CSF Flow Study of Normal Cranio cervical Neuraxis
Using the Cine Phase Contrast MR Technique

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Introduction

Although some fundamental features of cerebrospinal fluid (CSF) flow physiology have been known for some time, a more detailed understanding of CSF motion has been gained with the use of magnetic resonance (MR) imaging. Evaluation of intracranial and intraspinal CSF flow was accomplished by the use of cardiac gated cine phase contrast magnetic resonance (PC-MR) technique. Normal patterns of pulsatile flow within the ventricles, cisterns, cervical subarachnoid
space, and lumbar cistern were established by this technique and these observations were compared to prior description of CSF flow.

With systole there is downward (caudal) flow of CSF in the aqueduct of Sylvius, the foramen of Magendie, the basal cisterns and the dorsal and ventral subarachnoid spaces while during diastole, upward (cranial) flow of CSF in these same structures is seen. The relationships between the cardiac cycle and the CSF pulsation are demonstrated on both magnitude reconstruction and phase reconstruction MR images. Calculations of actual fluid velocity within CSF containing spaces can be obtained from the phase reconstruction images and hold promise for a more accurate analysis of CSF flow.

This investigation was undertaken to characterize and quantitate normal CSF flow at key locations in the intracranial and spinal neuraxis by means of a phase-contrast cine pulse sequence, and further precision can be obtained by plotting the temporal velocity information from the images as a waveform (CSF flow waveform). This important basic information may be useful for understanding altered physiology in disease states such as syringomyelia and the various forms of hydrocephalus.

**Methods**

Ten healthy volunteers were selected free from neurologic disease, without cerebrovascular risk factors, using no medication, and performing well on a neuropsychologic test battery. The subjects were examined using a standard head coil: the head was not tilted in any specific way. Using a 1.5(Signa, General Electrics, USA) superconducting magnet, head and spine cine images were obtained in the mid-sagittal plane and axial plane. All the CSF flow studies were cardiac gated and use a reduced flip angle (15 degrees) gradient echo technique with a TR determined by the patient's R-to-R interval, a TE of 15ms, and a section thickness of 5mm. Multiple images ("cine frames") in the same plane were obtained during an R-to-R interval, starting immediately after the R-wave and acquiring successive images at 40 ms intervals to within about 200ms of the next R-wave. Clearly, with a slower heart rate, more frames would be obtainable. Images are acquired following 2 to 4 excitations, on a 192 x 256 matrix and displayed on a 512 x 512 matrix. The information was then displayed in a 'real time' closed loop cine format. Patients with cardiac arrhythmias are not ideal candidates for the gated studies because of the varying R-to-R interval.

The qualitative cine studies were examined for evidence of marked signal void within various CSF pathways indicative of pulsating and rapidly flowing CSF. Intracranially, we examined primarily the aqueduct of Sylvius, the third ventricle, fourth ventricle, dorsal and ventral subarachnoid spaces at the cervico-medullary junction, and intraspinally, the cervical and lumbar level. The CSF pathways were judged to be patent whenever a normal flow void was observed during a portion of the gated cycle. The following scans were performed on all 10 volunteers.

1. Sagittal TI-weighted locator(500/15/2 [repetition time/echo time/excitations], 5-mm scan thickness).

2. Sagittal midline CSF study to include aqueduct, third and fourth ventricle, and cervical subarachnoid spaces to the level of C-4.

3. Axial CSF study through third ventricle, the inferior collicular level of aqueduct, 4th ventricle, and dorsal and ventral subarachnoid spaces at the cervico-medullary junction.

The analysis of phase-contrast images alone was not sufficient to assess the subtle physiologic to assess the subtle physiologic details of the CSF flow. Further precision can be obtained by plotting the temporal velocity information from the images as a waveform (CSF flow waveform). The waveforms from all the CSF and blood flow studies were plotted with velocities in millimeters per second plotted on the y-axis and fractions of the cardiac cycle on the x-axis. Fractions of the cardiac cycle were chosen to normalize subjects with different heart rates. The following velocity and temporal parameters were also evaluated.
1. Amplitude parameters:
   Maximum craniocaudal velocity-maximum CSF systolic velocity (Vmax)
   Maximum caudocranial velocity-maximum CSF diastolic velocity (Vmin)
   Difference between Vmax and Vmin (Vdif)

2. Temporal parameters:

   1) Systolic
   R-wave to the onset of craniocaudal flow (R-onset of CSF systole: R-S)
   R-wave to maximum systolic velocity (R-MSV)

   2) Diastolic
   R-wave to the onset of caudocranial flow (R-onset of CSF diastole, R-D)
   R-wave to maximum diastolic velocity (R-MDV)

   The measurements R-S and R-D for the CSF flow waveforms were obtained at time points when zero velocity was noted (Fig. 1).

Results

1. Qualitative assessment

   1) Ventricles
   Velocity changes in the frontal horns were minimal and did not have a clear oscillatory pattern.

   In most patients no significant motion was detected. There were no flow channels except at the foramen of Monro. This observation is explained by the fact that CSF flowing through large areas within the lateral ventricular system does so with a lessened fluid velocity and negligible turbulence.

2) Aqueduct
   The velocity profile of CSF in the aqueduct was similar to that of CSF in the foramen of Monro although velocities were greater (Fig. 2). Peak systolic flow occurred at 25.2% through the cardiac cycle, whereas peak diastolic flow occurred at 74.4% through the cardiac cycle. Flow was reversed simultaneously in the foramen of Monro and aqueduct at 56% through the cycle. Mean peak signal changes were nearly equivalent during the systolic and diastolic phases: 204 (SD=±124) and -212 (SD=±131), respectively.

3) Fourth ventricle
   The fourth ventricle represented a mixing chamber for CSF exiting the ventricular system and CSF flowing in from the cisterna magna.

4) Cisterna magna
   The cisterna magna represented the other major site of mixing CSF of the ventricular system with that of the subarachnoid space. Systolic and diastolic phases could be identified but were less well defined than those of the other areas studied. Craniocaudal and caudocranial flow could often be detected simultaneously. Because of the anatomy and mixing characteristics, pulsation amplitude had little meaning in this location.

5) Cervical spine
   The CSF pulsation dynamics in cervical spine showed well-defined systolic and diastolic components. Peak velocity during CSF systole occurred at 3% (SD=±3.1%) through the cardiac cycle, and peak diastolic velocity occurred at 66.5% (SD=±5.2%) through the cardiac cycle. It is noteworthy that peak systolic velocity in the cervical spine subarachnoid space preceded peak systolic velocity in the foramen of Monro and aqueduct by 22.2% of the cardiac cycle. Mean
peak signal intensity in the anterolateral recess was 145.1 (SD = ± 53.3), while peak diastolic signal intensity was -187.7 (SD = ± 60.8). The velocities in the subarachnoid space were heterogeneous because of the various compartments formed by dorsal and ventral roots, the dentate ligament, and dorsal arachnoid se-

Fig. 2. Sagittal plain and velocity-encoded images of aqueductal level in normal person. A sagittal plain MR image showing the anatomical detail around the aqueduct in 2a. Systolic peak flow (white) is seen in 2b, and diastolic peak flow (black) is seen in 2d. Inversion of systolic to diastolic flow is seen in 2c (Note signal changes starts at the center of aqueduct).
6) Lumbar spine

No flow was identified in the distal lumbar sac with the velocity range used in these measurements (Fig. 4).

2. Quantitative assessment (CSF flow waveforms)

The results of the configuration, amplitude, and temporal analysis of the CSF flow waveforms will considered separately. The flow was bidirectional. All the extraventricular and aqueductal CSF flow waveforms showed distinct CSF systolic and diastolic components. The extraventricular CSF flow waveforms were characterized by relatively narrow systolic peaks and broad diastolic troughs. The aqueductal CSF flow waveforms differed from those of the extraventricular CSF compartments in that the systolic peaks were broader than the diastolic troughs. There was some visible CSF flow in lumbar cistern, but not specific or reproducible.

Considerable variation of the amplitude parameters (MSV and MDV) were seen with a wide range between maximal and minimal values. But the temporal parameters (R-MSV, R-D, R-MDV and R-S) were much more constant than amplitude parameters. The temporal parameters of the extraventricular spaces were more reliable than that of aqueduct. The onset of the cranio-caudal (R-S) or caudo-cranial flow (R-D) in the postcord space was either simultaneous with or earlier than in the precord CSF space (p < .05). The onset of cranio-caudal or caudocranial flow in the pericord spaces was always earlier than in the pre-pontine and the interpeduncular cisterns (p < .05)

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Fig. 3. Axial velocity-encoded images of upper cervical level in normal person. Systolic peak flow (white) is seen in 3a, and diastolic peak flow (black) is seen in 3c. Inversion of systolic to diastolic or diastolic to systolic flow is seen in 3b or 3d (Note signal changes starts at the periphery of cervical pericord spaces. Dentate ligaments is seen in lateral part of pericord spaces.).
Fig. 4. Sagittal plain and velocity-encoded images of lumbar level in normal person. A sagittal Plain MR image showing the anatomical detail around the cauda equina in 4a. Systolic peak flow (white) is seen in 4b, and diastolic peak flow (black) is seen in 4d. Inversion of systolic to diastolic flow is seen in 4c (Note relatively indefinite signal changes through the cul de sac).
Table 1. Summary of variable parameters and statistical significance

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<th>Amplitude parameters</th>
<th>Temporal parameters</th>
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<tr>
<td></td>
<td>Vmax</td>
<td>Vmin</td>
</tr>
<tr>
<td>Aqeduct</td>
<td>53.2</td>
<td>-70.7</td>
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<tr>
<td>Ant pericord</td>
<td>50.4</td>
<td>-46.6</td>
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<tr>
<td>Post pericord</td>
<td>47.7</td>
<td>-49.8</td>
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Ant. or post. pericord, anterior or posterior cervical pericord space; Vmax, maximal systolic signal intensity; Vmin, minimal diastolic signal intensity; Vdiff, difference of Vmax-Vmin; R-SMV, R-wave to maximum systolic velocity; R-D, R-wave to the onset of caudocranial flow; R-DMV, R-wave to maximum diastolic velocity.

Fig. 5. The mean cerebrospinal fluid flow waves show different phase shift at various levels in normal persons. The waves representing flow dynamics of pericord spaces precede that of aqueduct(Ant or post SAS, anterior or posterior subarachnoid space) in the aqueduct(p<.05)(Fig. 5)(Table 1).

Discussion

Over the years, the nature and significance of pulsatile intracranial and intraspinal CSF flow has been the object of a number of investigations and much conjecture. In an attempt to clarify many of these issues, Du Boulay in 1966 and in 1972 reported the use of radiological techniques to measure pulsations of CSF during pneumoencephalography, myelography and ventriculography. He was led to conclude that CSF pulsations at the aqueduct arise from a pumping mechanism of the thalamus, that flow in the basal cisterns is a consequence of the rhythmic expansion and contraction of the brain during systole and diastole, that previously held theories concerning the choroid plexus and the source of CSF pulsations were incorrect, and that causes of CSF movement are ultimately related to the pressure and elasticity provided by the arteries and veins. Lane and Kricheff in 1972 published their observations on normal and abnormal cervical CSF pulsations using a videodensititor display of pantopaque myelography. Their measurements were taken directly off a television monitor and showed a wide range of deflection(3-30mm) in the upper cervical spine. Importantly, they demonstrated, in normal patients, caudal pulsations in systole and cranial pulsations in diastole while in patients with obstruction of the spinal CSF pathways, they demonstrated a lower pulsation amplitude above and below the block. The unavoidable problem involved in these early studies was the fact that measurement and evaluation of CSF flow involved the injection of contrast material into the CSF spaces and/or the evaluation of the movements of "foreign" material(e.g. oil-based contrast material) in the CSF spaces. Although such methods provided some information concerning CSF dynamics they were, by their very nature, invasive and therefore disturbed the very system they were meant to investigate. Furthermore, these investigations could not provide simultaneous characterization of flow dynamics in multiple areas of the subarachnoid space, nor could they easily calculate CSF velocity. Because no invasive procedure in performed and no contrast material is introduced, MR imaging is a nearly ideal modality for the assessment of CSF flow.

The onset of CSF systole in the subarachnoid space was synchronous with the onset of systole in the carotid artery. The systolic and diastolic components were different in the subarachnoid space, where systole occupied approximately 40% and di-
astole 60% of the cardiac cycle, compared with the ventricular system, where they were nearly equal. This difference results in systole in the intracranial and spinal subarachnoid spaces preceding that in the ventricular system; the same is true for diastole. The fourth ventricle and cisterna magna serve as mixing chambers. The high-velocity flow in the cervical spine and essentially no flow in the distal lumbar sac indicate that a portion of the capacitance necessary in this essentially closed system resides in the distal spinal canal. The patterns of CSF oscillation through the foramen of Monro and aqueduct confirm that the lateral ventricles, rather than a third ventricular "CSF pump", play the major role in normal CSF flow within the ventricular system. CSF pulsations at the foramen of Monro and aqueduct are in synchrony. CSF systole and diastole within the ventricular system are slightly out of phase with CSF systole and diastole in the subarachnoid space, the ventricular flow being slightly delayed compared with that of the subarachnoid space. This difference in flow results in the fourth ventricle and cisterna magna acting as mixing chambers. In most CSF spaces, fluid motion is uniform in one direction, but in the fourth ventricle and in the cisterna magna, motion is more complex, showing craniocaudal and caudocranial flow simultaneously in the systolic and diastolic time segments in the cardiac cycle. This pattern of flow shows that subarachnoid CSF moves unidirectionally and in synchrony during systole. In the ventricular system the oscillatory flow is such that systole and diastole each occupy approximately a half of the cardiac cycle and, not surprising, the velocities are nearly the same in both directions. This is true for the foramen of Monro and aqueduct. Since the brain is incompressible, this nearly equivalent oscillatory flow in systole and diastole is to be expected in a closed system with a low CSF production rate. During a single cardiac cycle, no significant inflow or outflow of CSF occurs in this essentially closed system. To allow for CSF oscillation there needs to be capacitance in the system. A portion of this capacitance appears to be in the lumbar sac and is associated with the asymmetry in CSF systole and diastole in the spinal subarachnoid space. That some capacitance exists intracranially is known because veins were seen to be compressed in the quadrigeminal cistern during CSF systole. A major site of capacitance must also be the distal lumbar sac because high-flow CSF can be detected from the cervical spine to the level of the conus. Below this level, little if any flow is detected.

Variable degrees of CSF flow within the posterior third ventricle are observed and occasionally flow at the level of the foramen of Monro is seen. The reason for the sporadic visualization of the foramen of Monro is explained by the fact that the structure may be out of the plane or may be volume averaged with aqueduct material by our standard 5mm thick mid-sagittal sections. The velocities in the subarachnoid space were heterogeneous because of the various compartments formed by dorsal and ventral roots, the dentate ligament, and dorsal arachnoid septations. The velocities in the anterior subarachnoid space were not significantly different from those of the anterolateral recesses. Velocities dorsal to the cervical cord were lower and more variable in some patients no flow was detected dorsal to the cord except during peak systole and diastole. The timing of the velocity changes, however, was uniform in these flow compartments. In most patients, CSF motion in the subarachnoid space anterior and dorsal to the spinal cord was in synchrony. It is common to observe more prominent ventral CSF flow because the ventral subarachnoid space is wider. Close inspection of these images show a variation in intensity of the signal voids across a given plane. This reflects the fact that near the dura or cord there is a wider range of phase shifts (i.e. dephasing) than there is in the center of the subarachnoid space. Itabshi reported peak CSF velocities in the cervical spine of 50 – 100 mm/s which increased when the neck was flexed and the change in direction of CSF flow occurred earlier with neck flexion. Differential flow at various spinal levels exists as the flow propagates inferiorly through narrow and then wider spaces. At disc space levels and wherever pathological narrowing occurs, CSF
velocities would be expected to increase. Enzmann\textsuperscript{7} found that in his normal population the highest CSF velocity in the cervical spine was at the C6 level because the canal area was smallest there. Typically, caudal flow within the cervical subarachnoid space commences approximately 100–150ms following the R wave and maximum velocity is, on the average, reached 75–100ms later (i.e. 175–250ms after the R wave)\textsuperscript{12}. Thereafter, the flow decreases and then reverses so that cranial flow of CSF occurs later in the cardiac cycle (400–500ms after the R wave)\textsuperscript{9}. Blockage of the spinal CSF pathways similar to what is observed on myelography is possible with cine MR. This diagnosis would be more simple in the cervical spine, where a prominent subarachnoid space flow void is normally observed. We believe that the use of cine MR provides a more direct and conclusive evidence of a CSF block in the spine that does the use of routine non-motion compensated T2 weighted images\textsuperscript{18}.

Non-synchronous flow can be observed occurring in both directions, and can be noticed in many segments of the CSF pathway. As stated above, the probable reasons for these normal variations are multiple but relate most likely to the size of nearby vasculature, the compliance of surrounding brain/spinal cord tissue, the anatomy of the CSF containing spaces, the volume and vascularity of the choroid plexus, and the systemic hemodynamics\textsuperscript{8}. We observed wide variations in the maximum systolic and diastolic velocity values of the CSF flow. Similar observations have been previously documented\textsuperscript{8,14–16}. So assessment of CSF dynamics with flow maps is, in our opinion a more accurate and more easily interpreted representation of fluid flow than the qualitative cine MR. Use of sagittal rather than of axial images for measurements may add potential source of underestimation of velocity values\textsuperscript{18}. Sagittal images, nevertheless, were used for this initial experiment so that different areas of extraventricular CSF pathways could be examined simultaneously during one sequence. Using small regions of interest on the sagittal images reduced the degree of partial volume averaging in the large extraventricular CSF spaces. However evaluation of the aqueduct and cervical pericord spaces required axial images.

Our preliminary experience indicates however, that large variations in normal velocities should be expected in all CSF spaces as in previous studies\textsuperscript{8,14–16,17}. The reason for the wide range of these values relates primarily to the anatomical size of the structure through which the CSF must pass and this of course, varies from patient to patient. Velocity measurements in the basal cisterns and upper cervical subarachnoid space are felt to be more reliable than those velocity measurements obtained from smaller spaces such as the aqueduct of Sylvius. No apparent difference was found with respect of age or sex within the group of volunteers, as was also the case in a previous study using a similar phase method which did not reveal significant changes in aqueduct CSF flow with increasing age\textsuperscript{16}. It is important for studies of CSF production and flow to take into account the circadian variation in CSF production, which is minimal around noon and reaches a maximum just after midnight\textsuperscript{17}. The measurements in the present study were all performed during the afternoon and hence probably reflect an intermediate level of production.

The analysis of cine PC MR CSF flow study may give us valuable points for understanding the CSF dynamics, determining the obstructive level, and even explaining the changes of CSF dynamics in pathologic conditions in vivo through the image, curve configuration, and phase shift of velocity curve.

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