HIGH LIGHT

CSF pressure assessed by lumbar puncture agrees with intracranial pressure

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Abstract—The accuracy of estimating intracranial pressure in brain tissue (ICP_{BT}) via lumbar space was investigated using preset pressure levels in the interval 0 to 600 mm H_2O in patients with communicating hydrocephalus. Lumbar space ICP correlated excellently to ICP_{BT}, demonstrated by a measured mean difference of 10 mm H_2O (0.75 mm Hg) and a regression coefficient of 0.98. The concurrence supports the lumbar puncture as an accurate technique to determine ICP in patients with communicating CSF systems.

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There are several neurologic conditions where assessment of intracranial pressure (ICP) is clinically important. In contrast to intensive care, where ICP is measured directly inside the cranium, ICP is under these circumstances often estimated indirectly via lumbar space, a procedure starting with a lumbar puncture.

The lumbar puncture technique was introduced in 1891[1] and resulted in new options to investigate the intrathecal environment. Although not explicitly proven, the technique is believed to accurately estimate ICP when CSF circulates freely,[2] a supposition that laid the foundation of the development of lumbar infusion tests to assess, it is assumed, intracranial hydrodynamics and pressure.[3]

Unfortunately, the definition of ICP is ambiguous, regarding both where and how it is measured. Hitherto, ventricular CSF pressure has been considered the gold standard.[4] However, in state-of-the art neurosurgery and intensive care, brain tissue microprobes are used when determining ICP, redefining the ICP standard to brain tissue pressure.

This challenges the lumbar puncture technique: Is it applicable when measuring brain tissue pressure as well? We present a study comparing the two over a pressure range of 0 to 600 mm H_2O using our unique computerized lumbar infusion apparatus, aiming to establish their absolute and relative relationship.

Methods. *Clinical material.* The study was based on 10 patients with idiopathic normal pressure hydrocephalus (INPH). Their mean age was 72.4 years, and they had symptoms of gait disturbance, memory deficiency, and urinary incontinence. MRI showed communicating hydrocephalus without stenosis and no significant ischemic or white matter lesions. All patients later received a CSF shunt, and at a follow-up all patients but one had improved. Informed consent was obtained from each patient, and the local ethics committee approved the study.

ICP measurement and data sampling. The set-up and execution of the parallel ICP measurement are shown in figure 1. An intraparenchymal catheter tip sensor (Codman MicroSensor™ Johnson & Johnson Professional, Raynham, MA) inserted into the roof of the right ventricle measured the direct ICP (ICP_{BT}). The patients were then subjected to overnight ICP registrations.

The indirect ICP (ICP_{LS}) measurement and infusion test via lumbar space have previously been described.[5] In short, with the brain tissue sensor still present, two 1.2-mm needles were inserted into the lumbar subarachnoid space, and the patient was placed in supine position. One needle was used for CSF pressure measurement by a transducer (Becton Dickinson, Franklin Lakes, NJ) and the other for pressure control by CSF volume alteration.

The vertical separation distance (D_{Sep}) between the sampling positions was measured on CT scans and translated to its corresponding pressure difference (P_{Sep}) according to the formula $P_{Sep} = p*g*D_{Sep}$, where p = water density and g = gravitational constant (table).

Pressure data were sampled at 100 Hz using an acquisition card (MIO16X50; National Instrument, Austin, TX) and recorded on a computer. The pressure investigation was divided into three stages depending on the pump direction, and each stage was sliced into 1-minute intervals, of which the average pressures were calculated. Together, 1,273 1-minute intervals were included in the analysis.

Statistics. The difference of each 1-minute sample pair was calculated, and the patients' individual and total mean differences and SDs were estimated. Additionally, the differences were correlated to pressure.

The regression coefficient k (slope) between ICP_{LS} and ICP_{BT} was determined by applying the following general linear model (GLM) to the data: $ICP_{LS} - P_{Sep} = k*ICP_{BT} + m_{Pump} + m_{Patient}$.

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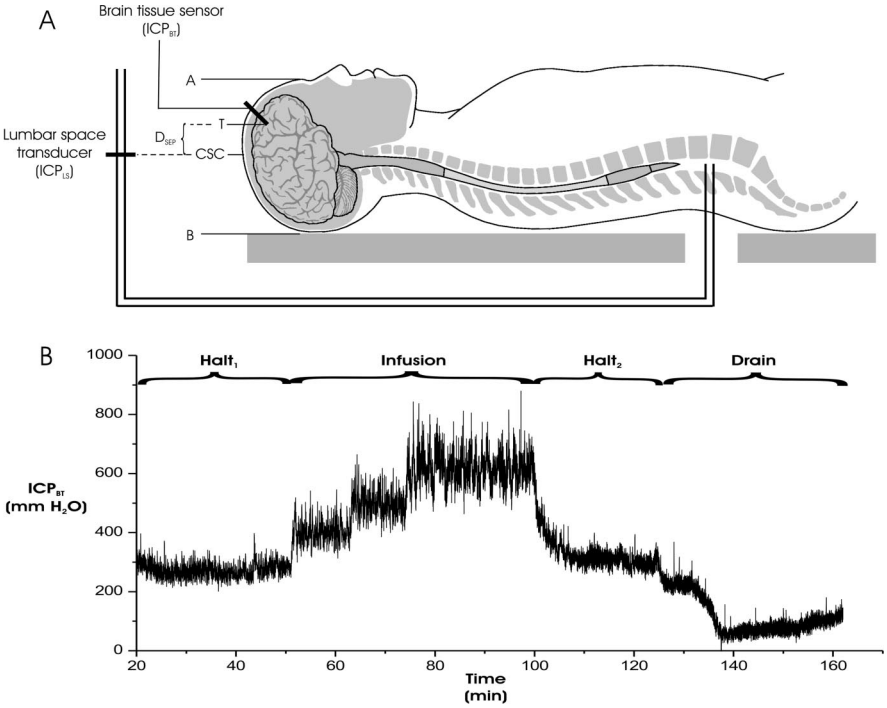

Figure 1. (A) The set-up of the intracranial pressure (ICP) measurement and the internal relationship between the measurement positions. ICP in brain tissue (ICP_{BT}) was measured by a brain tissue sensor having its tip (T) located in the anterior roof of the right ventricle. ICP via lumbar space (ICP_{LS}) was measured by a lumbar space transducer zeroed at the level of the cranial sagittal center (CSC), defined as the midpoint between the highest (A) and lowest (B) points of the head in the supine position. The vertical separation distance (D_{Sep}) between the measurement positions was defined as the vertical distance between point T and CSC. (B) The execution of the ICP measurement in a patient. Note the several preset pressure levels that were maintained by the computerized lumbar infusion apparatus. The sampling started after a 20-minute preparation period. On the y-axis, ICP is represented by ICP_{BT}. The curve was divided into three stages: Halt, Infusion, and Drain. During Halt, the pump was at rest, and it included two parts: $Halt_1$ corresponding to the measurement of resting pressure and $Halt_2$ to the pressure relaxation from the top level. The Infusion stage was characterized by net CSF inflow and the Drain stage by net outflow. Patient 7 had no Drain stage registered owing to problems with the needle.

By subtracting P_{Sep} from ICP_{LS}, the pressures were compared at a horizontal level, and the model also included a pump factor (m_{Pump}) and a patient-dependent factor ($m_{Patient}$). With use of analysis of variance, three values for m_{Pump} was determined: m_{Halt} preset to zero as a reference, $m_{Infusion}$ corresponding to net CSF inflow, and m_{Drain} to outflow. Similarly, 10 individual values, m_1 to m_{10}, were determined for $m_{Patient}$.

The pressure data carried a first-order autoregressive covariance structure that was accounted for in the correlation analysis and GLM. The significance level was set at 5%.

Results. The total mean and SD of the measured differences between ICP_{LS} and ICP_{BT} are -10 ± 29 mm H_2O (-0.75 ± 2.10 mm Hg). The corresponding individual means are similar (table), except for two cases falling below -40 mm H_2O, but the SDs are smaller.

The measured differences are homogeneously distributed (figure 2A), and the correlation to increasing pressure is minute ($r = 0.16$, slope $= -0.02$, $p < 0.001$). The extremes are -90 and $+84$ mm H_2O, and 95% of the observations fall in the interval -69 to $+35$ mm H_2O (-5.1 to $+2.6$ mm Hg).

The GLM determination coefficient is 0.996, and all parameters contribute to determine ICP_{LS} ($p < 0.001$ for ICP_{BT} and $m_{Patient}$, $p < 0.01$ for m_{Pump}). The slope is 0.98 (CI: 0.97 to 0.99), and the pump factors are $m_{Infusion} = 3$ mm H_2O and $m_{Drain} = -6$ mm H_2O, the latter significant in relation to $m_{Halt} = 0$. The patient-dependent factors (table) are significant, except in two cases.

Discussion. This is the first systematic and simultaneous comparison of ICP measured via lumbar space (ICP_{LS}) to ICP in brain tissue (ICP_{BT}), and the results demonstrate the accuracy of the lumbar puncture technique to determine ICP in both absolute and relative terms (figure 2). Instead of analyzing trauma patients with spontaneous ICP variation, we have analyzed patients with communicating CSF systems over a vast pressure interval utilizing our unique pressure control technique. The rising of ICP above physiologic range is standard procedure when diagnosing INPH patients[6] and was well tolerated by the patients.

The total mean of the measured differences, -10 mm H_2O, is clinically irrelevant, and their unbiased distribution (figure 2A), diminutive correlation to pressure, and 95% observation interval of (-69, $+35$) mm H_2O further support the measurability of ICP via lumbar space. The individual SDs (table) were smaller than the total, indicating that the main contributor to the magnitude of the 95% observation interval was the varying individual means, not a common large variation.

The GLM-analysis showed that ICP_{BT}, pump factors, and patient-dependent factors all significantly contributed to explain the variation in ICP_{LS}, although the pump effect was marginal. Importantly, CSF infusion did not cause misreading of ICP_{LS}, a prerequisite when determining CSF outflow resistance via lumbar space in the course of diagnosing INPH[6] and evaluating shunts.[7] The determination coefficient of 0.996 and slope of 0.98 suggest that changes in brain tissue pressure are equally well recognized via lumbar space, an obligation for viable ICP detection by lumbar puncture.

Table *Vertical separation pressures and individual pressure data*

Pat. no.	P_{Sep}	Individual measured differences, mean ± SD	Patient-dependent factors	
1	27	−11 ± 10	m_1	−29*
2	NA	−10 ± 9	m_2	NA
3	36	−1 ± 5	m_3	−30*
4	40	−26 ± 8	m_4	−57*
5	17	−44 ± 16	m_5	−52*
6	25	8 ± 13	m_6	−11*
7	24	−9 ± 12	m_7	−25*
8	23	−60 ± 12	m_8	−75*
9	35	26 ± 12	m_9	−2
10	27	23 ± 10	m_{10}	2

The P_{Sep} column holds the pressure differences corresponding to the vertical separation distances (D_{Sep}). The scans of Patient 2 could not be recovered, and therefore P_{Sep} was not assessed in that patient. P_{Sep} is always positive, representing that the brain tissue sensor was located above the lumbar space transducer in all patients. The next column contains the individual means of the measured differences between ICP_{LS} and ICP_{BT} , i.e., the differences when no adjustments of measurement position or pump action have been made to the data. The right column holds the patient-dependent factors derived from the general linear model. In contrast to the former column, they approximately represent the individual mean differences between the lumbar space and brain tissue ICP, had the sampling positions been horizontal, the pump off, and pressure in the lower range. Negative values imply lumbar space intracranial pressure being lower than in brain tissue. All numbers are given in mm H_2O.

* Significant factors on a 5% level.

NA = not assessed.

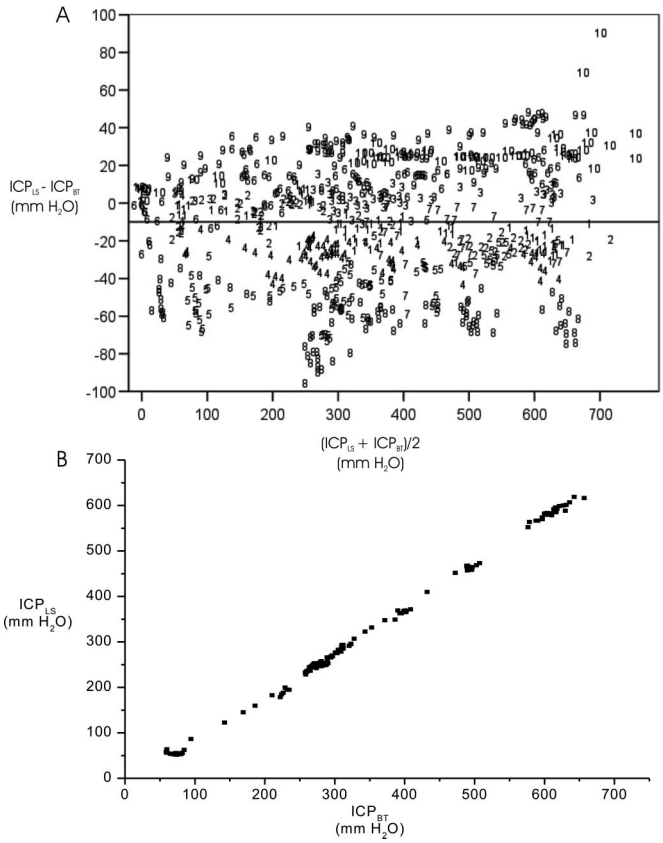

Figure 2. (A) Plot showing the distribution of the measured differences in the entire pressure range. The digits represent samples from the corresponding patient (1 to 10), and the horizontal line indicates the total mean of the measured differences. ICP_{LS} = intracranial pressure (ICP) measured via lumbar space and ICP_{BT} = ICP measured in brain tissue. (B) Plot demonstrating that ICP measured indirectly via lumbar space (ICP_{LS}) intimately follows ICP measured directly in brain tissue (ICP_{BT}) in the entire pressure range. The data presented were sampled from Patient 4.

In the INPH-associated pressure range,[6] the patient-dependent factors (table) can be interpreted as the horizontal individual mean differences between ICP_{LS} and ICP_{BT}. Notably, these were more negative than the original, and for measurement position unadjusted, ICP readings. Apparently, additional factors must affect the ICP readings. One such factor fitting the pattern is the predominantly positive drift of this brain tissue sensor.[8] However, the drift magnitudes required to completely make ends meet are unusual. Furthermore, drift in the air-referenced lumbar space transducer is unlikely. A small gradient between brain tissue and CSF would close the circle; however, such claims are controversial and must be elucidated in future research.

The validated clinical applicability of the lumbar infusion test in INPH[9] is confirmed by the demonstrated accuracy of the lumbar puncture technique to determine ICP over large pressure ranges, a necessity when assessing baseline ICP, CSF outflow resistance,[6] and compliance[10] in hydrocephalus patients. However, the application does not stop there, but pertains to any neurologic condition where ICP measurement is considered, for instance, chronic headache, meningitis, and intracranial pediatric disorders, provided they have communicating CSF systems.

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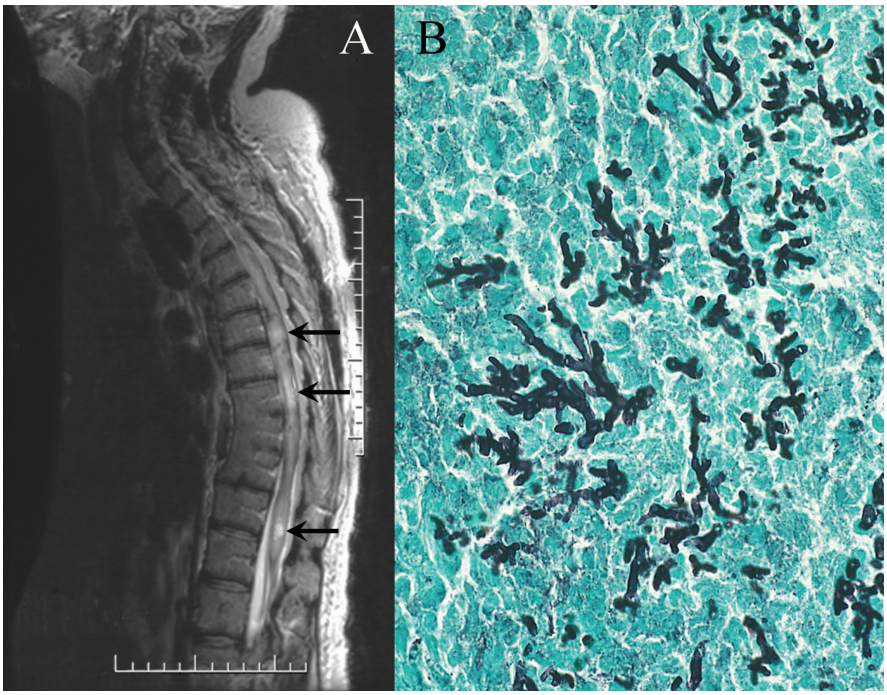

Figure. (A) MRI of the spine 8 months after the onset of paraparesis, indicating multiple enhancing intradural, extramedullary masses (arrows). (B) High-power view of spinal cord biopsy, demonstrating fungal hyphae consistent with Aspergillus species. Gomori methenamine silver stain.

Paraplegia caused by invasive spinal aspergillosis

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A 40-year-old woman with a history of multiple sclerosis (MS), asthma, and Crohn disease suddenly developed paraparesis, which was attributed to MS. She had received infliximab for Crohn disease 14 days prior to the onset of paraparesis, as well as methotrexate and corticosteroids in the more distant past for asthma. Eight months later, she developed progressive upper extremity weakness and sensory changes. Physical examination revealed flaccid paralysis in both lower extremities, and sensation was absent below T3. MRI revealed an edematous spinal cord from C5 through the conus and multiple enhancing extramedullary masses (figure, A). Spinal cord biopsy revealed a caseating granuloma with fungal hyphae morphologically consistent with *Aspergillus* species (figure, B), although cultures were negative. Chest and abdomen CT performed within 3 days of hospital admission revealed no source of aspergillosis. Despite 7 months of therapy with voriconazole and caspofungin for presumed spinal cord aspergillosis, gradual progression of the spinal cord lesions was noted on MRI. Nine months after switching to posaconazole, she remains clinically stable with no further radiographic deterioration by serial MRI scans. There is a risk of granulomatous infections following tumor necrosis factor antagonist therapy,[1] which may be caused by invasive fungi[2] and may present with severe neurologic manifestations (figure).

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