REFERENCES:


We would like to thank Connie Luna, Lead MRI technologist at the Cardiovascular Diagnostic Center, Monterey, CA, and Steve Saeger, Imaging Services Manager from Central Ohio Primary Care Physicians, Columbus, OH for their contributions to this paper.
The leading cause of renal impairment is diabetes, afflicting over 20 million people in the United States alone, with millions more undiagnosed. Diabetes and other vascular afflictions can require aggressive interventional treatment, necessitating repeat MR Angiography exams through the course of a patient’s lifetime. However, renal impairment is a major risk factor for Nephrogenic Systemic Fibrosis (NSF), a progressive and debilitating disorder that has been linked to gadolinium-based MR contrast agent exposure. Thus, eliminating all gadolinium-based contrast agents in these MRA examinations is vital. Time-Spatial Labeling Inversion Pulse (Time-SLIP) is a non-contrast MRA technique that provides high resolution angiograms, with image quality equal to, or superior to, CE-MRA for evaluating complex vasculature, identifying stenosis, and planning treatments for patients.

**TIME-SPATIAL LABELING INVERSION PULSE (TIME-SLIP)**

Time-SLIP is an Arterial Spin Labeling (ASL) variant that can be combined with 3D SSFP or FASE* sequences to depict bright blood vessels within a targeted region in any imaging orientation. Time-SLIP tags the blood and uses it 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. Vessels of interest can be depicted even if the blood is flowing in multiple directions. Time-SLIP can easily be adapted for use in multiple anatomical regions by adjusting parameters pertaining to tag position and delay time, known as Black Blood Time Interval (BBTI). (*FASE is Toshiba’s advanced fast spin echo with partial Fourier acquisition*).

The choice to use SSFP or FASE with Time-SLIP depends mostly on the properties of the region being imaged. In general, SSFP is used for fast flow, whereas FASE is used for slow flow in the target region. The leading cause of renal impairment is diabetes, afflicting over 20 million people in the United States alone, with millions more undiagnosed. Diabetes and other vascular afflictions can require aggressive interventional treatment, necessitating repeat MR Angiography exams through the course of a patient’s lifetime. However, renal impairment is a major risk factor for Nephrogenic Systemic Fibrosis (NSF), a progressive and debilitating disorder that has been linked to gadolinium-based MR contrast agent exposure. Thus, eliminating all gadolinium-based contrast agents in these MRA examinations is vital. Time-Spatial Labeling Inversion Pulse (Time-SLIP) is a non-contrast MRA technique that provides high resolution angiograms, with image quality equal to, or superior to, CE-MRA for evaluating complex vasculature, identifying stenosis, and planning treatments for patients.

**The choice to use SSFP or FASE with Time-SLIP depends mostly on the properties of the region being imaged. In general, SSFP is used for fast flow, whereas FASE is used for slow flow in the target region.**
region. High blood-to-tissue contrast from the inherent flow compensation of SSFP on all three axes yields bright blood angiograms of the renal arteries and portal venous system. FASE is used in the pulmonary system to avoid susceptibility artifacts caused by the air/tissue interface.

The placement of the Time-SLIP pulse controls the selection of the region to be highlighted as the blood flows into or out of the imaging region. This spatially selective tag pulse is applied in the orientation which best targets the blood flow pathway. For example, as seen in Figure 1A, the tag pulse (red) is placed at the top of the kidney to select the blood flowing into the kidneys from the abdominal aorta. A presaturation band (blue) is placed inferior to the renal arteries to suppress the venous flow signal. When imaging the portal system, the tag pulse is applied at approximately a 45 degree angle, the orientation that best targets the blood flowing into the liver, as seen in Figure 1B.

The BBTI is the delay time between the application of the Time-SLIP pulse and the start of the main imaging sequence. This controls the amount of time available for the tagged blood to travel into the imaging region and can be optimized to coincide with suppression of the background signal. Figure 2 describes the blood and background tissue signals before and after the Time-SLIP pulse is applied. The ideal BBTI selection balances both the travel time of tagged blood and the suppression of background signal. In addition, tertiary branches in the parenchyma, which are difficult to visualize with CE-MRA due to fast venous return, are usually easily depicted with Time-SLIP. Conversely, a poor choice of BBTI can drastically affect vessel conspicuity. As depicted in Figure 3, if BBTI is too short, not enough time is allowed for fresh blood to travel into the imaging region. If the BBTI is too long, venous and background signals return. Since no contrast agent is used, it is also possible to obtain several acquisitions with different parameters and orientations as desired.

Time-SLIP is easily adaptable to suit multiple imaging requirements. When Time-SLIP is applied to image inflow (Figure 4A), such as blood flow to the renal arteries, a selective IR pulse is applied which inverts the entire signal in the region. Then, the inflow of fresh, unsaturated blood can be depicted clearly while the background remains suppressed. When Time-SLIP is applied to image outflow (Figure 4B), such as blood flowing out from the heart into the pulmonary system, the tag pulse is applied which inverts the entire background. Then, a selective IR pulse is applied to restore longitudinal magnetization at the source of the fresh blood (e.g., the heart). When imaging after the BBTI delay, blood flowing from the heart into the pulmonary system will appear bright while the background remains mostly suppressed. To visualize

**PRACTICAL TIPS FOR RENAL TIME-SLIP**

- **Time-SLIP** is a quick and easy exam to perform within a 30 min. time slot
- **Time-SLIP** tag placement:
  - The tag placement determines the range of distance blood travel in the acquisition area
  - Align the top of the **Time-SLIP** tag pulse with the top of the kidney
  - The **Time-SLIP** pulse is axial for a renal exam for the highest inflow

- **BBTI** selection:
  - BBTI corresponds to the distance and time needed for blood to travel to the renal arteries
  - BBTI also serves to suppress the background signals by setting it equal to the null point of kidney tissue, which is approximately 1100 ms at 1.5T
  - At 1.5T a default BBTI value of 1200 ms works well for most patients

- **Cases of suspected renal artery stenosis (RAS)** may need to be increased up to 2000 ms
- **Consider increasing BBTI** by increments of ~200 ms until best visualization of RAS is achieved

By Connie Luna, RT, Cardiovascular Diagnostic Center, Monterey, CA
**Time-SLIP: Safe, Simple and Effective Non-Contrast MR Angiography**

**OTHER BENEFITS OF NON-CONTRAST ANGIOGRAPHY**

The above safety and convenience properties of Time-SLIP are easily appreciated, but Time-SLIP provides financial benefits as well by substantially reducing or eliminating the amount of contrast media and associated supplies needed for CE-MRA exams. After just one year of non-contrast peripheral runoff and renal MRA exams, Dr. Timothy Albert and the Cardiovascular Diagnostic Center, Monterey, CA, saved more than $35,000 on 250 patient exams by eliminating the contrast agent ($100), IV tubing and starter kits ($23), and nursing assistance ($60/hour). Furthermore, pre- and post-dialysis, and creatinine scoring tests are eliminated for high risk patients.

**APPLICATIONS OF TIME-SLIP**

A renal angiography exam perfectly demonstrates the capabilities of Time-SLIP, as well as the appropriate placement of the tag pulse for highlighting in-flow and selection of BBTI.

**HEALTHY CASE 1**

A renal Time-SLIP MRA exam of a healthy patient confirms the absence of renal stenosis.

**NOTES**

- **BBTI**
  - Black Blood Time Interval. Delay time between the application of the Time-SLIP pulse and the acquisition. Allows the acquisition to begin at the optimal point for acquiring bright blood and suppressing background.

- **Tag On/Off Option**
  - An Alternative Mode option for Time-SLIP. Alternates between data collection with the tag on and off to acquire two datasets.

**Table 1: Important Time-SLIP terminologies.**

<table>
<thead>
<tr>
<th>Definition</th>
<th>Notes</th>
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| 3D SSFP    | Steady State Free Precession: A balanced gradient echo sequence in which blood maintains very high signal compared to background tissue. Useful for fast flowing regions.
| 3D FASE    | Fast Advanced Spin Echo: A fast spin echo sequence that uses Partial Fourier. Useful for slow flowing regions.
| Selective Tag Pulse (Time-SLIP Pulse) | A tag pulse that is applied to a region of interest which inverts only those signals within the region. User selects the region for which the Time-SLIP pulse is applied. Flowing blood from the target vessel is selectively tagged.
| Non-Selective IR pulse | An inversion recovery pulse that indiscriminately saturates the entire signal in the field of view. Available with 3D FASE Time-SLIP. Background can be completely removed by inverting all the signal in the FOV before the selective tag pulse restores the signal.
| BBTI       | Black Blood Time Interval. Delay time between the application of the Time-SLIP pulse and the acquisition. Allows the acquisition to begin at the optimal point for acquiring bright blood and suppressing background. |
| Tag On/Off Option | An Alternative Mode option for Time-SLIP. Alternates between data collection with the tag on and off to acquire two datasets. Two 3D data sets are acquired, one with the Time-SLIP pulse “On” and another with the Time-SLIP pulse “Off”. Subtraction removes the background completely. Arteries and veins can be acquired and viewed separately. Does not require a pre-saturation band. |

**Table 2:**

<table>
<thead>
<tr>
<th>Tag On/Off Option</th>
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<td>Tag On</td>
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<td>Tag Off</td>
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**Figure 4:** Sequence timing and signal properties for imaging bright blood signal due to A) inflow, B) outflow, and with C) complete cancellation of background.
volunteer is shown in Figure 5, which demonstrates the balance between inflow arterial signal and background suppression. A BBTI of 1200 ms was selected to allow visualization of the renal arteries as the blood flows into the kidneys while the background signal remained suppressed. The arterial flow in the abdominal aorta and renal arteries is clearly visualized with bright signal, while the background signals are nulled. This subject was noted to have a second left renal artery.

CLINICAL CASE 1
A 42-year-old patient with uncontrolled hypertension underwent an abdominal MRA exam to assess renal artery stenosis. The non-contrast Time-SLIP abdominal MRA was followed by CE-MRA. The exam was performed on an XGV Vantage 1.5T MRI scanner using the Torso Speeder coil. 3D SSFP Time-SLIP was acquired in the axial plane with a BBTI of 1200 ms. Representative maximum intensity projection (MIP) images are shown in Figure 6.

Both Time-SLIP and CE-MRA exams confirmed that the abdominal aorta was normal in caliber. Bilateral duplicated renal arteries were seen using both techniques. They were normal in caliber and no aneurysm or stenosis was identified. While both techniques depicted the origins of the renal arteries very well, even the tertiary branches are conspicuous well into the kidney using the Time-SLIP technique, whereas only the initial renal branches were visualized using CE-MRA, as seen in Figure 6.

CLINICAL CASE 2
A 77-year-old woman with renal insufficiency and hypertension underwent a non-contrast renal MRA exam using Time-SLIP. The study was performed on a ZGV Vantage Atlas 1.5T MRI scanner using one Atlas Body coil centered over the kidney. 3D SSFP Time-SLIP was acquired in both the coronal and axial orientations using the BBTI of 1300 and 1200, respectively.

Moderate atherosclerotic plaque was seen in the abdominal aorta and the infrarenal aorta had ectasia. A mild eccentric ostial plaquing was noted at the origin of the left renal artery and a long segment of narrowing was found in the proximal portion of the right renal artery. Using a distal segment as a reference, the narrowing appeared to be approximately 70% occluded. The MIP and analysis is shown in Figure 7.

As the sole MR angiography technique used to diagnose this patient, Time-SLIP spared this woman from the risk of developing NSF as well as the requirement to undergo screening procedures which may have been necessary if the exam included CE-MRA.

CLINICAL CASE 3
The MIP from a Time-SLIP renal exam performed on a 61-year-old patient

Figure 5: MIP of the renal arteries and its branches are well visualized into the kidney tissue using the 3D SSFP Time-SLIP technique. This image was acquired on a healthy volunteer in the axial plane with a BBTI of 1200 ms. Surface volume rendered MIP images were processed on the Virtual Explorer workstation.

Figure 6: Direct comparison between CE-MRA (A) non-contrast renal Time-SLIP (B) acquired in the same patient. Note: the conspicuity of the arterial branches is clear well into the kidney tissue with Time-SLIP, but is limited with CE-MRA. Images courtesy of Central Ohio Primary Care Physicians.

Figure 7: Time-SLIP non-contrast MRA of the renal arteries revealing a left-sided stenosis. Center/Right: MIP images processed on Virtual Explorer workstation. Analysis revealed that the 4.1 mm diameter vessel narrowed to 1.5 mm.
suffering from abdominal pain is shown in Figure 8. The exam was performed on an XGV Vantage 1.5T MRI scanner using the Torso SPEEDER coil. 3D SSFP Time-SLIP with a BBTI 1200 ms was used. Data was acquired in the axial plane.

The mesenteric vasculature and renal arteries were evaluated during the MR exam. Mild irregularity of the distal infrarenal abdominal aorta suggested underlying atherosclerotic involvement. No high-grade stenosis of either renal artery is identified from its origin through to the renal hila. However, fluid-filled bilateral renal cysts are clearly evident on the 3D SSFP Time-SLIP images, which indicate that they are accumulating fluid during the BBTI.

CLINICAL CASE 4
Time-SLIP was performed on a 46-year-old woman with severe and poorly controlled hypertension in both the axial and coronal planes. The study was performed on a ZGV Vantage Atlas 1.5T MRI scanner using one Atlas Body coil centered over the kidneys and the Atlas Spine coil. The source and MIP images are shown in Figure 9. The renal arteries were found to be normal. Both renal arteries and branches were clearly visualized in axial and coronal planes. Other causes for the hypertension were investigated.

CONCLUSION
CE-MRA has been considered the gold standard in MR Angiography for many years. In the United States there had been little motivation to adopt novel non-contrast imaging techniques given the comfort level of vascular radiologists with contrast-enhanced techniques, the reasonable reimbursement for MRA, and the relatively low cost of gadolinium. However, with recent changes in reimbursement structure and new concerns about the link of NSF with gadolinium, it is now necessary to consider the adoption of novel non-contrast MRA protocols such as Time-SLIP.

Prior to concerns about nephrotoxicity of gadolinium-based contrast agents, Toshiba invested many years in the development of cutting-edge non-contrast angiography techniques that addressed constraints on medical practice in Japan. Fortunately, Time-SLIP is a straightforward vascular imaging technique that can be substituted for CE-MRA methods. For diabetic patients who are susceptible to renal impairment, and patients with renal insufficiency, Time-SLIP is invaluable for obtaining high temporal and spatial resolution images for evaluating vessel patency, diagnosing aneurysms, and planning treatment.

Toshiba has many ways to eliminate gadolinium from MR Angiography exams, and Time-SLIP is leading the field for non-contrast MRA.

Figure 8: Time-SLIP surface volume rendered MIP images of the renal arteries and branches processed on the Virtual Explorer workstation. In addition to the excellent clarity of the renal arteries, bilateral fluid filled cysts are seen within the kidneys. Images courtesy of Central Ohio Primary Care Physicians.

Figure 9: Source and MIP images from a patient with diabetes and severe poorly controlled hypertension. Top row: Axial source image and 3D maximum intensity projections. Bottom row: Coronal source image and 3D maximum intensity projections. Surface volume rendered MIP images were processed on the Virtual Explorer workstation.
REFERENCES:

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