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Intracranial compartment volumes in patients with enlarged ventricles assessed by magnetic resonance–based image processing

MITSUNORI MATSUMAE, M.D., PH.D., RON KIKINIS, M.D., ISTVÁN MÓROCZ, M.D., ANTONIO V. LORENZO, PH.D., MARILYN S. ALBERT, PH.D., PETER MCL. BLACK, M.D., PH.D., AND FERENC A. JOLESZ, M.D.

Departments of Neurosurgery and Radiology, Brigham and Women's Hospital, and Department of Neurosurgery, Children's Hospital, and Harvard Medical School, Boston, Massachusetts; Department of Neurosurgery, Tokai University School of Medicine, Kanagawa, Japan; and Department of Psychiatry, Massachusetts General Hospital, Boston, Massachusetts

Magnetic resonance image–based computerized segmentation was used to measure the volumes of the brain, gray and white matter components, and to identify regions with prolonged enhancement on T_2-weighted imaging, such as periventricular or deep white matter hyperintensities. The authors also determined the volumes of the ventricles and subarachnoid space in control subjects and in patients with: 1) aqueductal stenosis (AS); 2) other causes of obstructive hydrocephalus (OH); 3) Alzheimer's disease (AD); and 4) normal-pressure hydrocephalus (NPH). In AS the volume of the brain was smaller, whereas that of ventricles and subarachnoid cerebrospinal fluid space was larger than that of controls. The decrease in brain volume was due primarily to white matter loss. Although in OH the ventricles were larger, the subarachnoid space was smaller than in controls, presumably due to encroachment by the brain, in which the volume remained unchanged. In AD, loss of both gray and white matter resulted in a smaller brain volume, whereas that of ventricles and subarachnoid space was larger than in controls. In NPH patients, only ventricular volume was greater, whereas all other compartments were similar to controls. The brain normally occupies 87% to 92% of the intracranial volume and consequently, as observed in our patients, relatively small decrements in brain size lead to large increments in ventricular and/or extraventricular volumes. The magnitude of such changes differed markedly among our patient groups, and whether such changes prove useful in clinical assessment and differentiation needs to be determined.

KEY WORDS • hydrocephalus • magnetic resonance imaging • computerized image processing • brain • gray and white matter volume • cerebrospinal fluid volume

MAGNETIC resonance (MR) image–based computerized image processing segmentation[38] provides the first noninvasive, *in vivo* approach for measuring accurately the volumes of the various intracranial components, including that of the cortical gray and white matter and the cranial subarachnoid space.[12,27] Using MR image–based segmentation to measure these volumes in healthy volunteers (controls), the authors[41] recently reported that the cranial subarachnoid space volume was not only considerably larger than volumes determined by traditional methods[9,16,37] but also that it was approximately five times greater than that reported for the extraventricular cerebrospinal fluid (CSF). Moreover, in agreement with others using conventional[59] or more recent MR imaging methods[25,35] we were able to document that the brain volume of both males and females declines with age. In view of the ability of this technique to define the volume of the various intracranial compartments, we attempted to determine whether parallel measurements in patients with enlarged ventricles might reveal important differences between the various types of hydrocephalus and possibly provide a better insight into the pathophysiology of these abnormalities.

The CSF compartments may enlarge because of blockage of the fluid pathways or fill in for lost cerebral substance. It may be difficult, especially in the elderly, to distinguish dilation of the fluid spaces due to impaired absorption of the fluid from that due to loss of cerebral substance, hydrocephalus *ex vacuo*. It is now possible to measure the ventricles, subarachnoid fluid volumes, and the brain volume, as well as the constituent proportions of gray and white matter using noninvasive MR image–based computerized segmentation.

Periventricular and deep white matter hyperintensities were also identified in T_2-weighted images of patients with hydrocephalus or with Alzheimer's disease (AD). The hyperintensity is probably the result of a pathological increase in tissue water and subsequent prolongation of T_2 relaxation time.[8,70] In hydrocephalic patients periventricular hyperintensities are due to transependymal migration

TABLE 1

Characteristics of age- and sex-matched controls and patients with enlarged ventricles due to aqueductal stenosis, other causes of hydrocephalus, normal-pressure hydrocephalus, or Alzheimer's disease

Group	Sex	No. of Cases	Age Range (yrs)	Average Age (yrs)*
age-matched control	M	4	27–56†	38 ± 8
	F	9		
aqueductal stenosis	M	2	33–47	40 ± 6
	F	4		
other causes of hydrocephalus	M	2	28–53	41 ± 10
	F	5		
age-matched control	M	7	56–80†	41 ± 10
	F	9		
normal-pressure hydrocephalus	M	8	60–80	71 ± 7
	F	6		
Alzheimer's disease	M	5	57–80	72 ± 7
	F	9		

* Values are given as means ± standard deviation.

† Both 56-year-old control subjects were men and each was assigned to a different age group on the basis of establishing an adequate age and sex distribution for the respective patient groups.

of CSF from the enlarged ventricles. This phenomenon was described in experimental models of hydrocephalic animals[55,56] and demonstrated by computerized tomography (CT) as periventricular lucency.[29,32,46] Transependymal CSF migration was also demonstrated by MR imaging. Both patients with AD and age-matched controls present with hyperintensities in the deep white matter seen on T_2-weighted images.[42,58] Histopathologically, the denudation of the ventricular ependyma and the gliosis are more severe in AD than in controls, and there is a trend toward more loss of myelinated axons in the deep white matter of the brains of patients with AD.[58] In healthy elderly subjects, the incidence of white matter lesions tends to increase with age.[5,48,52,61,66]

Clinical Material and Methods

Patient Characteristics

This study was reviewed and approved before its inception by the institutional human research committee. Twenty-eight men and 42 women ranging in age from 27 to 80 years were studied. The patients included six with clinical and radiographic diagnoses of aqueductal stenosis (AS), seven with other causes of obstructive hydrocephalus (OH), 14 with a clinical diagnosis of idiopathic normal-pressure hydrocephalus (NPH), and 14 with a clinical diagnosis of probable AD. All patients underwent MR studies between June 1988 and November 1991 at the Brigham and Women's Hospital in Boston. They were compared with normal volunteers who were studied during the same time period. These normal controls, who were selected to provide the best match for the sex and age distribution of the respective patient groups, are volunteers in the large database of the Normative Aging Study at the Boston Veterans Administration Out Patient Clinic.[1] The initial entry criteria for the group of volunteers were that at the time of the study volunteers had to be free of any severe neurological and psychiatric disorders including drug abuse or alcoholism.

Ventricular enlargement due to AS was distinguished on MR images by the usual criteria: normal fourth ventricle and enlarged third and lateral ventricles, associated with absence of CSF flow void in the sylvian aqueduct. Cases of OH included two germ-cell tumors in the pineal region, two pineoblastomas, one cerebellar astrocytoma, one cerebellar meningioma, and one pontine glioma. They had a clinical syndrome of increased intracranial pressure (ICP) with serious hydrocephalus. The patients with a clinical diagnosis of probable AD met the National Institutes of Neurological Disorders and Stroke/Alzheimer's Disease Research Association criteria[43] and that used by the Alzheimer study group at the Brigham and Women's Hospital. All NPH cases exhibited recent memory disturbances, 11 had gait disturbances, and four had incontinence. Of the 10 who had received ventriculoperitoneal shunts at our institution, five patients improved dramatically and five showed partial improvement. The characteristics of the control subjects and the various patient groups are shown in Table 1.

Magnetic Resonance Imaging Procedures

Axial MR images of the brains were obtained on a 1.5-tesla Signa Imaging System (General Electric Medical Systems, Milwaukee, WI) using double-echo (echo times 30 and 80 msec), long-repetition time ((TR) 2000–4000 msec), multislice (interleaved 3- or 5-mm thick slices), spin-echo data and 192 phase encoding, and a half Fourier technique. The images covered the entire brain from the vertex to the foramen magnum, and after transfer via a network the data were processed on an MR console (Sun Microsystems, Mountain View, CA) with programs developed by General Electric Medical Systems and the Surgical Planning Laboratory of the Brigham and Women's Hospital. Details of the segmentation procedure, accuracy, and reliability are cited in previous reports.[10,11] Figure 1A and B shows paired proton density and T_2-weighted images obtained in a normal subject. A scatterplot (Fig. 1C) is derived by plotting the pixel signal intensities from the proton and T_2-weighted images. Proton density images were used to identify air and bone (for background), gray and white matter, and extracranial tissue. The T_2-weighted images were used to identify brain and CSF. The selected loci for gray matter were the frontal cortex, cerebellar cortex, dentate nucleus, and head of the caudate nucleus. Loci for white matter were the internal capsule, cerebral peduncle, splenium, and genu of the corpus callosum, whereas those for CSF were the cerebellopontine and prepontine cisterns, both of the anterior horns, and the trigone of the lateral ventricles. Each selected locus appears on the scatterplot, and computer interpolation is used to calculate the nearest neighbor and to create a feature map (Fig. 1D). The latter is then used to derive the segmented images (Fig. 1E) from which the computer automatically extracts the signal for extracranial tissues. Correction for ventricular CSF is made semiautomatically with a connectivity program[10] that generates the final segmented image (Fig. 1F). The areas in centimeters squared are then calculated from the final segmented image by counting pixels. The volumes in centimeters cubed are generated by

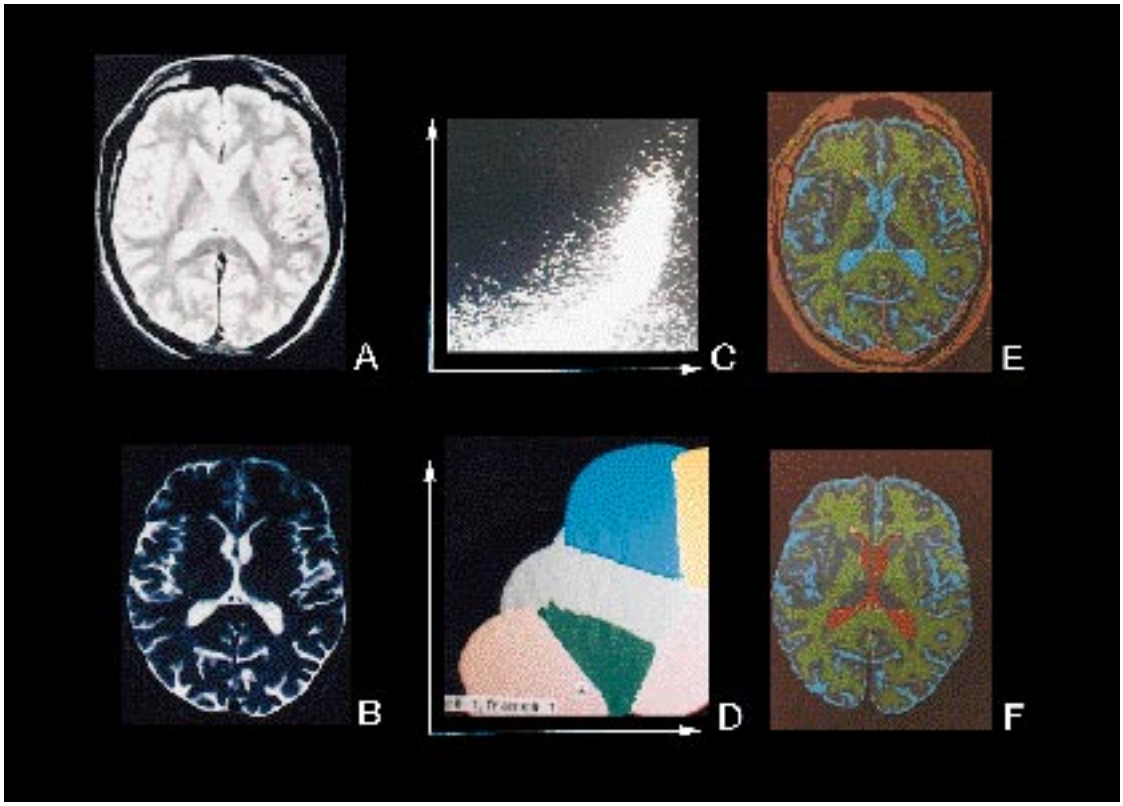

FIG. 1. A and B: Proton density and T_2-weighted magnetic resonance images showing the brain in a 67-year-old normal individual. C: Scatterplot derived from the proton density (y-axis) and the T_2-weighted (x-axis) images. D: Calculated feature map derived from the scatterplot depicting background as black, extracranial tissue as orange, gray matter as gray, white matter as green, lesions as yellow, and cerebrospinal fluid (CSF) as blue. E: Segmented image derived from the calculated feature map. F: Final segmented image depicting background in black, gray matter in gray, white matter in green, lesion in yellow, ventricular CSF in red, and extraventricular CSF in blue.

multiplying the segmented image by the slice thickness. Unfortunately, values of gray and white matter could not be accrued from patients in the OH group because the variance in tumor volume and type precluded meaningful segmentation. Thus, in these patients segmentation has been selected for brain tissue only. Gray and white matter, ventricular and extraventricular CSF, and brain lesion volumes were determined separately and their sum yielded the intracranial volume. Brain volume was the sum of gray and white matter. All values are reported as means ± standard deviation (SD) of the means.

Finally, the authors developed three-dimensional reconstructed images of ventricles and lesions from the segmented images using the MR console program in each group to determine the relationship between the lesions and the ventricles.

Two different values were used for the TR and for the slice thickness. No significant difference was observed in the absolute and relative values for brain volume, extraventricular CSF, and ventricle volume when these two parameters were interchanged in control subjects.

Assessment of Error

To assess the error (SD/mean) of these measurements, segmentation and volumetric determinations were repeated three times in two controls, two NPH cases, one AD case, and one AS case randomly selected from our groups. To reduce bias repeat, measurements in each of these individuals were separated by intervals of more than 3 weeks. Repeat segmentation and volumetric determination of the six selected cases indicated a measurement error of 3.2%, 3.5%, 5.5%, and 7.9% for the gray and white matter, ventricle and extraventricular CSF volumes, respectively.

Statistical Methods

The nonparametric Mann–Whitney U-test was used to determine significance between the control and patient group values because the distribution of each patient group was observed to be skewed and not normal. A commercially available software package (Statview; Abacus Concepts, Inc., Berkeley, CA) was used to make the analysis.

Results

Table 1 shows that the average age and sex distributions of the younger and older patient groups were comparable to those of the respective control groups. The average volumes for the intracranial compartments in the respective control and patient groups are shown in Table 2.

TABLE 2

Average intracranial volumes in age- and sex-matched controls and patients with aqueductal stenosis, other causes of hydrocephalus, normal-pressure hydrocephalus, or Alzheimer's disease

Group	Volume (cm^3)				
	Intracranial	Brain	Gray Matter	White Matter	Lesions
age-matched control	1401 ± 217	1296 ± 211	652 ± 107	644 ± 128	>1
aqueductal stenosis	1532 ± 94	1124 ± 29*	653 ± 25	471 ± 40*	>1
other causes of hydrocephalus	1472 ± 158	1274 ± 69			6 ± 4*
age-matched control	1359 ± 119	1188 ± 104	626 ± 40	558 ± 83	3 ± 2
normal-pressure hydrocephalus	1423 ± 141	1163 ± 129	620 ± 81	531 ± 96	12 ± 11*
Alzheimer's disease	1326 ± 162	1056 ± 153*	569 ± 87†	468 ± 101†	19 ± 13*

* $p < 0.01$.
† $p < 0.05$.

It is apparent that the mean intracranial volumes of the younger and older control groups are comparable and that there is no significant difference between the intracranial volumes of the various patient groups and their respective controls. There is no difference in the brain volume of the two control groups, OH and NPH patients. However, brain volumes of AS and AD patients are significantly smaller than those of their respective controls ($p = 0.0005$; $p = 0.01$) and although in AS patients the decrement is attributable primarily to white matter loss ($p = 0.0029$), in AD it is due to loss of both gray ($p = 0.0417$) and white matter ($p = 0.015$). The volume of brain lesions increases with age in controls ($p = 0.0001$). In the patient groups the volume of these lesions, which most often have a paraventricular distribution, is markedly increased in OH ($p = 0.001$), NPH ($p = 0.001$), and AD ($p = 0.0001$) but not in AS.

Table 3 shows the total (cranial), ventricular, and subarachnoid space CSF volumes of the control and various patient groups. Marked and highly significant increases in the cranial CSF volumes are noted for AS, OH, AD, and NPH when compared to their respective controls ($p = 0.0006$, $p = 0.039$, $p = 0.0003$, $p = 0.001$). As anticipated, these differences were due primarily to the marked volume expansion of the extraventricular CSF volume, although in patients with AS and AD ($p = 0.0012$ and $p = 0.0001$, respectively), but not NPH ($p = 0.2985$), moderate expansion of the subarachnoid space was also a contributory factor. Paradoxically, in patients with OH the subarachnoid space was significantly smaller than that of the age- and sex-matched controls ($p = 0.0043$). Also, it is of interest to note that the cranial CSF volume is significantly greater ($p = 0.0004$) in the older (56–80 years) than in the younger (27–56 years) control group.

Table 4 expresses the size of the ventricles and the subarachnoid space compartments as percentages of the total cranial CSF volume. It becomes apparent from this transformation that the proportion of CSF volume in each of the two cranial compartments changes dramatically in hydrocephalus. Whereas in patients with AS, OH, and NPH the ratio of ventricular to cranial CSF volume increases dramatically over that of the respective controls ($p = 0.0021$, $p = 0.0003$, $p = 0.0001$), the subarachnoid space to cranial CSF volume ratio in these patients becomes significantly smaller ($p = 0.0021$, $p = 0.0003$, $p = 0.0001$).

In contrast, in AD cases both ventricular and extraventricular ratios are similar to the ratios derived for the respective control groups. A further transformation and

TABLE 3

Average cerebrospinal fluid (CSF) volume in age- and sex-matched controls and patients with aqueductal stenosis, other causes of hydrocephalus, normal-pressure hydrocephalus, or Alzheimer's disease

Group	CSF Volume (cm^3)*		
	Cranial	Ventricular	Extra-ventricular
age-matched control	105 ± 30	17 ± 9	89 ± 27
aqueductal stenosis	407 ± 86†	253 ± 96†	172 ± 63†
other causes of hydrocephalus	191 ± 111‡	142 ± 112†	50 ± 19†
age-matched control	169 ± 49	27 ± 10	142 ± 43
normal-pressure hydrocephalus	248 ± 58†	116 ± 42†	133 ± 42
Alzheimer's disease	252 ± 49†	55 ± 20†	196 ± 48†

* Values are means ± standard deviation.
† $p < 0.01$.
‡ $p < 0.05$.

TABLE 4

Cerebrospinal fluid (CSF) values as percentages of the total cranial CSF volume in age- and sex-matched controls and patients with aqueductal stenosis, other causes of hydrocephalus, normal-pressure hydrocephalus, or Alzheimer's disease

Group	CSF Value (%)*		
	Cranial	Ventricular	Extra-ventricular
age-matched control	100	15.7 ± 7	84.3 ± 7
aqueductal stenosis	100	41.1 ± 19.5	58.9 ± 19.5
other causes of hydrocephalus	100	67.0 ± 17.8	33.1 ± 17.8
age-matched control	100	16.1 ± 4.6	83.9 ± 4.6
normal-pressure hydrocephalus	100	46.2 ± 11.2	53.8 ± 11.2
Alzheimer's disease	100	22.3 ± 8.6	77.7 ± 8.6

* Values are means ± standard deviation.

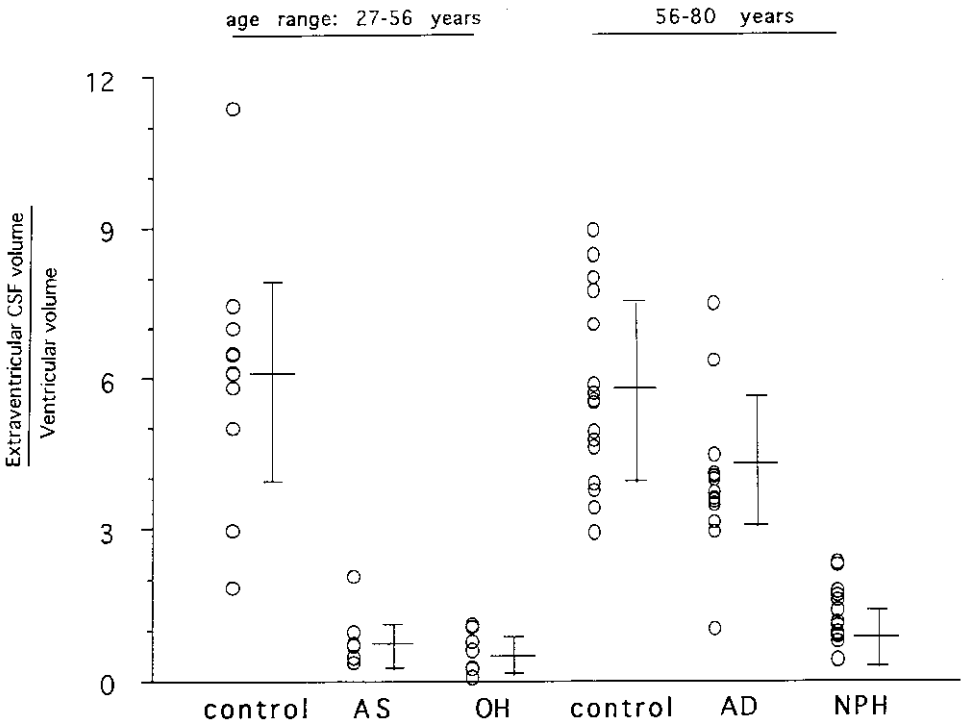

FIG. 2. Graph depicting the ratio of the extraventricular-to-ventricular cerebrospinal fluid (CSF) volumes in patients and their respective age- and sex-matched controls. *Open circles* designate individual values for each group. *Horizontal* and *vertical bars* represent the mean and standard deviation of the mean. Significance for control versus AS: $p = 0.0021$; control versus OH: $p = 0.0003$; control versus NPH: $p = 0.0001$; control versus AD: $p = 0.0112$. AD = clinical diagnosis of probable Alzheimer's disease; AS = aqueductal stenosis; NPH = normal-pressure hydrocephalus; OH = other causes of hydrocephalus.

comparison is provided in Fig. 2, in which the respective CSF volumes for controls and patients are expressed as extraventricular (subarachnoid space) to ventricular ratios. It is apparent that with the exception of values for AD patients (3.94 ± 1.51 cm^3), individual and average ratios for each patient group generally are lower than the respective values for controls (5.68 ± 1.87 cm^3; $p = 0.0112$). Also, the average ratios for patients with AS (0.88 ± 0.61 cm^3) and OH (0.59 ± 0.41 cm^3) are lower ($p = 0.0009$, $p = 0.0003$) than the respective values for age-matched controls (6.2 ± 2.26 cm^3). Moreover, in contrast to the younger group of patients, in which no significant difference is noted between the ratios for AS and OH patients ($p = 0.4751$), the ratio for the NPH group (1.29 ± 0.59 cm^3) was significantly smaller ($p = 0.0001$) than the ratio for patients with the clinical diagnosis of probable AD (3.94 ± 1.51 cm^3).

The three-dimensional reconstructions of the ventricle and brain lesions in OH, AS, and AD patients show that the thick, irregular bands of lesions were distributed around the ventricles, whereas in the NPH cases the lesions were smooth and limited to ventricular areas extending from the anterior horn to the body of the lateral ventricles. Interestingly, lesions in AS were not detected but were seen in the age-matched control group. In contrast to NPH patients, the lesions in AD cases extended into the subcortical region predominantly around the trigone and temporal horn of the lateral ventricles (Fig. 3).

Discussion

The observation that brain volume or weight decreases with advancing age in individuals deemed to be neurologically intact, or showing little or no obvious morphological abnormality at autopsy, has been made by various investigators.[15,21,30,59] It has also been noted that during the last century the stature and thus the brain weight of humans has increased significantly.[21,45] This long-term increase in brain weight acts to confound the results of cross-sectional studies because it is not clear to what extent age-related decreases in brain volume or weight are attributable to this phenomenon or to the aging process. However, the fact that in many such studies the age-related decrease in brain volume or weight is accompanied by a marked increase in the volume of the cranial CSF[25,35] strongly suggests that long-term changes may play a less significant role than age-related biological processes that contribute to the normal shrinkage of the adult brain. We recently addressed these issues in a cross-sectional aging study of normal volunteers of both sexes in which MR image–based processing was used to measure brain and cranial CSF volumes.[41] The results of the study showed that the average brain volume was considerably larger in males than in females but that cranial CSF volumes were not significantly different. In addition, both the volume of the brain and of the cranial CSF compartments changed with age.

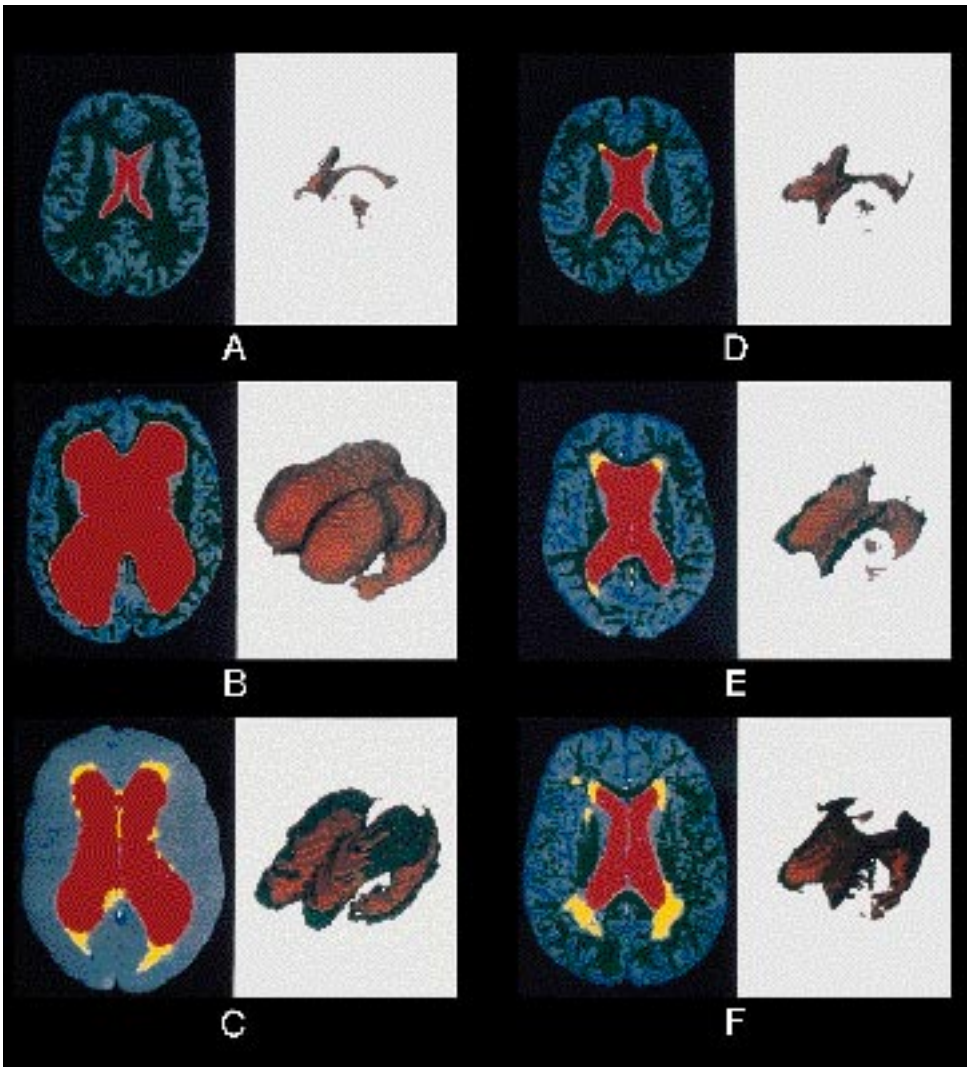

FIG. 3. Images showing a representative axial segmented image *(left)* and the respective three-dimensional reconstruction image of the ventricle and lesions *(right)* for each category. In the three-dimensional reconstruction the ventricular system is depicted in red and the lesions in green. A: Twenty-four-year-old normal woman. B: Forty-nine-year-old woman with primary aqueductal stenosis. C: Twenty-nine-year-old man with obstructive hydrocephalus secondary to a germ-cell tumor in the pineal region. D: Sixty-seven-year-old normal man. E: Eighty-year-old man with Alzheimer's disease. F: Eighty-year-old man with normal-pressure hydrocephalus.

In the present study, no significant decrease in brain volume is observed when the values for the younger and older group of controls are compared ($p = 0.1001$). However, when such volumes are normalized to the intracranial volume, the difference between the younger ($92.4\% \pm 2.1\%$) and older ($87.4\% \pm 3.3\%$) group mean values becomes significant ($p = 0.0001$). Such changes in brain and CSF volume with age are important when evaluating the significance of cranial CSF compartment alterations that typically occur in patients with enlarged ventricles.

The results of this study indicate that significant differences exist among AS, OH, NPH, and AD patients with respect to cranial, brain, and CSF extraventricular and ventricular volumes. It is generally accepted that when a CSF pathway becomes obstructed, expansion of the CSF compartments theoretically occurs above the point of obstruction. However, it is also recognized that this dictum may not hold in all situations. Teasdale, *et al.*,[63] reported that brain atrophy with ventricular enlargement in AS patients is often accompanied by a significant expansion of the cranial extraventricular CSF volume. Moreover, it is also well established that enlargement of the ventricles is not a uniform process, being dependent on the site of the CSF circulation blockage as well as on the duration of the hydrocephalus.

Generally, patients with AS have a long clinical history,[2,39,47] often covering many years, and show evidence of chronic increase in ICP as demonstrated on plain skull x-ray films.[28] Such cases of hydrocephalus are characterized by a decrease in brain volume, marked ventricular dilation, and a slight or moderate enlargement of cortical sulci

as revealed by CT studies.[68] The decrease in brain volume is attributed by most to the marked thinning of the white matter, because the cortical gray matter and basal ganglia are often observed to be spared under these conditions.[50,54,67] Our results (Table 2) are consistent with these observations. The sparing of gray matter in the presence of white matter atrophy has been attributed to the relatively low blood supply to the white matter, which presumably becomes compromised as a result of the increased intraventricular pressure.[17,50] Another interesting result seen in this study is that no lesions were detected in AS. It is widely accepted that the increase of water content in the periventricular region in patients with ventricular enlargement is related to transventricular CSF absorption.[6,8,29,32,55,56,71] The subependymal glia usually undergoes a variable degree of gliosis associated with AS.[54] Presumably, the absence of lesions around the ventricles may be due to increased ependymal thickness or subependymal gliosis due to long-standing hydrocephalus. Subsequently diminished transependymal absorption can be presumed in AS cases.

Vanneste and Hyman[68] reported on nine cases of long-standing adult AS. Enlarged cortical sulci were noted in eight of nine cases, seven of eight cases were slightly enlarged, and one case had moderate enlargement of cortical sulci. Expansion of the extraventricular volume in AS patients was demonstrated by MR imaging.[63] From these studies it is not clear why the extraventricular CSF volume increases. One possibility is that in long-standing ventricular enlargement the brain atrophies and as a consequence the cranial subarachnoid space expands. The other possibility is that absorption of extraventricular CSF is compromised, leading to an increase in the volume of the subarachnoid space. Radioisotope cisternography studies, however, show the passage of the isotope from the basal cisterns to the convexities to be unimpeded and isotope clearance to be within normal limits.[68] Thus, it would appear that expansion of the extraventricular space in AS patients is not due to an absorption deficiency but most likely to brain atrophy. This does not imply that shunt placement is not indicated in such patients, because many present with symptomatic hydrocephalus.

Unlike AS patients, those with OH have smaller subarachnoid space volumes on average than their respective controls, even though the magnitude of the ventricular dilation in both AS and OH is similar. These patients present with relatively acute symptoms of increased ICP that may be due not only to ventricular blockage of CSF flow but also to a diminished subarachnoid space or the existence of a "double block."[14,44,57] Such phenomena, however, have also been reported in patients with AS,[65] and it is not clear why in our study a diminished subarachnoid space is most often limited to OH patients. Possibly, in such patients the increasing tumor mass and associated edema leads to encroachment of the brain on the subarachnoid space.

Most of the volumetric studies of AD patients have emphasized the moderate-to-severe brain atrophy that is accompanied by the expansion of both the ventricles and subarachnoid space.[13,19,20,50,53,64] Although our results are consistent with these observations, unlike those that indicate that brain shrinkage is due primarily to loss of white matter, they show that loss of both gray and white matter contributes to this shrinkage (Table 2). The controversy surrounding this issue is illustrated by recent studies. Decreases in gray matter ranging from 10.2% to 31.6% have been reported by Høedt-Rasmussen and Skinhøj[31] and Rusinek, *et al.*[53] Creasey, *et al.*,[13] suggested that gray matter loss was mainly cortical because no changes occurred in subcortical nuclei or white matter volumes. In contrast, de la Monte[18] reported a 10% to 29% reduction of the total cortical volume with a 3% to 19% decrease in white matter but no change in nuclear structures in patients with histopathological evidence of AD. However, the volumes of white and gray matter in preclinical AD cases are controversial. De la Monte[18] reported that in preclinical AD cases only white matter loss with preservation of cortical areas was observed, indicating that atrophy of white matter preceded that of cortical gray matter. On the contrary, Prohovnik and coworkers[51] reported a loss of relative cortical gray matter volume in the early stages of presenile AD but not in AD of senile onset.

Consistent with earlier pneumoencephalography and CT studies[26,60,62] as well as subsequent MR imaging reports,[63] patients with NPH in our study exhibited a greater dilation of the ventricles than those with AD. However, unlike the latter group of patients ventricular expansion was not associated with brain shrinkage or expansion of the subarachnoid space. The fact that there is little or no change in the subarachnoid space is curious because cisternography studies often show failure of radioisotope movement over the cerebral convexity, accompanied by ventricular filling and retention.[34,49] This has led to the suggestion that CSF flow and absorption within the subarachnoid space is hindered in the patient with NPH.[60] The obstruction, however, may represent a dynamic relative block that allows filling of the subarachnoid space in the presence of greater resistance. There is no question that obstruction of CSF flow and absorption due to subarachnoid hemorrhage, meningitis, or trauma is the most likely etiological factor in NPH of known cause.[3] Indeed, in such cases Vessal, *et al.*,[69] were able to document a generalized thickening of the leptomeninges with moderate-to-marked obliteration of the subarachnoid space. Curiously, in our patients with idiopathic NPH the volume of the subarachnoid space is similar to that of control subjects, even though as in cases of known cause, it is well established that the rate of CSF absorption is reduced.[4,7,33,40,60] Even

TABLE 5

*Summary of changes of brain, ventricular, and extraventricular cerebrospinal fluid volumes in conditions leading to ventricular enlargement**

	Volume (cm^3)				
Group	Brain	Gray Matter	White Matter	Ventricular	Extra-ventricular
controls	normal	normal	normal	normal	normal
AS	decreased	unchanged	decreased	increased	increased
OH	unchanged	—	—	increased	decreased
NPH	unchanged	unchanged	unchanged	increased	unchanged
AD	decreased	decreased	decreased	increased	increased

* Abbreviations: AD = Alzheimer's disease; AS = aqueductal stenosis; NPH = normal-pressure hydrocephalus; OH = other causes of hydrocephalus; — = not assessable.

though DeLand, *et al.*,[22] have reported a case of idiopathic NPH in which diffuse fibrosis ". . . completely obliterated the subarachnoid space," fibrosis of the leptomeninges is not a general feature in idiopathic NPH.[23,36]

The results of this study, as summarized in Table 5, show that the corresponding volumes occupied by the brain and the cranial CSF, which in normal subjects measure 89% and 11% of the intracranial volume, respectively,[41] are markedly altered in patients with hydrocephalus. Moreover, the proportional distribution of the cranial CSF between the ventricles and the cranial subarachnoid space, which in control subjects is approximately 16% and 84%, respectively,[41] also undergoes marked and dramatic changes in these patients. These alterations in patients with AS and AD are attributable primarily to shrinkage of brain volume, which accounts for most or all of the cranial CSF volume expansion in both groups. In contrast, in patients with OH and NPH in whom there is little or no change in brain volume, expansion of the cranial CSF volume must be related to expansion of the ventricular volume. In patients with AS and AD, who typically experience significant decreases in gray and/or white matter volumes, the expansion of cranial CSF volume must be related to expansion of both ventricular and extraventricular CSF volumes.

We may now ask whether these changes detected by MR image–based computerized segmentation can prove to be useful adjuncts in discriminating between the various types of hydrocephalus. Clearly, one of the central questions concerning this issue is whether the process underlying ventricular and/or subarachnoid CSF volume expansion is due primarily to atrophy of the brain, as in AD or to an increase in ventricular pressure with secondary atrophy of adjacent brain areas, as in AS. Teasdale, *et al.*,[63] used a ventricular-to-cortical sulcal CSF ratio as an index to discriminate between patients presenting with dementia attributable to communicating hydrocephalus (NPH) from those with dementia due to brain atrophy (AD). They found that such measures may be of prognostic value in determining which patients will respond to treatment. In our study (Fig. 2) the extraventricular (subarachnoid space)/ventricular volume ratio for AD cases (3.94 ± 1.51 cm^3) is three times greater than that for NPH cases (1.29 ± 0.57 cm^3), and there was a tendency for this ratio to be lower in patients responding dramatically to shunting (0.97 ± 0.15 cm^3) than in those showing only partial improvement (1.47 ± 0.4 cm^3, five patients). However, the difference was not significant ($p = 0.10$), possibly because of the small number of patients in each group or because the comparison should be to nonresponders. Fazekas, *et al.*,[24] suggested that the "halo" type of periventricular hyperintensity may be of diagnostic value for AD, although in an earlier publication by this group[71] it was stated that ". . . the pattern of periventricular hyperintensity has proven to be of limited value in clinical assessment of hydrocephalic patients." The results of our three-dimensional reconstruction of the white matter lesions and ventricles show that the shape and distribution of these periventricular lesions were different. For instance, in patients with NPH the band of lesions was smooth and limited in its distribution around the lateral ventricles, whereas in patients with AD the lesions were distributed as irregular bands around the lateral ventricles and extended into the deep white matter regions. Although such observations may prove of value, Davson, *et al.*,[16] have noted that the literature is replete with reports identifying particular tests or features of NPH auguring favorable response to shunting but subsequently proving to be less promising, particularly in cases of idiopathic NPH.[3,16] In view of this, the question of whether the measures alluded to above can be used as predictive indices of treatment outcome must be approached with caution because shunting is often associated with serious complications.

Magnetic resonance image–based computerized segmentation provides a noninvasive *in vivo* technique to measure the volumes of the brain, the gray and white matter components, and the various cranial CSF compartments. It is anticipated that this technique will provide information that will help our understanding of physiological and biochemical processes that affect these cranial compartments throughout life. In addition, the technique provides a powerful tool to better understand and manage clinical problems associated with the various causes of ventricular enlargement.

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Address reprint requests to: Ferenc A. Jolesz, M.D., Department of Radiology, Brigham and Women's Hospital, 75 Francis Street, Boston, Massachusetts 02115.