Time-Spatial Labeling Inversion Pulse

Safe, Simple and Effective Non-Contrast MR Angiography

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TOSHIBA'S CONTINUOUS DEVELOPMENT OF NON-CONTRAST ANGIOGRAPHY USING TIME-SPATIAL LABELING INVERSION PULSE*

- **2002:** The first application of time-spatial labeling inversion tag (t-SLIT) technique with selective tag on/off demonstrated with pulmonary artery imaging[1].
- **2004:** Time-SLIP was combined with parallel imaging to improve visualization of the arteries from the aortic arch to the basilar artery[2].
- **2005:** Time-SLIP was used to evaluate pre and postprandial flow changes under pathological conditions[3].
- **2007:** Time-SLIP was evaluated for its ability to depict the renal arteries[4].
- **2009:** Time-SLIP was optimized for producing selective and high-contrast visualization of the hepatic arteries, which enabled visualization of the arteries without the need for an exogenous contrast agent or breath-hold[5].
- **2009:** Time-SLIP using SSFP and FASE were compared for imaging the portal venous system[6].
- **2009:** Multiple Time-SLIP acquisitions were used to provide a time-resolved representation of intracranial blood flow[7].
- **2009:** Improvements in renal artery conspicuity were shown by using an inversion recovery pulse to suppress fat[8].

**Selected publications*

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.

Contrast Enhanced MRA (CE-MRA) methods are commonly used because contrast agents are relatively inexpensive, are widely available and were at one time considered to be very safe and non-nephrotoxic. However, the non-reimbursed expense of contrast media for MRA exams hampered its adoption in Japan. Toshiba addressed this need and developed a suite of advanced non-contrast techniques including Time-SLIP, to provide high temporal and spatial resolution MRA exams of complex vascular anatomies, such as the renal arteries shown in this paper. Time-SLIP is also effective for imaging the portal-venous system, spleen, pulmonary system, carotid and intracranial arteries, and slower flowing vessels of the hands and feet. Time-SLIP produces bright blood angiograms that are diagnostically equivalent to CE-MRA without the drawbacks and safety concerns. Time-SLIP has already become the standard angiography technique in many hospitals and diagnostic imaging centers throughout the world.

Time-SLIP is essential for those patients with renal insufficiency and vascular disease who are most susceptible to NSF. In addition, Time-SLIP is a safe and highly effective way to image all patients with unknown or suspected vascular disease. Furthermore, call-backs due to patient motion during a CE-MRA exam are eliminated, since Time-SLIP can be repeated immediately without waiting for contrast agent clearance.

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. 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 lungs, a non-selective IR pulse is first 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 of 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 effect, although the acquisition area can be coronal or axial
- 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

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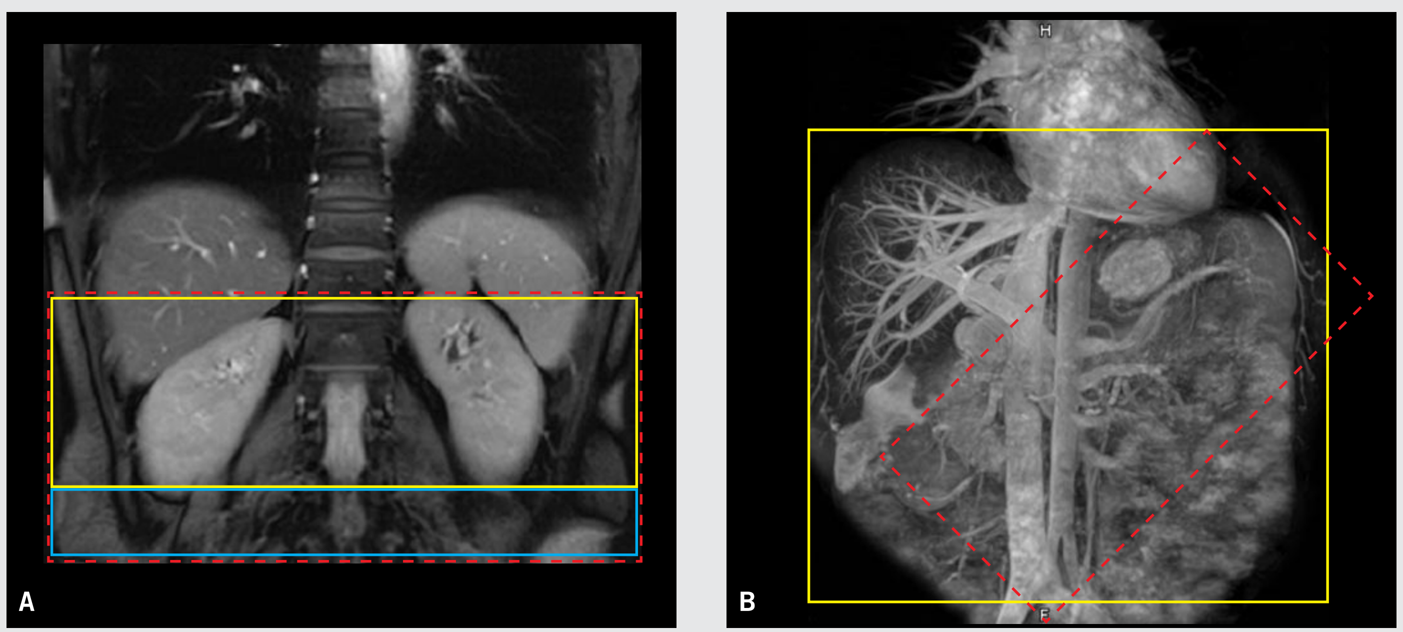

Time-SLIP Pulse   Acquisition Area   Pre-saturation Band

Figure 1: Time-SLIP positioning for renal artery acquired in the axial plane (**A**) and portal venous system acquired in the coronal plane (**B**). The orientation of Time-SLIP selective tag can be manipulated to best suit the target flow. A pre-saturation band is not required for the portal venous system because it is best depicted using alternative mode (See Table 1).

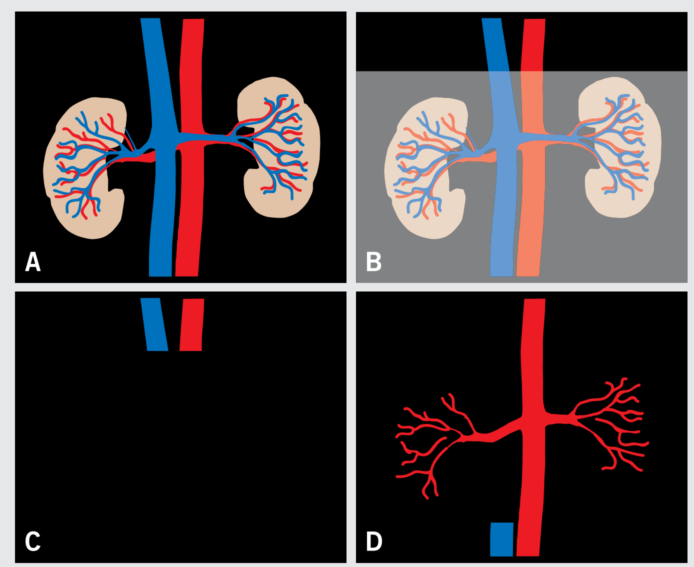

Figure 2: Series of steps taking place during the Time-SLIP sequence. **A)** The region of interest. **B)** The region in which the Time-SLIP pulse will be applied is highlighted. **C)** The dark signal in the region of interest represents the decrease in signal following the Time-SLIP pulse. **D)** Blood that is not affected by the Time-SLIP pulse flows into the imaging region and appears as bright signal when acquired at the optimal BBTI.

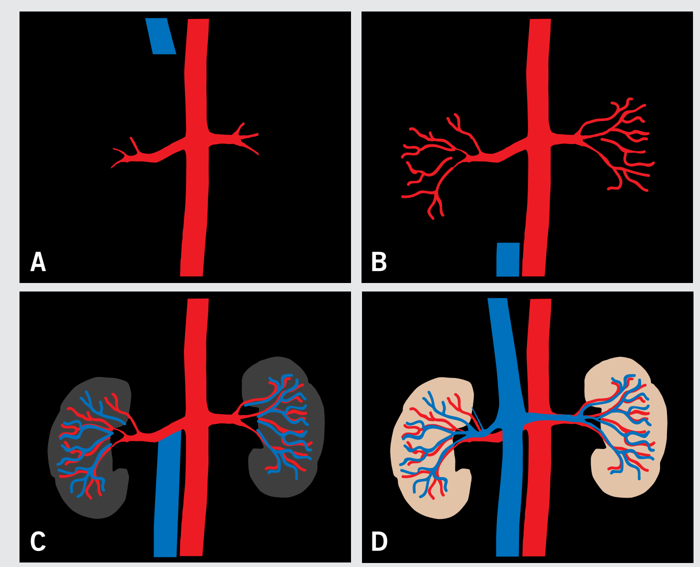

Figure 3: BBTI must be appropriately chosen to balance high arterial signal with background suppression. **A)** BBTI too low: insufficient travel time for inflow of fresh blood results in low arterial signal. **B)** Optimal BBTI: sufficient travel time for inflow of fresh blood results in high arterial signal. **C)** BBTI slightly high: some venous and background signals begin to recover. **D)** BBTI too high: venous and background are fully recovered.

extremely slow blood flow, or for complete removal of background signals, Time-SLIP can be implemented in an alternate mode (**Figure 4C**), in which the data is acquired once with and once without the tag. This alternate mode implementation also allows for arteries and veins to be acquired simultaneously and displayed separately. For example, if the tag was placed to target the portal venous system, it will be depicted in the "tag on" acquisition. All of the hepatic vasculature (arteries and veins) will be depicted in the "tag off" acquisition. Finally, subtraction of the two datasets removes the background, cancels out the veins to depict the hepatic arteries.

Time-SLIP image quality can be further enhanced by using respiratory gating to acquire the data during the quiescent periods, which is especially important for the abdominal region. Image resolution can be optimized with parallel imaging and increasing the number of segments. **Table 1** summarizes the various parameters and implementations of Time-SLIP.

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

	Definition	Notes
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. Provides bright blood signal.
3D FASE	Fast Advanced Spin Echo: A fast spin echo sequence that uses Partial Fourier.	Useful for slow flowing regions and/or regions that are prone to susceptibility artifacts, such as the pulmonary system.
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 suppressed 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 1: Important Time-SLIP terminology.

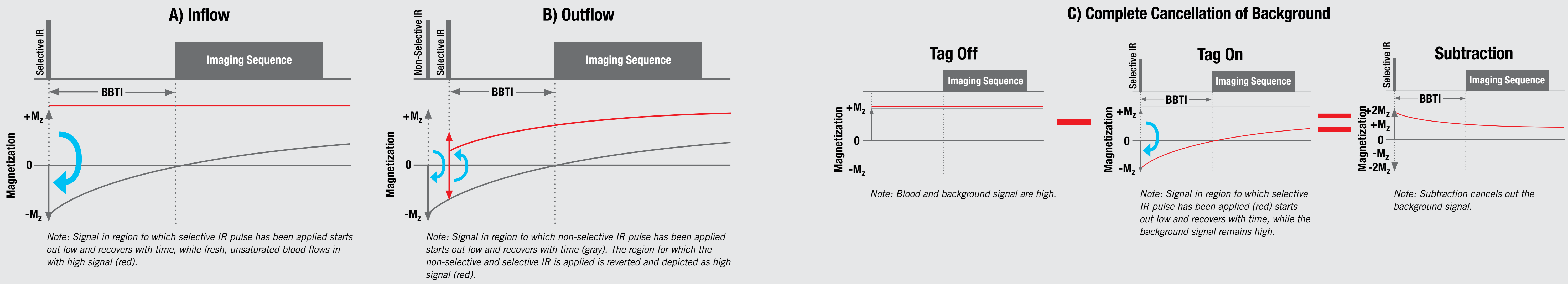

Figure 4: Sequence timing and signal properties for imaging bright blood signal due to **A)** inflow, **B)** outflow, and with **C)** complete cancellation of background.

KEY FEATURES OF TIME-SLIP

- Time-SLIP is a vascular imaging technique that provides bright blood angiograms without the use of a contrast agent
- Time-SLIP is based on the Arterial Spin Labeling technique
- Time-SLIP is a quick, easy, repeatable and adaptable exam that is safe for all patients
- Time-SLIP balances blood signal against background suppression by adjusting the time delay (BBTI) between the selective IR pulse and the imaging sequence
- Time-SLIP can be used to image inflow or outflow
- Respiratory gating allows data to be collected during the quiescent periods of the respiratory cycle

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.

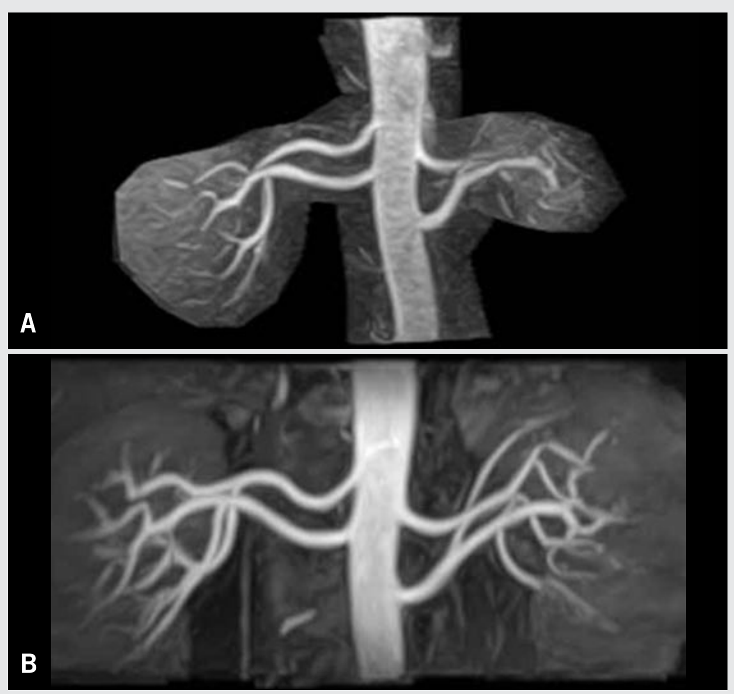

Figure 6: Direct comparison between CE-MRA (**A**) non-contrast renal Time-SLIP (**B**) acquired in the same patient. Note: the conspicuity of the arterial branches is clear well into the kidney tissue with Time-SLIP, but is limited with CE-MRA. *Images courtesy of Central Ohio Primary Care Physicians.*

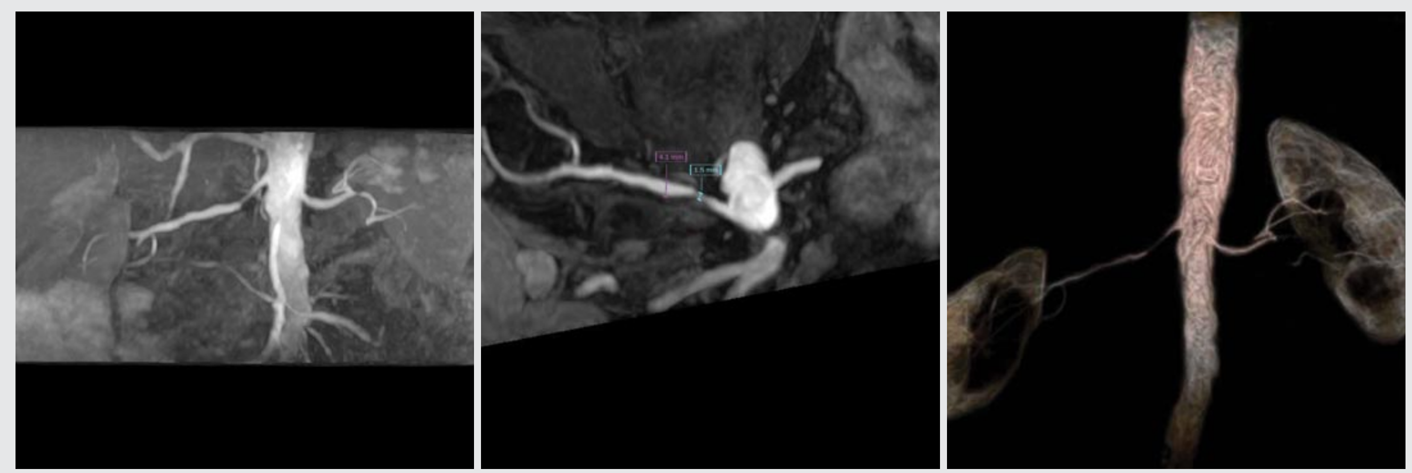

Figure 7: Time-SLIP non-contrast MRA of the renal arteries revealing a left-sided stenosis. Center/Right: MIP images processed on Virtual Explorer workstation. Analysis revealed that the 4.1 mm diameter vessel narrowed to 1.5 mm.

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.

BENEFITS OF NON-CONTRAST MRA

- The safest choice for your patients
- Time-tested, proven technology
- Reproducible
- Requires less setup time compared to contrast enhanced MRA
- Can be reacquired on the spot for non-compliant patients who move during the scan
- Can be acquired with a high resolution matrix because it is not limited by acquisition timing constraints
- More versatile than CE-MRA because it can also acquire a venogram in the same acquisition
- Does not require the use of contrast agent
- Does not require an IV injection
- Does not rely on bolus timing of the injection by the technologist
- Cost savings:

Contrast agent	$100 per study
Nurse assistance	$20 per study
IV supplies	$23 per study
Total*	**$143 per study**

**Study reported by Dr. Timothy Albert, CVDC, 2009.*

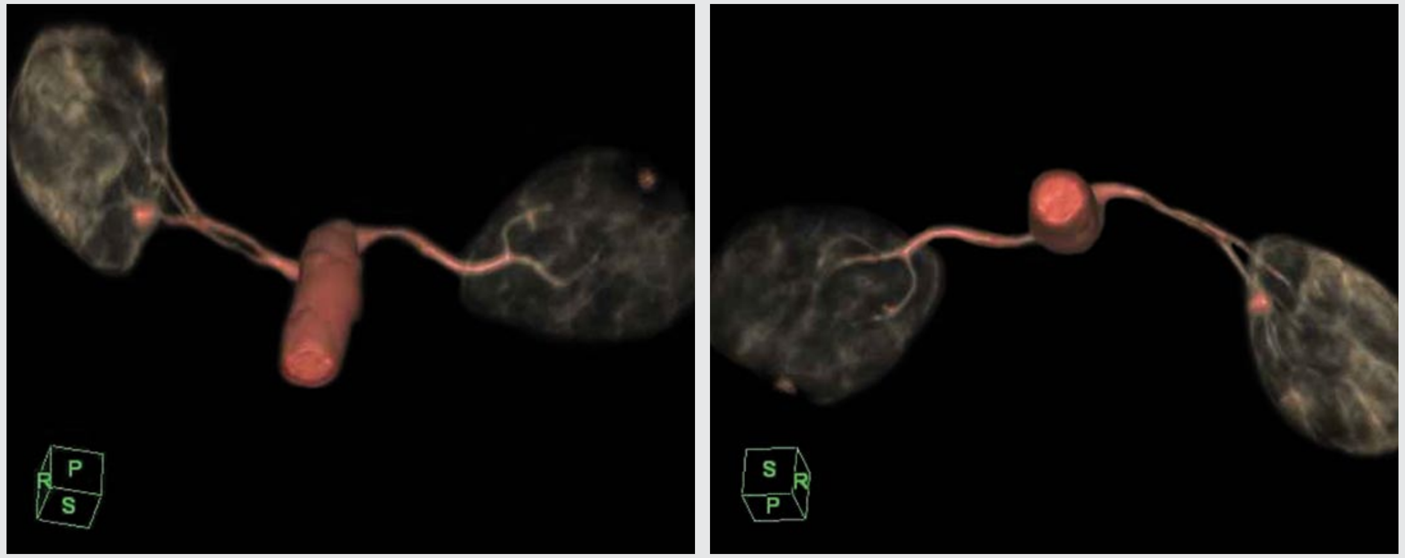

Figure 8: Time-SLIP surface volume rendered MIP images of the renal arteries and branches processed on the Virtual Explorer workstation. In addition to the excellent clarity of the renal arteries, bilateral fluid filled cysts are seen within the kidneys. *Images courtesy of Central Ohio Primary Care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

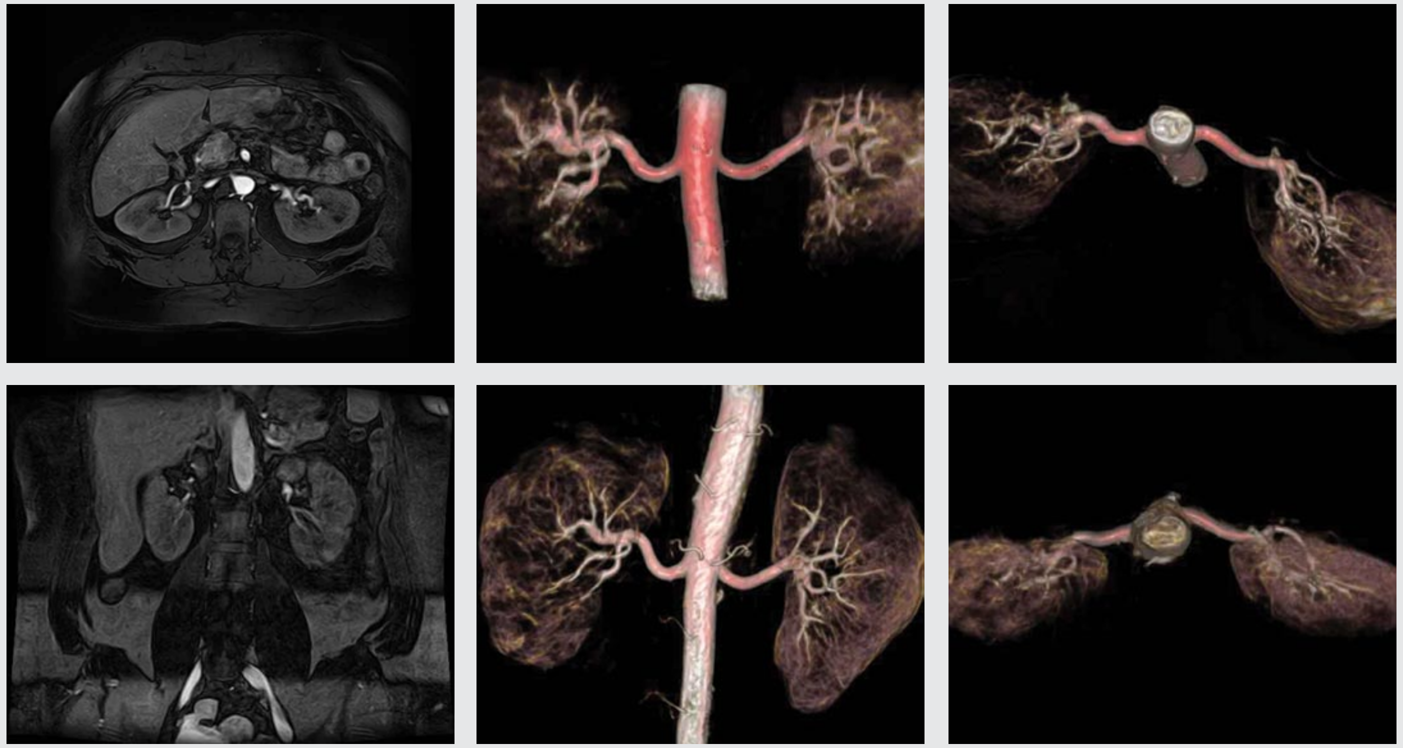

Figure 9: Source and MIP images from a patient with diabetes and severe poorly controlled hypertension. **Top row:** Axial source image and 3D maximum intensity projections. **Bottom row:** Coronal source image and 3D maximum intensity projections. Surface volume rendered MIP images were processed on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

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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.

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