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Fresh Blood Imaging:

Setting the Standard for Non-Contrast Peripheral MR Angiography

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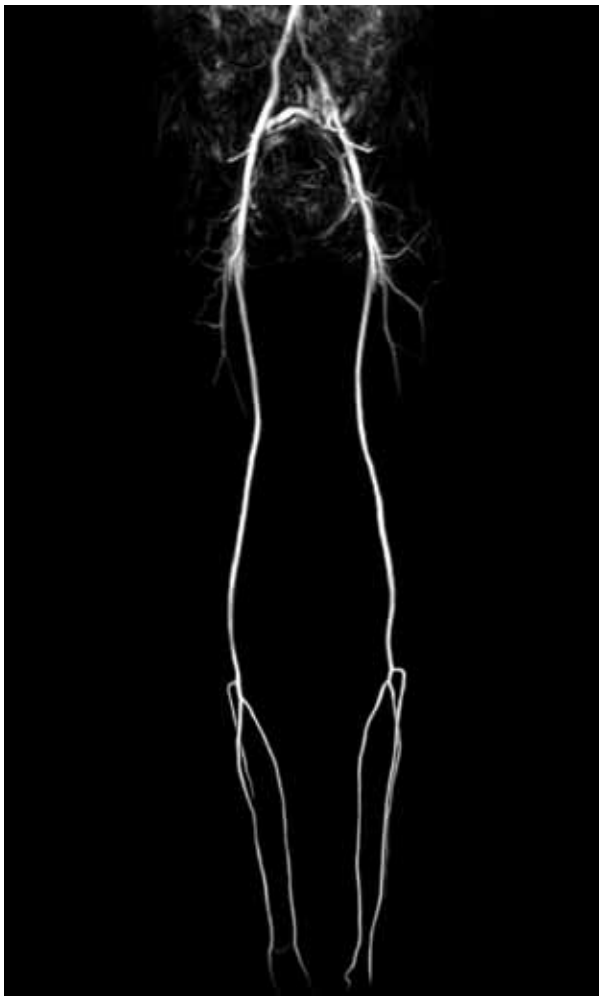


TOSHIBA'S CONTINUOUS DEVELOPMENT OF FRESH BLOOD IMAGING*

- **1998:** SPEED (Swap Phase Encode Extended Data) improves blood vessel resolution while simultaneously reducing the signal loss caused by flow dephasing[1]
- **1998:** Fresh Blood Imaging (FBI) produces 3D natural blood contrast MRA in a single breath hold at 0.5T[2]
- **1999:** The first experiences of non-contrast lymphography to image the thoracic duct along the thoracic aorta[3]
- **2000:** Introducing 3D ECG-gated FBI technique with Half-Fourier FSE at 0.5T and 1.5T[4]
- **2001:** A clinical evaluation of non-contrast enhanced FBI in 75 patients with aortic disease[5]
- **2002:** Evaluating pulsatile flow during the cardiac cycle in the pulmonary arteries with non-contrast FBI[6]
- **2003:** Introducing Flow-spoiled FBI which improves the separation of arteries from veins in slow flow regions like peripheral vasculature[7]
- **2009:** The clinical demonstration of fast iliac to peripheral MR venography without contrast medium using 3D-FBI[8]

**Selected publications*

Nephrogenic Systemic Fibrosis (NSF) is a debilitating and potentially fatal man-made disease for patients with renal insufficiency who are exposed to gadolinium-based MR contrast media. Gadolinium is commonly used in contrast enhanced MR Angiography (CE-MRA) exams, because this agent enables rapid scanning over a large field of view (FOV) at the required high spatial resolution to assess lumen narrowing. CE-MRA is considered to be the gold standard technique in MR Angiography. Alternatively, contrast-agent-free angiography techniques with exquisite depiction of the vasculature were developed and improved in Japan, where the cost of contrast agents is expensive. These techniques, known as Fresh Blood Imaging (FBI), were commonly applied in clinical practice throughout the world for several years before the first cases of NSF were reported. FBI, which does not employ toxic heavy metals like gadolinium, is a simple and effective approach that maintains the highest level of care to patients without the risk of NSF.

NON-CONTRAST ANGIOGRAPHY: BRIGHT BLOOD IMAGING BY FRESH BLOOD ENHANCEMENT

Intrinsic image contrast mechanisms have the capability to provide bright blood MR angiograms without gadolinium and due in part to NSF, they have received renewed interest in recent years. Prior non-contrast angiography techniques, such as Time-of-Flight (TOF) and Phase-Contrast (PC) have limitations. FBI is a fast, high resolution, robust and versatile non-contrast technique based on the physics of flowing blood.

FBI is generally applicable for imaging the aorta and major runoff vessels of the abdomen and legs. For improved depiction of slower blood flow, vessels in the lower leg, hands and feet are studied with Flow-Spoiled Fresh Blood Imaging (FS-FBI). Both techniques produce excellent bright blood angiograms. This is a considerable benefit for those patients with renal insufficiency and vascular disease who are most susceptible to NSF. In addition, the FBI technique 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 FBI can be repeated immediately and does not require time for contrast agent clearance.

FRESH BLOOD IMAGING

FBI is an ECG-gated* 3D T2-weighted bright blood partial Fourier Fast Advanced Spin Echo (FASE) technique. ECG gating captures the data at the optimal point in the cardiac cycle.

**Peripheral pulse gating may be used instead of ECG gating, but ECG-gating detects the R-wave more precisely and accurately.*

SUMMARY OF FBI

- An angiography technique that does not require exogenous contrast media
- Based on the FASE 3D ECG gated sequence
- Produces two sets of three-dimensional data – one during systole and one during diastole
- Can use ECG gating to optimally acquire the data during systole and diastole
- Suppresses signal from stationary anatomy like parenchyma with an IR pulse
- Produces bright blood angiograms with minimal venous and background signals
- Allows large anatomical coverage because the data can be collected in the sagittal or coronal planes
- Uses short echo train spacing to preserve image resolution
- Uses a TR of at least two heart beats to allow sufficient T1 recovery
- Can use SPEEDER to shorten the data acquisition shot time

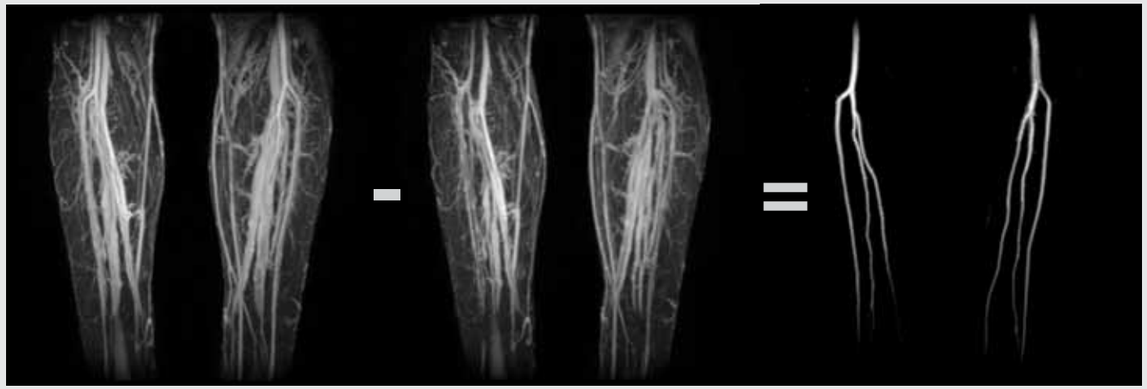


Figure 1: 3D arterial MIP images (right) are created via subtraction between the source data sets collected during diastole (left) and systole (center). Subtraction cancels the venous signal appearing during systole and diastole, revealing the bright arterial signal acquired during diastole.

The visualization of bright blood vessels in FBI is optimized by: using short echo train spacing to reduce resolution loss from T2 decay; suppressing the parenchyma with an inversion recovery pulse; and, enhancing image contrast by acquiring the data from near the center of k-space. Further resolution optimization employs partial Fourier methods, SPEEDER (Toshiba's parallel imaging technique) and increasing the number of shots from 1 to 2. Signal is enhanced by setting TR to at least twice the R-R interval. Large FOV coverage is possible, since FBI data can be acquired in the coronal or sagittal planes.

FBI separates veins from arteries by capitalizing on subtle differences in spin dephasing. Fast arterial flow typically results in complete dephasing of spins in systole, where the corresponding pixels will appear black in the image. Conversely, arterial flow during diastole and venous flow throughout the cardiac cycle will have less dephasing, where the corresponding pixels will appear bright. Subtracting images acquired at the extreme points of the cardiac cycle will yield a bright arterial image, as shown in **Figure 1**.

The optimal systolic and diastolic collection times can be determined with the ECG-prep scan. ECG-prep is an ECG-gated 2D FASE sequence, which repeatedly scans the same slice with an incrementing R-wave delay time (100, 200…700 ms, etc.). The optimal systolic time produces black blood arteries, while the optimal diastolic time produces bright blood arteries. **Figure 2** shows the optimal systolic ECG-prep image (left), the optimal diastolic image (center), and the subtracted result (right).

The FBI Navi tool** automatically determines the optimal delay times and stores them for use in the FBI gating window. **Figure 3** shows the FBI Navi graphical interface. (***This feature is available on Toshiba MR software versions 9.50 and above.*)

FLOW-SPOILED FRESH BLOOD IMAGING

Flow-Spoiled Fresh Blood Imaging (FS-FBI) improves the depiction of arterial images, especially in the lower extremities, by adding a small amount of dephasing gradient moment to the readout axis, which is oriented parallel to the direction of blood flow.

In the lower extremities and/or in patients with poor circulation, the signal differences can be small, which results in poor arterial signal after subtraction. Dephasing along the readout axis enhances the arterial signal loss during systolic imaging, which improves the signal differences between the arteries and veins as demonstrated in **Figure 4**.

The optimal dephasing gradient, represented as percentages of half the area of the readout gradient, varies for different anatomical regions and pathology. General recommendations

ECG PREP ACQUISITION AND ANALYSIS

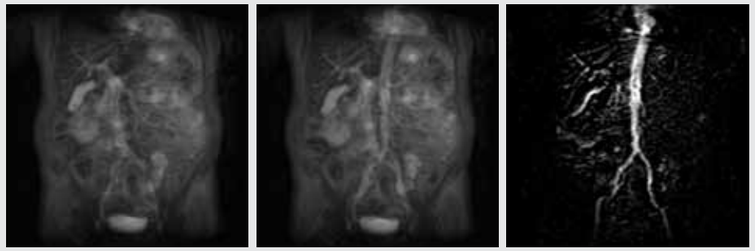


Figure 2: Example of systolic (left) and diastolic (center) ECG-prep images acquired at 100 ms and 600 ms from the R-wave, respectively. These delay times were chosen because they provide the best indication that the subtraction will provide a bright blood angiogram (right).

Figure 3: FBI Navi is a tool provided on the system console that automatically selects the systolic and diastolic delay times based on the image intensity waveform (top right). The user can adjust the systolic and diastolic times to verify that the arterial image created via subtraction (bottom left) offers the best arterial clarity.

for iliac, popliteal, tibial and foot regions are shown in **Table 1**. Further optimization is possible with Flow-prep. Flow-prep incrementally checks a range of dephasing gradients to find the optimal arterial signal. **Figure 5** depicts select Flow-prep images collected during diastole (top row), systole (middle row) and the subtraction images (bottom row). The fourth column shows the optimum result, which balances conspicuity of arteries against background and venous contamination.

OTHER BENEFITS OF NON-CONTRAST ANGIOGRAPHY

In addition to the primary safety benefits of a contrast-agent-free MRA study, there is also a significant financial gain. 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 FBI

A three station peripheral run-off MRA exam demonstrates the capabilities of FBI, as well as the appropriate use of the dephasing gradients in FS-FBI. The straightforward sequence of procedures required to perform a three station FBI exam can be broken down into a few simple steps, as shown in **Figure 6**, based on the experience of Connie Luna, Lead Technologist at the Cardiovascular Diagnostic Center, Monterey, CA. Patient preparation is very important, since a comfortable patient is more likely to remain still during the exam. Obtaining a good ECG trace is necessary for accurate detection of the R-wave during the exam. Locator images allow the operator to visualize the vessels for planning the main 3D FBI acquisition. The operator also has the option to tailor the delay times and dephasing gradient strengths for each station by running ECG-prep and Flow-prep, each of which can be completed in less than a minute. The locator and 3D acquisition sequences can be simply copied and repeated for multi-station runoffs.

The visual appearance of healthy and diseased vasculature can be strikingly dissimilar. The MIP images of a peripheral run-off FS-FBI study performed on a healthy volunteer are shown in **Figure 7**, in which the vessels are bright, and highlight an unobstructed blood flow pathway. The following three clinical cases demonstrate the clinical strength of FBI and FS-FBI for evaluating severe vascular disease.

CLINICAL CASE 1

An 80-year-old patient with a history of peripheral vascular disease and claudication was evaluated with FS-FBI.

PRACTICAL TIPS FOR RUNNING AN FBI EXAM

- Patient Comfort
  - A comfortable patient is more likely to lie still during the exam
  - Cushion every patient while providing support to their limbs
  - Encourage patients to listen to music
  - An empty bladder prior to scan start is a must
- Choosing the dephasing gradient strength
  - Use the recommended dephase strengths as an initial baseline
  - Consider the patient's age, medical condition (e.g., claudication, diabetes), and degree of activity
  - Select a higher value for older and/or less healthy patients who might have slower arterial flow
- Tailoring FBI
  - For unilateral disease, the initial scan may demonstrate flow on the healthy side only
  - To remedy this issue, increase the dephase strength to demonstrate flow on the absent side
  - If flow is missing in either anterior station, use higher dephase strength for the lowest station

NOTE: To decrease the possibility of fluids in the bowel interfering with the quality of the pelvic FBI, patients are asked to refrain from drinking or eating 2 hours prior to scan time.

Practical tips for FBI based on the experience of Connie Luna, lead technologist at the Cardiovascular Diagnostic Center, Monterey, CA.

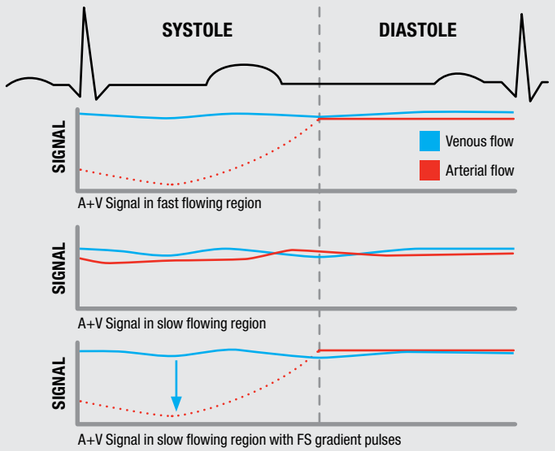


Figure 4: Illustration of the dephasing of the arterial signal that occurs in the FBI exam during systole in a fast flowing region (top) in comparison to a region in which the arterial flow is slow without (center) and with (bottom) the use of flow spoiler pulses. In regions where arterial and venous flow rates are similar, the flow spoiler pulses increase the difference in arterial and venous signal (arrow) to improve the separation between arteries and veins.

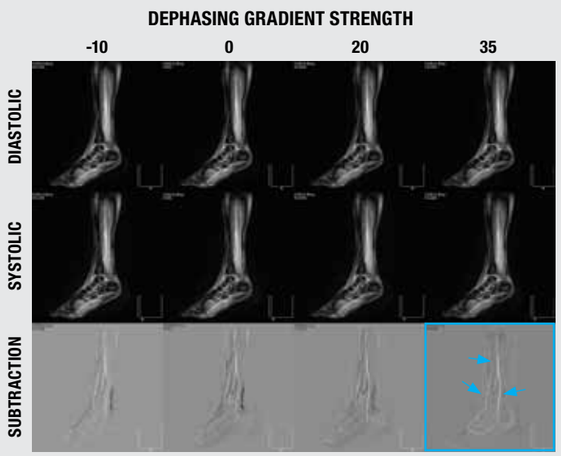


Figure 5: Selected Flow-prep images acquired during diastole (top row) and systole (middle row) with FS gradient pulse values -10, 0, 20, and 35 (left to right). Subtraction of the systolic series from the diastolic series depicts the arteries only (bottom row), and these Flow-prep images assist in determining the optimal dephasing gradient pulse strength. In the example above (bottom right), a dephasing gradient strength of 35 was chosen because it resulted in the most conspicuous representation of the arteries and cancelled the venous signal.

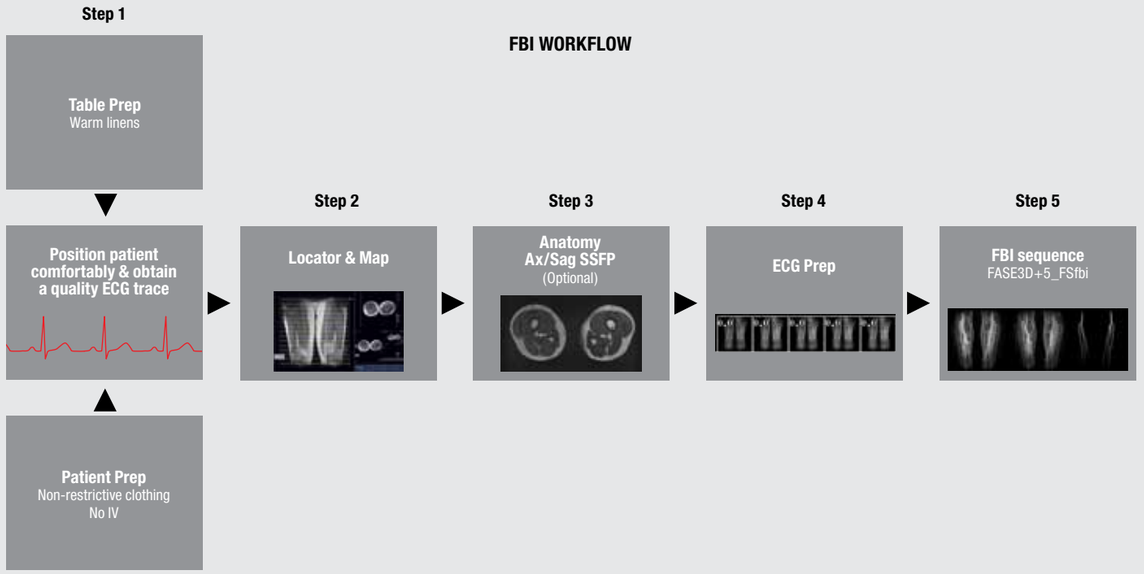


Figure 6: Typical step by step guide for a peripheral runoff non-contrast FBI exam. Note: Flow-prep has been omitted because with experience, a user can make an educated guess on the appropriate flow spoiler pulse. For multiple imaging stations, the operator can simply repeat steps 2 and 5.

	Dephasing Pulse Strength	**ECG Delay Time** (systole/diastole) (unit: ms)
Iliac	-10 -0	50/600
Popliteal	0 -15	100/600
Tibial	10 -25	100/600
Foot	+35	100/600

Table 1: Suggested values for the dephasing pulse strengths and ECG delay times for an average RR interval of 800 ms to 1000 ms. In healthy or younger populations, the lower dephasing pulse yields the optimal results. However, in elderly and/or flow compromised patients, the higher FS gradient strength helps to improve the arterial signal (based on Toshiba Imaging Manual 2B900-366EN and user experience). For patient tailored FS gradient strengths and delay times, use ECG Prep and Flow Prep.

Contrast agent avoidance was especially important due to baseline renal insufficiency and the associated risks of gadolinium for developing NSF. The FBI exam was performed on a ZGV Vantage Atlas™ 1.5T MRI scanner. Coverage from the abdomen to below the popliteal trifurcation was provided by using two Atlas Body coils and the Atlas Spine coil.

The resulting MIP images from the three station FS-FBI exam are shown in **Figure 8**, revealing complex lower extremity disease. Despite the presence of a bilateral iliac stent, the pelvic flow appeared to be normal. However, bilateral superficial occlusions were evident with collaterals and distal reconstitution by way of the profunda vessels. In this patient exam, systolic

times were 100 ms, 100 ms, and 100 ms and the diastolic delay times were 500 ms, 500 ms, and 550 ms for the iliac, femoral, and calf regions, respectively. Dephasing gradient strength values of 0, 15, and 25 were used in the iliac, femoral, and calf regions, respectively.

CLINICAL CASE 2

FS-FBI was used to evaluate the abdominal and peripheral runoff vessels of a 78-year-old man with diabetes, diminished distal pulsations, and claudication (**Figure 9**). The ZGV Vantage Atlas 1.5T MRI scanner was used for this exam. Two Atlas Body coils and the Atlas Spine coil were used to provide coverage from the abdomen to below the popliteal trifurcation.

In this study, the pelvic inflow vessels were found to be patent with evidence of moderate plaque along the vessel walls. In both the left and right legs the SFA and profunda are free of significant luminal obstruction, but moderate ectasia of the distal SFA leading into the popliteal segment was found.

CLINICAL CASE 3

This case compares non-contrast FBI with invasive X-ray Digital Subtraction Angiography (DSA), the gold standard angiographic technique. DSA is an invasive procedure that exposes the patient to X-rays while injecting a contrast dye. While DSA clearly visualizes blood vessels to diagnose occlusions, stenosis, and aneurysms, non-contrast FBI also produces the same diagnostic information non-invasively and without radiation. FBI and DSA can be visually compared in **Figure 10**. The FBI exam was performed on a ZGV Vantage Atlas 1.5T MRI scanner. Systolic and diastolic delay times were 100 ms and 600 ms, respectively, and a dephasing gradient strength of 0 was used for this patient.

The non-contrast FBI technique revealed a tortuous and atherosclerotic distal abdominal aorta with bilateral pelvic inflow disease. Critical narrowings of the left internal and external iliac arteries were noted with less severe narrowing appreciated in the right iliac arteries. As seen in the comparative images, DSA confirmed these findings with a high degree of correspondence.

HEALTHY CASE

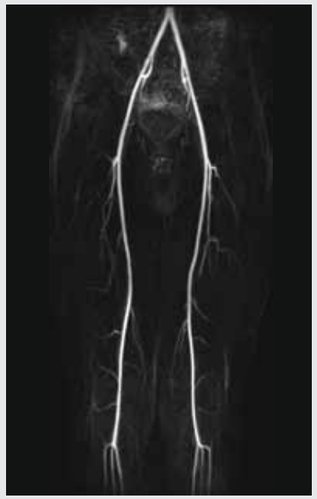


Figure 7: 3D MIP image from a three station runoff non-contrast FS-FBI exam of a healthy volunteer. As seen, the arteries from the iliac region down through the popliteal trifurcation are clearly visualized.

CLINICAL CASE 1

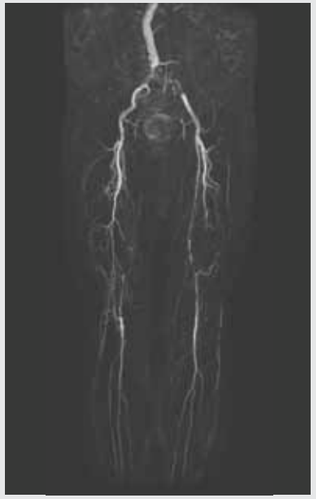


Figure 8: FS-FBI runoff of a patient with a severe peripheral vascular disease and chronic renal insufficiency. Despite the bilateral iliac stent, the non-contrast runoff exam showed otherwise normal pelvic arterial flow.

CLINICAL CASE 2

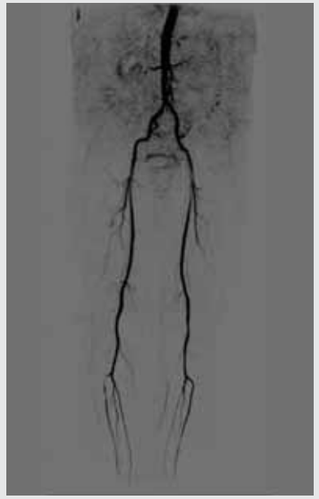


Figure 9: Three-station peripheral non-contrast runoff MRA of a patient with diabetes, weak arterial pulsations in the distal regions and claudication.

CLINICAL CASE 3

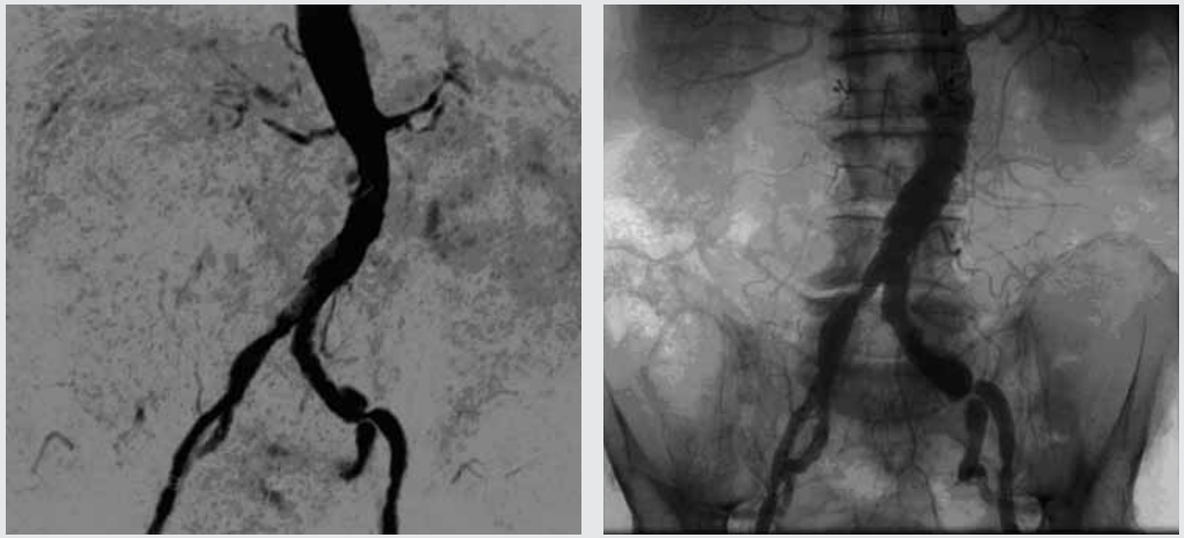


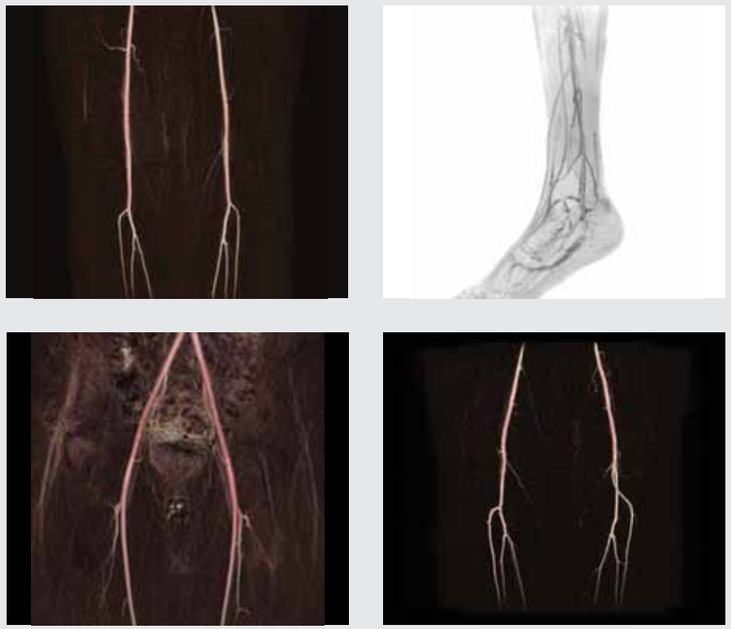
Figure 10: Coronal FBI reverse MIP of the pelvis (left) and corresponding invasive angiogram MIP (right). The non-contrast MRA technique showed critical narrowings of the left internal and external iliac arteries, with less severe narrowing appreciated in the right iliacs. Angiography confirmed these findings with a high degree of correlation.

CONCLUSION

Due to the limitations of conventional non-contrast angiography techniques, such as TOF and PC, CE-MRA emerged as the gold standard in MR Angiography. In the United States, the cost of gadolinium is relatively inexpensive, the cost of the MRI examinations is reimbursable, and CE-MRA is well understood by vascular radiologists. Therefore, there was little motivation to change the fundamental features of a CE-MRA exam. However, recent findings exclusively link NSF to gadolinium, which necessitated urgent changes to the practice of MR Angiography.

Prior to concerns about nephrotoxicity of gadolinium-based agents, Toshiba invested many years into the development of robust non-contrast angiography techniques that addressed constraints on medical practice in Japan. Fortunately, FBI and FS-FBI are vascular imaging techniques that do not require a contrast agent to produce bright blood angiograms and thus can be substituted for the more common CE-MRA methods.

Toshiba's non-contrast enhanced MRA techniques are powerful tools for eliminating gadolinium-based contrast agents in MR angiography. Non-contrast angiography is safe, established and repeatable, and FBI techniques are leading the standards for non-contrast MRA.



Example FS-FBI images of the femoral to popliteal arteries, pedal arteries, iliac and popliteal trifurcation (left to right, top to bottom). MIP images were processed on the Virtual Explorer Workstation.

BENEFITS OF NON-CONTRAST MRA

- The safest choice for your patients
- Does not require the use of contrast agent
- Repeatable
- Does not require an IV injection
- Requires less setup time compared to contrast enhanced MRA
- Does not rely on bolus timing of the injection by the technologist
- 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
- Cost effective:

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.*

REFERENCES:

1. Miyazaki M, Ichinose N, Sugiura S, et al. A novel MR angiography technique: SPEED acquisition using half-Fourier RARE. J Magn Reson Imaging. 1998; 8(2):505-507.

2. Miyazaki M, Tateishi F, Sugiura S, Machida Y, Kassai Y, Abe H. Fresh blood imaging at 0.5-T: natural blood contrast 3D MRA within single breathhold. In "Proceedings, ISMRM, 6th Annual Meeting" Sydney, Australia, p780, 1998.

3. Hayashi S, Miyazaki M. Thoracic duct: visualization at nonenhanced MR lymphography-initial experience. Radiology. 1999; 212(2):598-600.

4. Miyazaki M, Sugiura S, Tateishi F, et al. Non-contrast-enhanced MR angiography using 3D ECG-synchronized half-Fourier fast spin echo. J Magn Reson Imaging. 2000; 12(5):776-783.

5. Urata J, Miyazaki M, Wada H, et al. Clinical evaluation of aortic diseases using nonenhanced MRA with ECG-triggered 3D half-Fourier FSE. J Magn Reson Imaging. 2001; 14(2):113-119.

6. Kawanami S, Nakamura K, Miyazaki M, et al. Flow-weighted MRI of the lungs with the ECG-gated half-Fourier FSE technique: evaluation of the effect of the cardiac cycle. Magn Reson Med Sci. 2002; 1(3):137-147.

7. Miyazaki M, Takai H, Sugiura S, et al. Peripheral MR angiography: separation of arteries from veins with flow-spoiled gradient pulses in electrocardiography-triggered three-dimensional half-Fourier fast spin-echo imaging. Radiology. 2003; 227(3):890-896.

8. Ono A, Murase K, Taniguchi T, et al. Deep vein thrombosis using noncontrast-enhanced MR venography with electrocardiographically gated three-dimensional half-Fourier FSE: preliminary experience. Magn Reson Med. 2009; 61(4):907-917.

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