection of the pointer of the meter, it is desirable either that the path of the cannula be chosen to pass only through white matter after penetrating the cortex (which can be accomplished readily in many cases by appropriate choice of the port of entry) or, as is done currently in the stereotactic experimental work on animals, the approximate position of the ventricular wall to be entered is estimated before penetrating with the cannula.

Electrically, the impedance of the medium, which provides the conducting path between the exposed tip of the center electrode and the surrounding sleeve, is determined by measuring the voltage across the terminals of the electrodes when a constant current AC signal is applied (Fig. 2). The change in impedance is detected as a deflection of the pointer of the meter from a value preset by adjusting the balance control on the instrument panel after the cannula has been inserted into the tissue. The presetting feature is desirable since the particular value of impedance presented to the assembly is determined both by the type of tissue in which its end is imbedded and by the diameter and configuration of the electrode assembly at the tip. By including such an adjustment, a single instrument can be provided with a range of sizes of probe assemblies

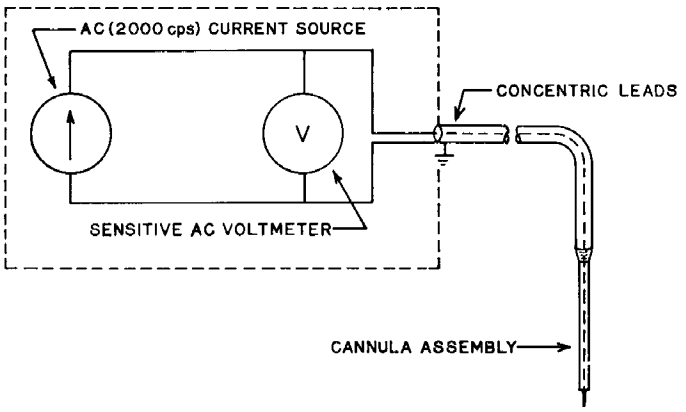

FIG. 2. Block diagram illustrating method of measuring electrical impedance. A Teflon-insulated flexible cable which may be autoclaved connects the cannula assembly to the electronic instrumentation package.

for work on widely different-sized brains and on different types of tissue.* Full-scale reading on the meter corresponds to a maximum of 250 mV. across the terminals which is small enough to avoid stimulating structures with the sizes of electrodes employed. The transient states produced at the terminals on switching on and switching off the instrument have a 2 msec. time constant and a maximum amplitude no more than twice the steady-state value. The type of electrical design employed has advantages over ordinary bridge methods of measuring impedance for the specific applications reported here. First, the change in impedance is indicated directly by deflection of the pointer of a meter without the necessity of accomplishing bridge balancing. Second, the electrical signal applied to the tissue is small and limited to a reasonable value at full-scale deflection. Most bridge arrangements do not so control the magnitude of the signal applied to the unknown impedance and many employ excessively high values. Since a null indication is used in the usual bridge arrangement, the observed reading of the meter yields no information regarding the actual signal being applied.

One additional convenient characteristic of the design of the present instrument is the provision of a dummy plug or plugs which can replace the probe to verify proper operation of the device before its actual use. The dummy plug can contain a resistor that yields approximately the same deflection of meter as the style of probe to be used (the exact value is immaterial). Of course, this simple test also verifies that the batteries are in proper operating condition.

* The specific range of values of impedance that the instrument in current use by the authors provides is from 500 ohms to 10,000 ohms. A 3-to-1 adjustment is available with the external balancing control and the additional adjustment of range is provided internally.

RESULTS OBTAINED AND FUTURE POSSIBILITIES

The authors have employed the instrument described in ventriculographic procedures on experimental animals and humans. Essentially all the work on placement of deep lesions of the brain in cats and monkeys currently in progress in the Biophysical Research Laboratory is now accomplished using landmarks on the ventricular system as coordinate references. The instrument and associated procedure described in this paper have made ventriculography on these animals practical and routine. Even routine ventriculography on rats is entirely feasible and the roentgenograms obtained permit identification of desired landmarks with no difficulty. Positioning of the tip of the cannula within the ventricular system is achieved in essentially all cases with a single passage of the needle through the intervening tissue.

The average quality of the lateral and vertical roentgenograms obtained on cats using Pantopaque as a contrast medium is illustrated in Fig. 3. The radio-opaque material, which is injected with the animal oriented on one side, fills a major fraction of the volume of one lateral ventricle, the 3rd ventricle, the aqueduct of Sylvius, and the 4th ventricle. The imprecision in measurement of anteroposterior and vertical coordinates of identifiable landmarks such as specific sites on the ventricular boundaries of the anterior and posterior commissures, the aqueduct of Sylvius and the 4th ventricle is no more than 0.1 mm. Measurements on the vertical roentgenogram (Fig. 3c) yield lateral coordinate values with respect to the anteroposterior axes of the 3rd ventricle, aqueduct of Sylvius, and 4th ventricle serving as mid-line coordinate references again with an accuracy of 0.1 mm. It should be noted here that for the purpose of placing electrodes for making electrical observations or production of

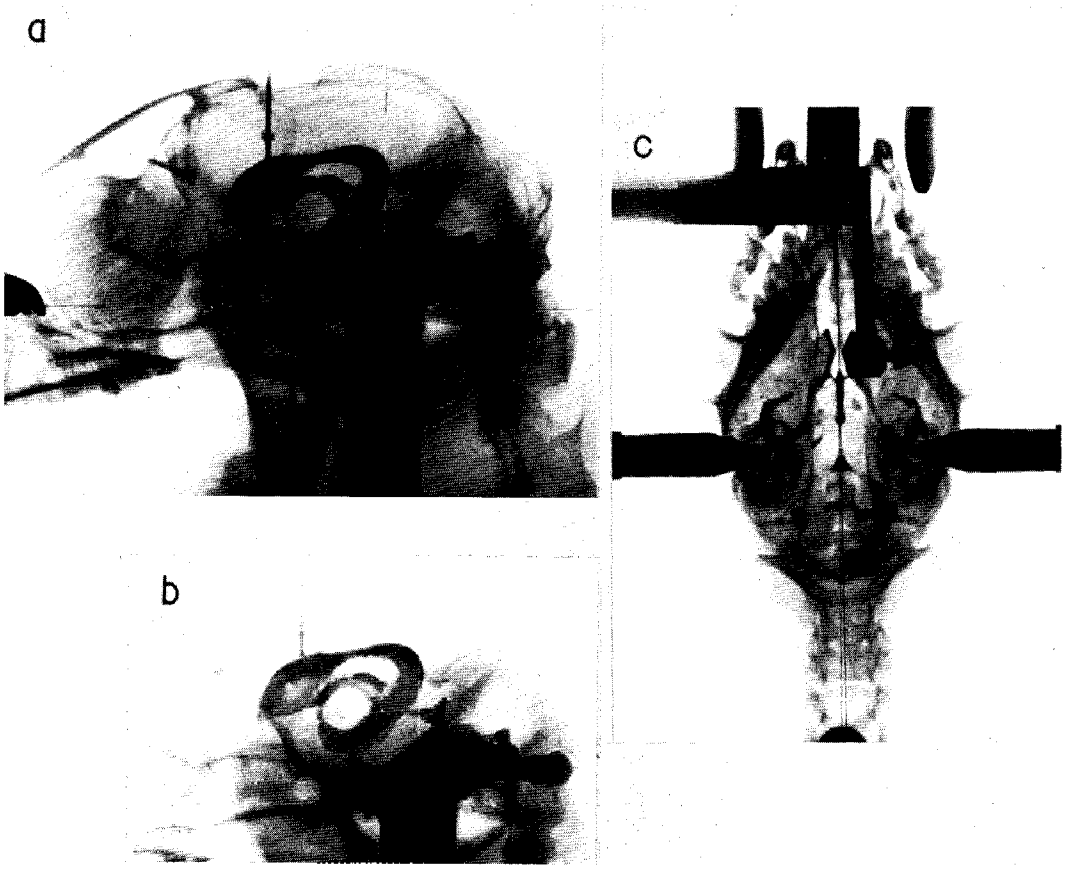

FIG. 3. Roentgenograms showing ventricular system of cat outlined with Pantopaque. (a, b) Lateral view at different roentgen-ray contrasts. (c) Vertical view. (These pictures illustrate the average quality of the ventriculographic results obtained routinely at the Biophysical Research Laboratory using Pantopaque as contrast agent.)

lesions it is of course not necessary to have the ventricular system free of Pantopaque and therefore this material can be employed for such work since the animals generally experience no neurological or physiological difficulties during or following ventriculography. However, when changes are to be induced by focused ultrasound it is not possible to have residual globules of Pantopaque remaining in the path of the beam since its acoustic properties (density and velocity of sound) do not match closely those of brain tissue. Therefore, in such work, it is necessary to use a medium that is miscible in cerebrospinal fluid. Accordingly, the authors presently use Conray* when ultrasound is to be employed. In fact this latter material is now the medium of choice of the authors for all stereotactic work on both animals and humans. Its use provides a very desirable combination of features: (1) excellent roentgenographic contrast—only slightly inferior to Pantopaque when appropriately employed, (2) rapid absorption and elimination, and (3) slight transient inconvenience to the patient.

An example of the quality of the roentgenograms obtained when Pantopaque is used to outline the ventricular system in the human is

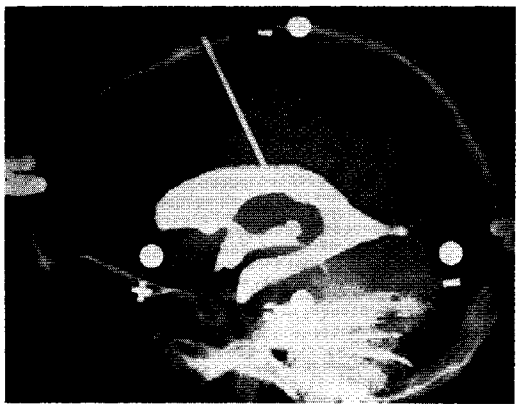

FIG. 4. Lateral roentgenogram of human ventricular system partially filled with Pantopaque.

* "Conray" is the Mallinckrodt Chemical Works' brand of methylglucamine methalamate.

illustrated in Fig. 4. Lateral, anteroposterior and a third "off-axis" roentgenograms are taken with the patient's head supported in a rigid holder[1] and with his body in a semireclining position. The Pantopaque is introduced into the "lower" lateral ventricle and after the major fraction of its volume has been filled it flows into the 3rd ventricle and down the aqueduct of Sylvius. The ventricular cannula is supported and guided for penetration by a carrier mounted on the head holder.

In addition to the use of the instrument to determine when a cannula assembly has penetrated the ventricular wall, other applications suggest themselves. For example, a slightly different configuration of the tip of the cannula, which the authors plan, is expected to provide a useful method for placement of the tips of needles in the subarachnoid space of the spinal canal. The method is of course not restricted in its applicability to procedures on the central nervous system but can be useful in determining for any region of the body when a probe or tip of a cannula passes from one type of tissue or inclusion to another characterized by a sufficiently different characteristic impedance.

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Reprinted from *Journal of Neurosurgery*
1962, Vol. XIX, No. 9
pages 793 -798