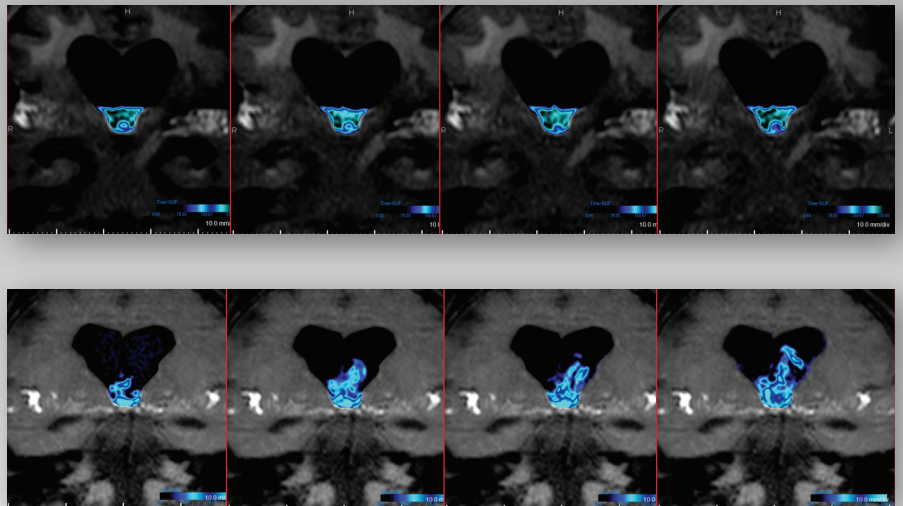


Time-Spatial Labeling Inversion

Cerebrospinal Fluid Flow Evaluation



INTRODUCTION

Impairment to the natural flow of cerebrospinal fluid (CSF), a clear, water-like fluid found within and surrounding the brain and spinal cord, can cause debilitating and catastrophic effects. Severe headaches, seizures, vomiting, increased head size, impaired vision, growth deficits and even death are some examples. While there is no cure, surgical treatment options are available for restoring CSF flow; however, they have a high failure rate and are not successful in all patients. Accurate and reliable non-invasive imaging techniques to evaluate CSF pathways are critical for proper patient management. For many years, Phase-Contrast Magnetic Resonance Imaging (PC-MRI) has been relied upon for such evaluation because it allows for visualization of the back and forth motion of CSF flow, as well as quantification of CSF flowing through a particular channel. Now, an alternate technique using Canon Medical Systems' 2D Time-Spatial Labeling Inversion Pulse (Time-SLIP) is emerging as a clinically useful tool for straightforward evaluation of CSF flow pathways. This technique has the ability to visualize CSF flow non-invasively in ways that have previously not been possible, and shows promise for improving patient care and management.

BACKGROUND

Hydrocephalus is a general term for an incurable but potentially treatable disorder characterized by an abnormal build-up of CSF typically associated with enlarged lateral ventricles. Hydrocephalus has historically been classified as either "communicating" (in which there is no distinct blockage to CSF movement) or "non-communicating"/"obstructive" (in which there is a distinct blockage of CSF movement). Normal Pressure Hydrocephalus (NPH) is a type of hydrocephalus that can occur later in life and is associated with dementia, gait disturbance and incontinence. CSF accumulation within pockets of tissue can form cysts or syrinxes in the brain or spinal cord. These cavities can be silent and cause no signs or symptoms. In other cases they can cause significant, even life threatening, problems. Pressure from impaired CSF flow in the brain and cord can also either cause, or complicate, a defect in the skull or spine, known as a Chiari malformation.

TYPES OF CSF FLOW

Pulsatile: a brisk cyclic back and forth motion driven by the cardiac cycle. With every heartbeat, blood is pumped into the brain during systole, forcing CSF to move caudally. During diastole, CSF moves cranially as the blood vessels relax. Average peak velocity: 5 cm/s.

Bulk: slow molecular motion driven by gravity and Brownian motions. Average velocity: 0.2 cm/s.

Reflux: turbulent backwards flow from the aqueduct into the third ventricle and/or from the third ventricle into the lateral ventricle.¹

ROLE OF IMAGING

Various attempts have been made over the past century, and continue to this day, to study CSF flow disorders in an effort to better characterize and predict which patients will respond well to treatments. Conventional tracer studies such as radioisotope cisternography and CT cisternography have been commonly used to observe CSF flow and/or leakage. However, these techniques are invasive, use ionizing radiation and require injection of a contrast agent. Perhaps the greatest caution for relying on these studies' accurate assessment of CSF flow comes from the mechanism of the technique itself. It is possible that the introduction of the contrast agent can introduce suspicion of whether the perceived CSF flow is actually CSF or simply diffusion of the contrast agent.

In the 1990s, PC-MRI emerged as a promising tool for providing quantitative measures of through-plane pulsatile CSF flow and qualitative evaluation of in-plane flow. PC-MRI was the first imaging technique which made it possible to study CSF flow patterns noninvasively by using ECG triggering and collecting a series of velocity images as a function of the cardiac cycle. Long-term studies have been conducted to evaluate treatment outcomes based on a collection of quantitative parameters, including stroke volume, flow rate and phase.

CSF flow studies using PC-MRI have demonstrated that the pulsatile component moves cranially and caudally in a cyclical fashion as a function of the cardiac cycle at a peak velocity between 3 and 7 cm/s² and the CSF stroke volume measured at the level of the aqueduct has been established to be between 30 and 50µl in healthy controls. PC-MRI studies of CSF flow in hydrocephalus patients have found up to a 10-fold increased pulsatile aqueductal flow. This finding has led to the establishment of "flow thresholds" to be used as predictions of shunt success; however, this has not proven to be clinically useful. Repeated studies failed to find any statistical significance between stroke volume and clinical improvement from shunting.

TIME-SPATIAL LABELING PULSE FOR IMAGING CSF FLOW

Time-SLIP has been used for vascular imaging for many years. A similar approach can be used to capture CSF flow, but in a unique way. Unlike PC-MRI, which collects images in multiple phases represented over a single cardiac cycle, 2D Time-SLIP acquisitions are incremental, allowing the bulk flow movement and turbulent components of CSF to be

seen for the first time non-invasively over several cardiac cycles. Using a 2D Fast Advanced Spin Echo (FASE) sequence as the fundamental acquisition scheme, a series of single-shot images with incremental inversion recovery delay times are acquired to visualize CSF bulk and turbulent flow without the administration of contrast material.

TECHNICAL ASPECTS

Time-SLIP is an Arterial Spin Labeling (ASL) variant that is typically used to depict blood vessels within a targeted region in any imaging orientation. For vascular imaging, Time-SLIP magnetically labels the blood with radiofrequency (RF) pulses and uses the labeled blood as a tracer to obtain vascular images in a relatively simple manner. The stationary tissue signal is suppressed by an inversion pulse and the final image contains only the contribution of the labeled flow, acquired after a delay time between the selective tag and the start of imaging known as the BBTI, or simply TI. Time-SLIP has been evaluated for use in the renal arteries, carotid arteries, pulmonary system and portalvenous system. It produces accurate angiograms using blood as an endogenous tracer, instead of a contrast agent.³⁻⁸ The application of Time-SLIP lends itself very well to imaging CSF flow.

CSF movement can be acquired with Time-SLIP in any sagittal, coronal, axial or oblique plane. Initially in the sequence, the entire signal within the field of view is inverted to $-Z$ magnetization by a non-selective inversion recovery

pulse. Immediately following the nonselective pulse, a user-prescribed slice-selective tag is applied so that only the magnetization within the tagged area is returned to $+Z$ magnetization. As the CSF signal within the entire field of view recovers, it passes through the null point, at which the CSF signal is zero, appearing dark on MR images. At the same time, the CSF within the tagged region is bright, producing excellent contrast between tagged CSF and untagged CSF as the tagged CSF flows out of the tagged region. CSF movement is captured by incrementally increasing the time delay between the second inversion pulse and the start of the acquisition, resulting in a series of single shot 2D images. The optimal acquisition period is between 1900 ms and 3500 ms, and increments can be set according to total scan timing constraints (typically 100 ms). After this period, the background signal recovery limits the contrast between tagged and untagged CSF. A resulting sagittal acquisition is shown in Figure 2, in which the targeted CSF flow is at the level of and perpendicular to the aqueduct.

The key to this imaging technique is that, by incrementing the delay time while ensuring that the acquisition remains within period near the null point, bright “tagged” CSF will be seen in contrast to dark “untagged” CSF and background. The bright CSF moving along the pathway could have only come from the original tagged region. Acquiring multiple images at incremental delay times enables the observation of slow CSF movement noninvasively. Using this technique, the tagged CSF can be traced from its origin to

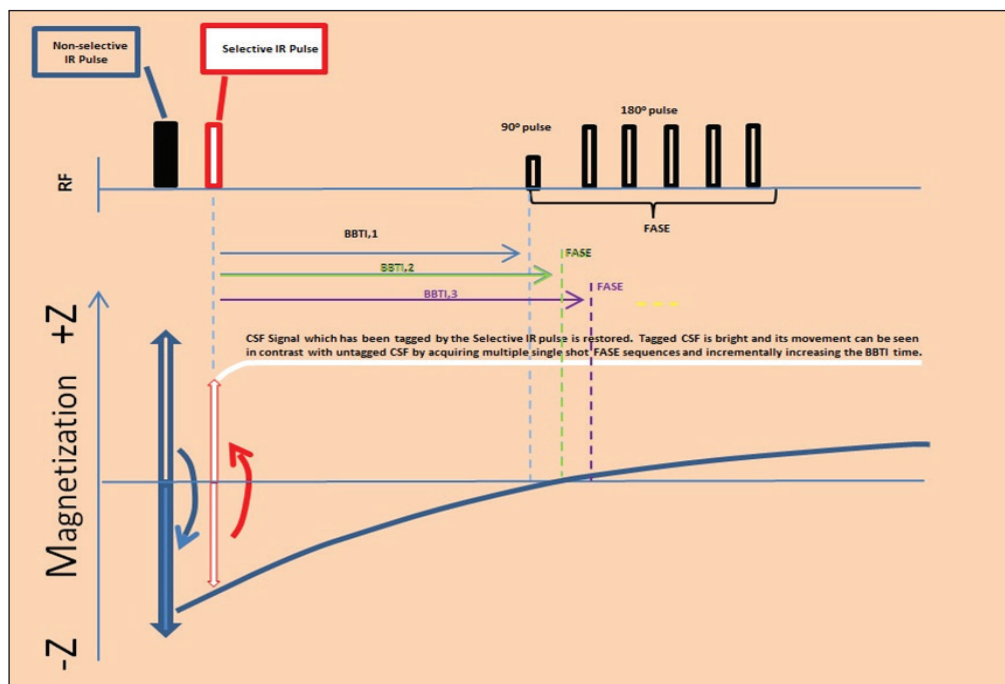


Figure 1: 2D Time-SLIP sequence diagram.

its destination. Lack of flow emerging from the tag region implies an obstruction.

Time-SLIP for imaging CSF flow is fundamentally different than PC-MRI, and both offer unique benefits. PC-MRI allows one to quantify parameters that may be helpful and aid in further research. Time-SLIP for CSF imaging is purely qualitative, but clearly depicts CSF flow 4 Time-Spatial Labeling Inversion for Cerebrospinal Fluid Flow along virtually any pathway of the operator’s choosing.

Time-SLIP is valuable because the information gleaned from this technique is the visualization of the bulk CSF flow itself, from its origin to its destination, or perhaps more importantly for diagnostic purposes, if it is not moving at all. Table 1 shows key features of both PC-MRI and Time-SLIP.

CLINICAL APPLICATIONS

Time-SLIP for CSF imaging has many clinical applications. Since the slice orientation and tag placement are arbitrary, flow pathways can be evaluated in ways that are difficult

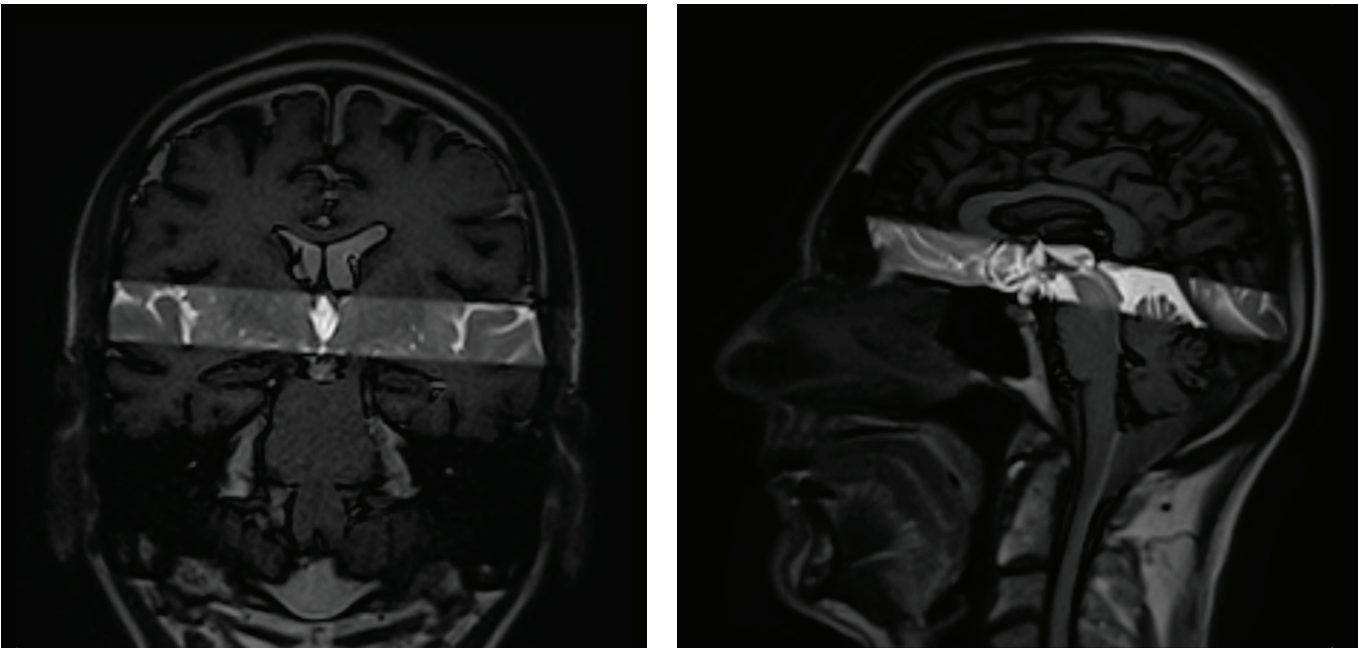


Figure 2: Series of single shot 2D Time-SLIP movies depicting CSF flow originating from the tagged region and flowing through the aqueduct into the 4th ventricle.

	PC-MRI	Time-SLIP
Gating	Yes, ECG or PPG.	Yes, ECG or PPG.
CSF flow	Yes, results in representation of pulsatile CSF flow collected over several cardiac cycles and displayed as one cycle.	Yes, results in visualization of bulk and reflux flow at incremental time points collected and displayed over several cardiac cycles.
Flow in Ventricles	Not possible.	Possible.
Flow in a Cyst	Not possible.	Possible.
Flow between Cysts	Not possible.	Possible.
Quantitative	Yes, in the axial plane only. Require post-processing.	Not possible.
Preparation	Selection of Venc, number of cardiac phases.	Setting initial BBTI and increment times, number of repeats.
Scan Plan	Axial at aqueduct, midline sagittal.	Any plan, tag placement in any orientation for best evaluation of flow.

Table 1: Comparison of PC-MRI and Time-SLIP.

with PC-MRI. For example, Time-SLIP routinely allows for visualization of flow into a cyst and the lateral ventricle. This is particularly challenging for PC-MRI due to signal to noise (SNR) limitations associated with the low velocity encoding value that would be necessary in these regions. CSF Time-SLIP is also useful for evaluating surgical outcome. For example, displayed in Figure 3, Time-SLIP was used before and after surgical intervention to restore CSF flow. Prior to surgery, Time-SLIP showed that there was no CSF flow into the lateral ventricles, as is apparent in normal findings. After intervention, Time-SLIP showed that the CSF flow into the lateral ventricles was restored.

Clinical applications include, but are not limited to:

- Evaluate patency of the aqueduct of Sylvius
- Characterize flow in Chiari malformation
- Evaluate CSF flow pathway
- Determination of CSF flow within arachnoid cysts
- Evaluate CSF leakage
- Assess surgical outcomes non-invasively

CSF TIME-SLIP PROTOCOL

Time-SLIP for CSF imaging is readily repeatable in the clinical setting, since no contrast agent is required. It is reproducible, because consistent results can be obtained from one exam to the next, with minimal changes following initial protocol

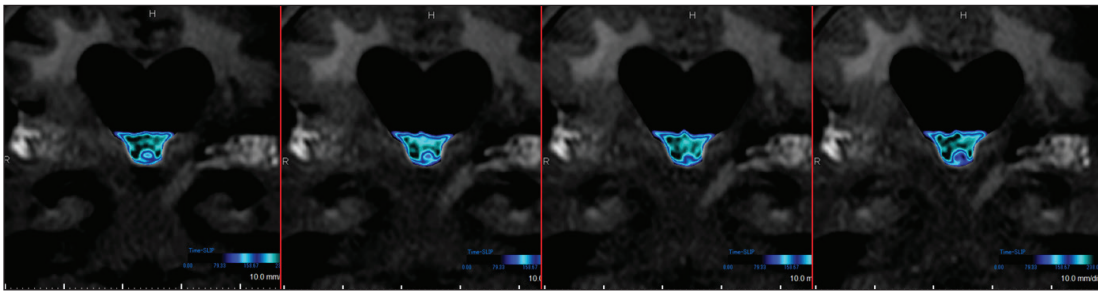
setup. The following parameters can be used for successful examinations. The user is free to manipulate the tag placement to best target the CSF region of interest.

In order to allow CSF recovery between each acquisition, it is critical to keep the TR at approximately 10,000 ms. In this sequence, the TR is controlled solely by the R-R interval (number of cardiac cycles), therefore, the user must increase or decrease the number of cardiac cycles based on the patient's heart rate in order to reach a TR of 10,000. The Repeat Time defines the amount of time the initial BBTI is incremented for every repetition (Repeat Number).

The Repeat Time and Repeat Number can be increased or decreased, keeping in mind that the optimal period is approximately between 1900 ms and 3500 ms on 1.5T. As outlined in the protocol below, the Initial BBTI is around 1900. The BBTI is incremented by 100 ms for every TR, and the process will be repeated 15 times. Therefore, image acquisition will occur at 1900, 2000, 2100, 2200...3300 ms. The scan time will vary depending on the heart rate and Repeat Number. The protocol is similar on 3T, although the lengthening of the T1 allows for an extended period of acquisition, and imaging can be acquired between 1900 and 4500 ms.

Thin slice sagittal and axial T2 weighted 3D acquisitions can be acquired prior to CSF scanning and used for localizers.

Pre-Shunt



Post-Shunt

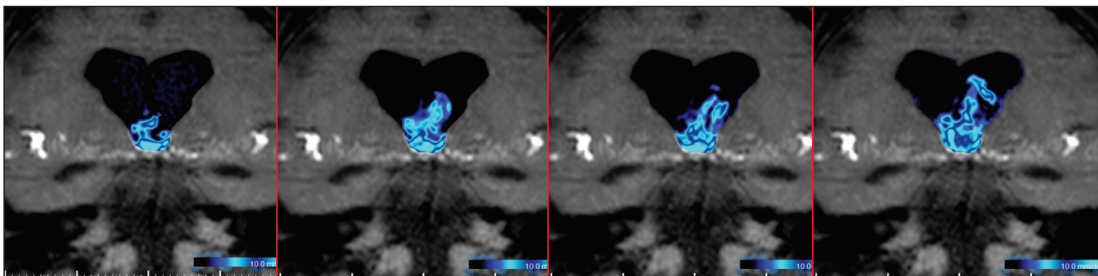


Figure 3: A series of single-shot Time-SLIP images are shown in a coronal view of the lateral ventricles before (top row) and after (bottom row) shunt placement in a patient suffering from NPH. In the pre-shunt series, CSF (blue) is unable to flow into the ventricle. Time-SLIP revealed that shunt placement was successful and CSF flow into the lateral ventricles was restored and the patient's symptoms improved.

(Courtesy of Dr. Yamada, Department of Neurosurgery, Tokai University Hospital).

Basic Imaging Parameters	
Imaging Technique	FASE+5
TR	10-15 RR (10,000 ms)
TE	80
Slice Thickness/Gap	5/0 mm
Imaging Plane	Aqueduct, 3rd, 4th Ventricle: Sagittal Craniocervical Junction: Sagittal Foramen of Monroe: Coronal Arachnoid Cyst: Best
Matrix	256 x 256
SPEEDER	2

Gate	
Gating Mode	BBTI Prep
Cardiac Cycle	10-15 (to get TR 10,000 -11,000 ms)
Delay Time	0
Initial BBTI	1900
Repeat Time	100
Repeat Number	15

Options	
Number of Shots	1
Acquisition Order	Forward
Flow Compensation	Off
Interleave	Interleave
Dynamic Scan / Visual Prep	Off / Off
Gate Source	Peripheral

SUGGESTED SCANNING ORIENTATIONS

The following imaging planes can be used for an overall evaluation of CSF flow, although it is possible to move the tag and slice orientation to suit individual clinical questions.

1. Aqueduct: Sagittal Acquisition with Axial Tag

This view is suited for evaluation of CSF flow through the aqueduct. A true midline slice must be chosen for accurate visualization of the aqueduct. The oblique-axial tag is placed above the aqueduct covering the third ventricle, since this is the source of the bulk CSF flow.

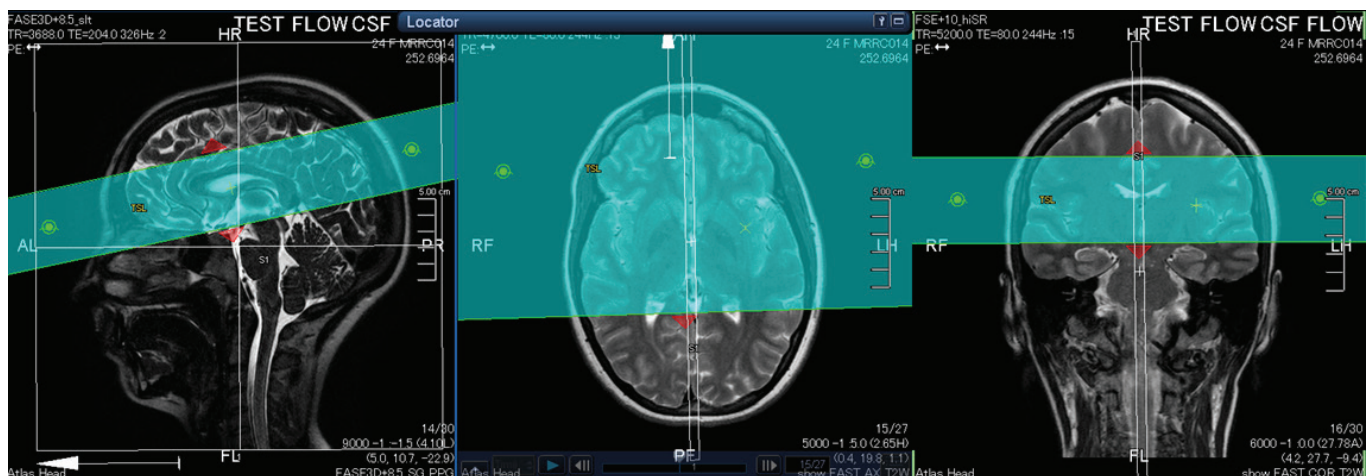


Figure 4: Sagittal scan plan (white lines) with oblique-axial tag placement (blue-green area) is used to target CSF bulk flow from the lateral and third ventricle into the aqueduct. Note: the tag size can be reduced and moved lower, targeting CSF flow originating from the aqueduct. A true midline sagittal slice must be used to accurately visualize the aqueduct.

2. Chiari: Sagittal Acquisition with Axial Tag

This view is suited for evaluation of Chiari malformation. A center slice should be chosen for visualization of CSF anterior and posterior to the spinal cord. The axial tag should be placed at the cranio-cervical junction.

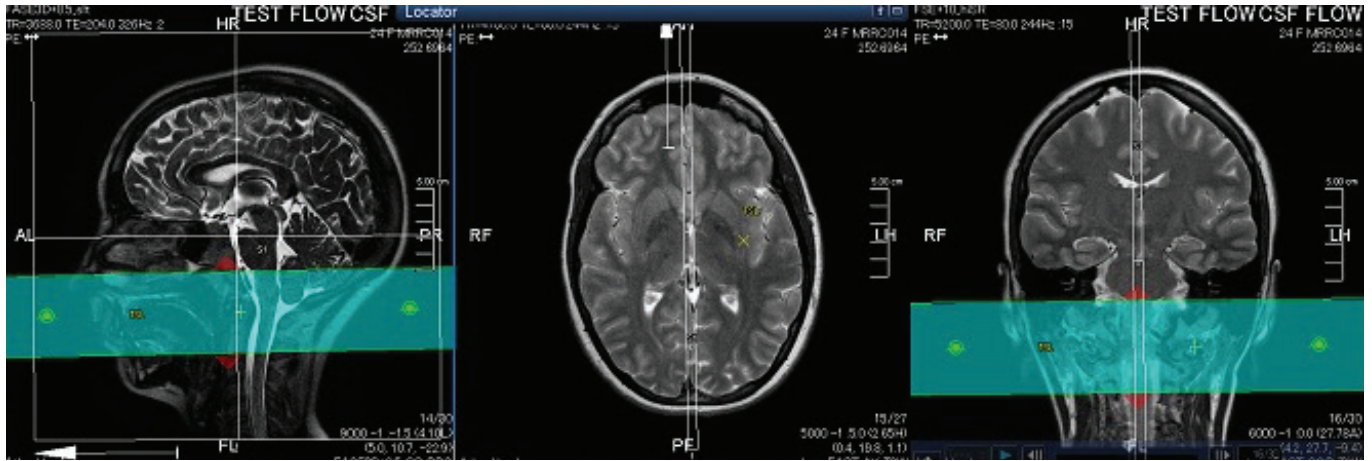


Figure 5: Sagittal scan plan (white lines) with axial tag placement (blue-green area) is used to view CSF bulk flow in the midline sagittal plane.

3. Lateral Ventricles: Oblique-Coronal Acquisition with Axial Tag

This view allows for visualization of CSF into the lateral ventricles through the foramen of Monro. The T2W axial localizer can be used to locate the foramen of Monro. Placing the oblique-coronal slice directly over the foramen of Monro based on the axial T2W localizer best allows for visualization of CSF in this plane.

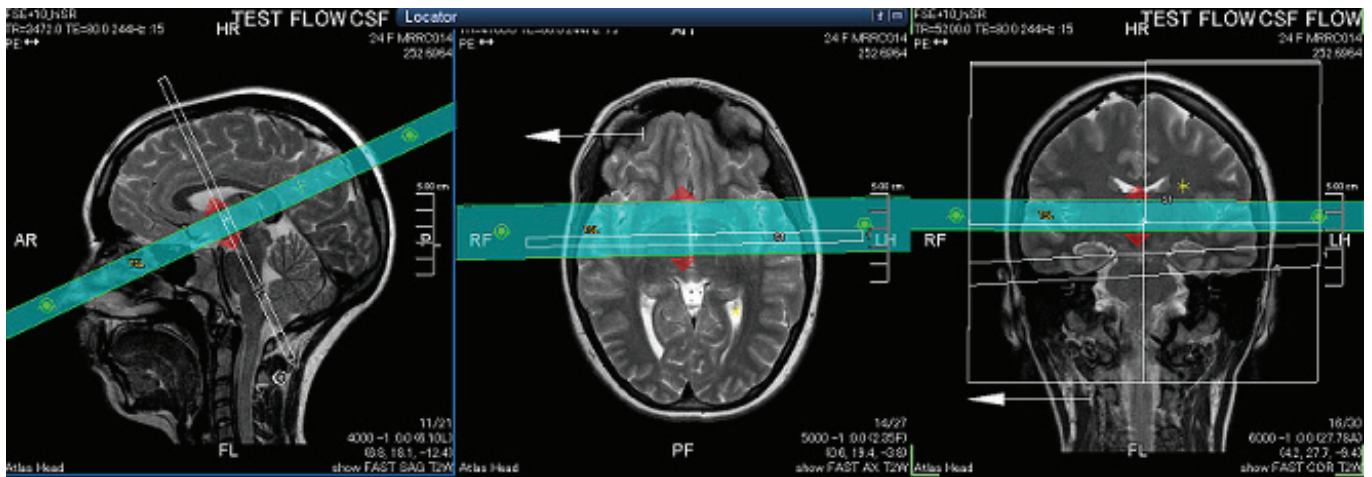


Figure 6: Oblique coronal scan plan (white lines) with oblique-axial tag placement (blue-green area) is used to target CSF bulk flow from the 3rd ventricle into the lateral ventricle.

SUMMARY

Time-SLIP is a technique that is readily available for immediate use in evaluating CSF flow disorders. It may have a big impact on patients who require a shunt to restore CSF flow, drain it from a cyst or open a pathway that is currently blocked.

Time-SLIP is versatile, non-invasive and repeatable. Time-SLIP allows CSF movement to be seen, studied and evaluated immediately and without post-processing.

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