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Intraoperative Imaging and Image Fusion for Venous Interventions

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ABSTRACT: Advanced imaging for intraoperative evaluation of venous pathologies has played an increasingly significant role in this era of evolving minimally invasive surgical and interventional therapies. The evolution of dedicated venous stents and other novel interventional devices has mandated the need for advanced imaging tools to optimize safe and accurate device deployment. Most venous interventions are typically performed using a combination of standard 2-dimensional (2D) fluoroscopy, digital-subtraction angiography, and intravascular ultrasound imaging techniques. Latest generation computer tomography (CT) and magnetic resonance imaging (MRI) scanners have been shown to provide high-resolution 3D and 4D information about venous vasculature. In addition to morphological imaging, novel MRI techniques such as 3D time-resolved MR venography and 4D flow sequences can provide quantitative information and help visualize intricate flow patterns to better understand complex venous pathologies. Moreover, the high-fidelity information from multiple imaging techniques can be integrated using image fusion to overcome the limitations of current intraoperative imaging techniques. For example, the limitations of standard 2D fluoroscopy and luminal angiography can be compensated for by perivascular and soft-tissue information from MRI during complex venous interventions using image fusion techniques. Intraoperative dynamic evaluation of devices such as venous stents and real-time understanding of changes in flow patterns during venous interventions may be routinely available in future interventional suites with integrated multimodality CT or MR imaging capabilities. The purpose of this review is to discuss the outlook for intraoperative imaging and multimodality image fusion techniques and highlight their value during complex venous interventions.

BACKGROUND

Conventionally, venous interventions are performed using a combination of imaging modalities such as 2-dimensional (2D) fluoroscopy/angiography from mobile C-arm or fixed angiography systems or ultrasound-based techniques such as duplex imaging and intravascular ultrasound imaging. An ideal intraoperative imaging modality provides dynamic morphological information about vascular and perivascular structures for accurate wire or catheter guidance and provides functional information for safe delivery of interventional therapies or devices. Current interventional imaging modalities, however, have several limitations and are far from ideal. Thus, interventionalists must analyze and integrate information from multiple imaging modalities in real time to make therapeutic decisions.[1-3] Furthermore, interventional imaging modalities must be efficient, user friendly, and cost effective to achieve seamless adoption into routine clinical practice.[3] A brief outline of various imaging modalities is provided below to understand their pros and cons from an interventional perspective. Then, the latter section of this review highlights how information from these imaging modalities can be complemented using image fusion techniques to facilitate the treatment of venous diseases. We cannot understate the need for robust training programs to enable better understanding of practical clinical applications and technical limitations of these interventional imaging and image fusion techniques.

INTRAOPERATIVE IMAGING MODALITIES

Ultrasound-Based Imaging Modalities

Duplex sonography is one of the sensitive, low-cost, commonly used imaging techniques for diagnosing and monitoring venous pathologies such as peripheral venous thrombosis or occlusions. Color Doppler flow imaging has been shown to be highly sensitive in detecting and characterizing stenosis, especially in peripheral venous system and hemodialysis access grafts.[4] However, the capabilities of ultrasound are limited in imaging the central venous system. Therefore, digital subtraction central venography has been considered the gold standard for diagnosing central venous thrombosis or occlusive disease because of its superior sensitivity.[5]

From an interventional perspective, ultrasound imaging of deeper and central veins is challenging in the presence of air (bowel gas, lung parenchyma), overlying bone, and patient body habitus.[6] One of the important limitations of ultrasound-based imaging includes interobserver variability in identifying the imaging planes, resulting in poor objective quantification of stenosis. Transesophageal imaging with 3D imaging may be performed for imaging the superior vena cava (SVC), but this technique, too, is limited by its smaller field of view and rather invasive approach. Another ultrasound-based imaging modality commonly used during interventions is intravascular ultrasound, which provides real-time cross-sectional imaging and measurement of physiological parameters such as flow reserve. However, this modality is limited in the presence of venous occlusion and requires a dedicated setup that comes with additional cost.

X-Ray–Based Imaging Modalities

A 2D angiographic roadmap is often performed during venous interventions because of its high spatial resolution and real-time imaging of iodinated contrast flow. Unlike ultrasound-based imaging techniques, this modality is not limited by the presence of air or bone. Some limitations of cineangiography or 2D digital-subtraction angiography are related to their intraluminal and planar imaging nature during interventions. For example, 2D angiographic assessment of narrowing in venous vasculature may be erroneous depending on the angiographic projection and changes in venous flow with respiration. Also, 2D angiographic imaging of complex venous structures using direct injection of iodinated contrast agent may be challenging due to contrast agent wash-out by nonopacified blood from various venous collateral channels and in the presence of thrombus. Hence, venous imaging using angiography typically requires multiple access sites for contrast agent injection proximal and distal to the lesion under evaluation.[4]

Three-dimensional rotational angiography and cone-beam computed tomography (CT) imaging capabilities are available in most advanced angiographic imaging systems equipped with recent flat-panel detector technology.[7-10] This novel intraoperative cone-beam CT imaging technique involves projection x-ray imaging with rotation of C-arm around the patient for ~200 degrees and reconstruction of a 3D CT-like cross-sectional dataset of vasculature and soft-tissue structures. In addition to vascular imaging with contrast injection, this technology can be used for imaging various interventional devices such as inferior vena cava filters and stents, and with appropriate software guidance, can enable safe percutaneous needle procedures in the interventional suite.[6] Any 3D landmark or vascular target annotated in the multiplanar cone-beam CT volumetric dataset can then be overlaid onto 2D fluoroscopy and tracked in real time for further guidance during interventions.

Case Example 1

A 63-year-old woman presented with facial puffiness and left upper extremity swelling. A diagnostic venogram revealed

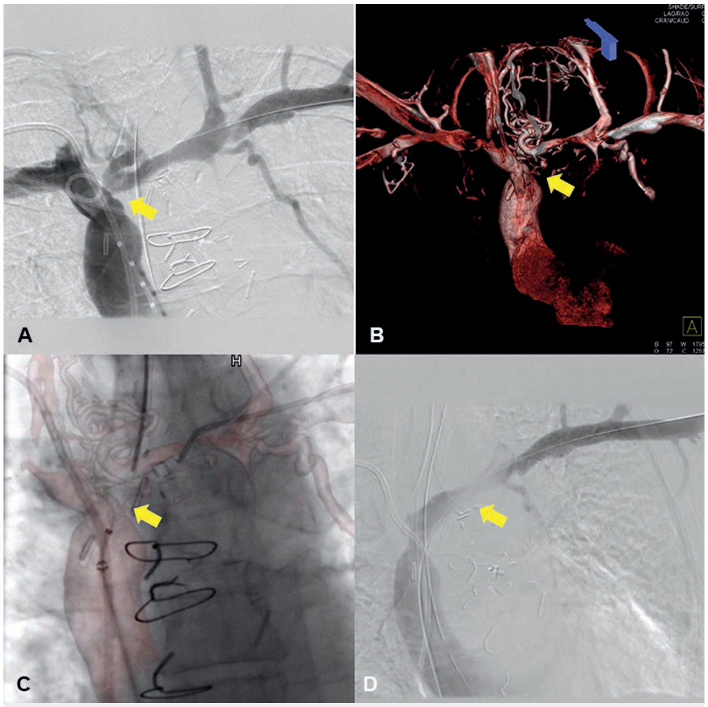

Figure 1.
Intraoperative cone-beam CT imaging of a 63-year-old female with facial puffiness and left upper extremity swelling. (A) A venogram revealed occlusion of the left innominate vein. (B) Intraoperative cone-beam CT with contrast injection showed the 3D anatomy of venous collaterals and the occluded portion of the native innominate vein as a narrow stub (yellow arrow). (C) The entire 3D volume-rendered cone-beam CT reconstruction was overlaid onto real-time fluoroscopy for image guidance during venous recanalization attempts. (D) A venogram after recanalization documenting contrast flow across the left innominate vein. CT: computed tomography

occlusion of the left innominate vein (Figure 1 A). Intraoperative cone-beam CT with contrast injection into right and left subclavian veins showed the 3D anatomy of venous collaterals and the obstructed portion of the native innominate vein as a narrow stub (Figure 1 B). Entire 3D volume-rendered data was then overlaid onto real-time fluoroscopy to provide image guidance during venous recanalization attempts (Figure 1 C). Finally, a post-recanalization completion venogram showed contrast flow across the native left innominate vein (Figure 1 D).

Despite providing high–spatial-resolution imaging of venous vasculature and devices, cone-beam CT imaging may be limited by a smaller field of view and relatively lower soft-tissue resolution compared to conventional multislice CT imaging,[11] which is superior in providing cross-sectional multiplanar reconstructions of venous structures with a larger field of view, especially in the presence of central venous occlusive disease and venous stents. In addition, recent third-generation CT scanners can acquire 3D images at a much faster acquisition speed while still providing better image quality at a lower radiation dose. Recent CT scanners, by using a dual-energy imaging technique, may also assist with lesion characterization in occlusive venous diseases.[12,13] However, CT imaging of complex venous occlusions can be challenging because of contrast-enhanced blood merging with unenhanced venous return from the lower body.[6] Unlike MRI with delayed imaging or blood pool imaging protocols, CT imaging for venous vasculature with appropriate contrast timing or bolus tracking can be difficult in the presence of venous collaterals.

Magnetic Resonance-Based Imaging Modalities

Magnetic resonance venography (MRV) has been demonstrated as an emerging modality for imaging and characterizing venous occlusive disease with excellent repeatability.[14-18] Studies have recently reported MR image-based characterization of thrombus in deep venous vasculature and measurement of thrombus age.[17,18] In addition, time-resolved MR venography has been shown to be helpful in central venous access in challenging patients.[19] These studies highlight the novel information that MR imaging reveals not only from a diagnostic perspective but also from an interventional perspective. Use of gadolinium contrast agent can be nephrotoxic in patients with chronic renal failure, with risk of nephrogenic systemic fibrosis. Thus, MR imaging of central veins using noncontrast techniques such as time-of-flight MRA sequence and 3D steady-state free-precession sequences have been developed.[20] More recently, respiratory gated noncontrast SPACE MRA sequence has been shown to image central veins with better signal- and contrast-to-noise ratios.[21] In patients with renal insufficiency, novel MR contrast agents such as iron-based ferumoxytol (Feraheme) may be used to provide blood pool imaging that is often well-suited for imaging central and peripheral venous diseases.[22,23] Time-resolved 3D phase-contrast MR imaging with three-directional velocity encoding, also called 4D-flow MRI, has shown clinical value in imaging hemodynamic flow patterns and quantifying flow in various vascular beds,[24-27] including the portal venous system.[28] Despite these promising techniques, MR imaging comes with its own limitations in the presence of metallic stents and has a relatively longer acquisition time compared to CT imaging. The underlying hypothesis behind MRV imaging for central venous occlusions is that, in addition to mapping the occluded venous segments, delayed imaging with blood-pool contrast agent may be able to visualize perivascular structures such as the vasa-vasorum of originally occluded veins. From an interventional standpoint, this key information may help with better patient selection for optimal therapeutic intervention when occluded venous segments are not well visualized by luminal angiography (Figure 2).

Upcoming novel imaging modalities based on fluorescence imaging, infrared-based imaging, and augmented reality-based 3D or 4D image visualization may provide better assessment of venous pathologies and assist with procedural planning and optimizing decisions regarding appropriate device implantation, thereby enhancing how venous procedures are performed in the future.[29-31]

IMAGE FUSION FOR VENOUS INTERVENTIONS

As highlighted in the last few paragraphs, individual interventional imaging techniques have their own advantages and limitations. Integration of information from multimodality imaging datasets may facilitate optimal diagnosis, procedural

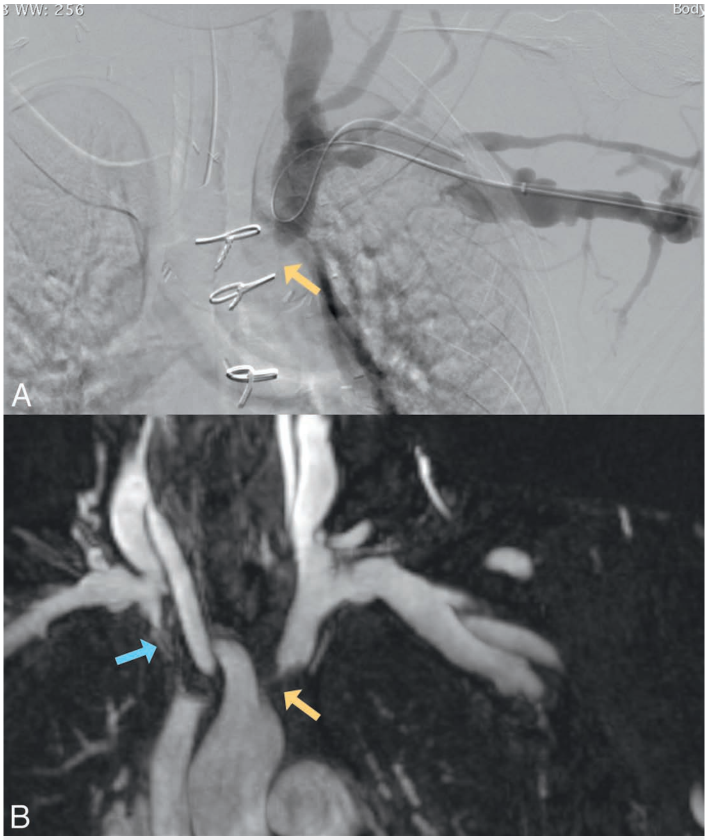

Figure 2.
(A) Digital subtraction angiography images acquired after iodinated contrast injection in left subclavian vein demonstrated occluded left innominate vein (yellow arrow). (B) Coronal maximum-intensity projection rendering of subtracted magnetic resonance venography images acquired after blood pool contrast agent injection (Feraheme) demonstrated perivascular information around the occluded right (blue arrow) and left innominate veins (yellow arrow) that were not visualized by luminal venography.

planning, and guiding treatment of complex venous steno-occlusive diseases. This task of combining information from multiple imaging modalities can be achieved by image fusion techniques, wherein images from different modalities are overlaid to better visualize the diseased vasculature. A subgroup of patients who currently undergo diagnostic venography using invasive imaging can instead be evaluated by a combination of noninvasive imaging modalities such as ultrasound, CT, and MR imaging techniques.

Enhancing 2D Fluoroscopy with Image Fusion

The expanding role of image fusion guidance for interventional imaging can be attributed to the recent growth of percutaneous novel implantable devices and adoption of minimally invasive surgical techniques. The limitations of one imaging modality can be offset by incorporating information from another modality, especially during complex venous interventions. The additional value of CT and MR image fusion with fluoroscopy has been demonstrated in various arterial and percutaneous interventions.[2,32-37] Although incorporation of multimodality imaging data for guidance is not performed routinely for venous interventions, recanalization for central venous occlusion would be a good setting for determining the additional value of such image fusion techniques.

CT fluoroscopy image fusion. Akin to intraoperative image guidance using CTA-fluoroscopy image fusion, venous morphology can be mapped from CT venography and projected as an overlay onto fluoroscopy using one of the two following methods: 3D-3D image fusion, where a preoperative CT venogram is fused with a noncontrast 3D intraoperative cone-beam CT image acquired during intervention,[35] or 2D-3D image fusion, where a preoperative CT venogram is fused using two fluoroscopic images acquired at least 30 degrees apart during intervention.[38,39]

3D-3D image fusion of a preoperative CT dataset and noncontrast cone-beam CT is often performed using bony landmarks, such as the spine, followed by vascular contours. Unlike CT image fusion for arterial interventions, critical landmarks for image fusion such as wall calcifications are not often visualized in venous vasculature.[40,41] 2D-3D image fusion is performed by aligning the vascular information from a venogram/arteriogram with a preoperative CT dataset. Whenever available, context-specific image registration can be performed based on relevant landmarks seen in fluoroscopy and CT images, such as pre-existing stents, surgical clips, or wires/catheters placed in the vessel of interest.[42]

MR fluoroscopy image fusion. MR imaging has the potential to integrate vessel wall information, such as outline of vasa-vasorum from originally occluded veins, obtained by fluoroscopy—for example, during endovascular recanalization of chronically occluded central veins. A few preclinical studies have shown that findings from MR imaging of the vessel wall and thrombus can be correlated to thrombus morphology by histopathology.[43,44] Such complementary information of occluded venous wall may be integrated as an overlay onto fluoroscopy during complex endovascular recanalization procedures for better 3D guidance. In addition, intraoperative cone-beam CT can provide soft-tissue information for troubleshooting in complex cases to better understand 3D catheter orientation relative to the target vessel and to rule out perforation during recanalization attempts.

MR image fusion with fluoroscopy is often considered challenging because most of the commercially available image fusion algorithms are optimized to work on joint histograms created from similar datasets such as CT and cone-beam CT. Software algorithms can create a synthetic pseudo-C–like image from MR datasets that can be used for optimizing image fusion for MR datasets. Currently, MRI-fluoroscopy image fusion is semiautomated compared to image fusion with CTA, which has already been routinely adopted for complex arterial interventions. 3D-3D image fusion can be optimized by aligning the bony landmarks or indwelling catheters/wire in the noncontrast cone-beam CT with central venous vasculature in the MRI dataset.[45] Once image fusion is completed, the electronically annotated vessel landmarks and centerlines can be overlaid onto fluoroscopy during recanalization attempts using dedicated coaxial support catheters (CXI, Cook Medical), sharp recanalization devices, or radiofrequency wire when the target is localized.[46] These electronic landmarks are automatically tracked with changes in C-arm positions, image zoom, and table movements. Using an MR fluoroscopy image overlay of the target vessel enhances procedural planning and provides addition guidance for the interventionalists to visualize the venous lesions better during complex procedures and has been shown to correlate with recanalization success in patients who underwent prior attempts without image fusion. In a recent publication, Schwein et al. illustrated clinical workflow, MR and cone-beam CT imaging parameters, and detailed procedural results suggesting that MRV image fusion is feasible and may improve procedural success and safety.[45]

Case Example 2

A 55-year-old woman presented with central venous occlusion after undergoing prior recanalization attempts. Figure 3 illustrates the steps of image fusion, in which occluded venous vasculature information from MRI were overlaid onto fluoroscopy. A baseline venogram demonstrated complete occlusion of the left innominate vein (Figure 3 A). Intraoperative

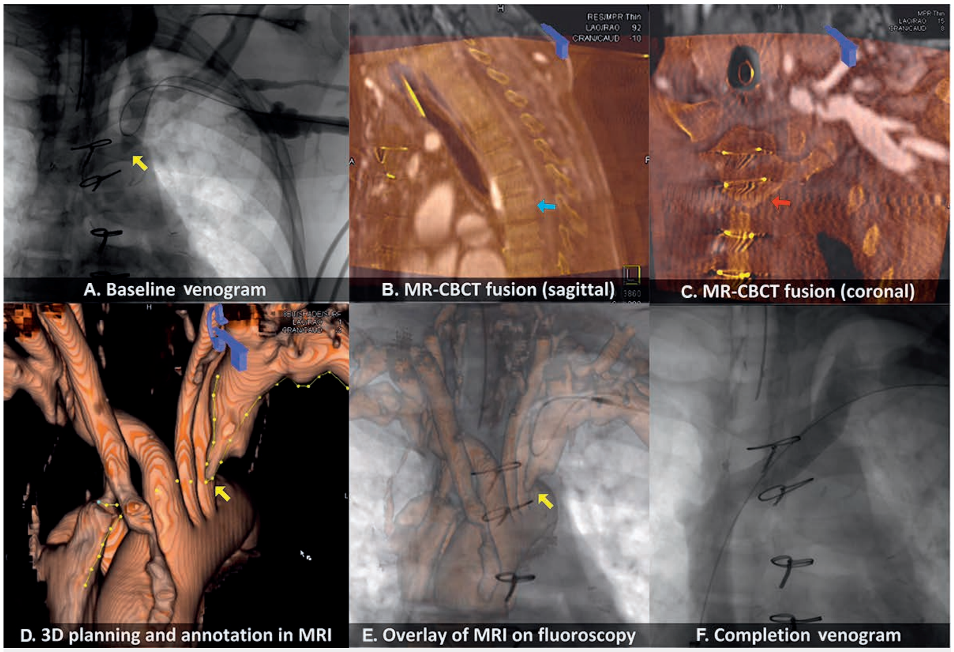

Figure 3.
Illustration of MRI-cone-beam CT image fusion and overlay on fluoroscopy for guidance during recanalization on a 55-year-old female with central venous occlusion after failed prior recanalization attempts. (A) A baseline venogram demonstrated complete occlusion of the left innominate vein (yellow arrow). (B, C) Intraoperative noncontrast cone-beam CT was acquired and coregistered with MRI dataset (T1-VIBE) using the spine (blue arrow) and sternum (red arrow) as alignment landmarks. (D) T1-VIBE and subtracted MR images demonstrated a venous lesion at the aortic arch level, where the path of the vein was electronically annotated. (E) This annotated vessel path was then overlaid on 2D fluoroscopy during the recanalization attempts. Accuracy of overlay was checked using wires/catheters at multiple fluoroscopic projections without the need for an additional venogram. (F) A completion venogram showed recanalized left innominate vein after stenting. MRI: magnetic resonance imaging; CT: computed tomography; CBCT: cone beam computed tomography

KEY POINTS

- Current imaging tools provide the capability to fuse and integrate 3-dimensional (3D) preprocedural computed tomography or magnetic resonance imaging datasets with 2D fluoroscopy for better image guidance during complex venous interventions, especially during central venous occlusions.
- Multimodality imaging studies using novel MR imaging sequences for lesion characterization are evolving to enable better understanding of the pathophysiology and to optimize therapeutic decisions for the complex venous diseases.
- Although future multimodality imaging suites have been integrated from a hardware standpoint, further seamless integration of complementary information and training of interventional team is essential for optimal use.

noncontrast cone-beam computed tomography was acquired and coregistered with a magnetic resonance imaging (MRI) dataset (T1-VIBE) using the spine (blue arrow) and sternum (red arrow) as alignment landmarks (Figure 3 B, C). T1-VIBE and subtracted MR images demonstrated a venous lesion at the aortic arch level, where the path of the vein was electronically annotated (Figure 3 D). This annotated path was then overlaid on 2-dimensional fluoroscopy during the recanalization attempts. During the procedure, the accuracy of overlay and the recanalization catheter/wire was checked at multiple fluoroscopic projections without the need for an additional venogram (Figure 3 E). A completion angiogram venogram shows the recanalized left innominate vein after stenting (Figure 3 F).

Towards Integrated Imaging and Devices

Despite the advantages of information gleaned from multimodality data overlaid onto fluoroscopy, the obvious limitation is that any prior dataset does not reflect the changes in vasculature during intervention. The interventionalist still needs to navigate wires and catheters based on limited information. In this context, intravascular ultrasound imaging can be coregistered with fluoroscopy or digital subtraction venography during the intervention to compare and understand the lesion morphology and features in both imaging modalities.[47,48] In addition to venous stents, novel recanalization devices have recently entered the market, bolstering venous device innovation[49] and highlighting the need for integration of cross-sectional 3D imaging with device deployment.

Any additional imaging data acquired during the procedure that can potentially influence interventional decision making can be integrated into the procedural workflow. In this context, future interventional suites or hybrid operating rooms are poised to gather and incorporate multimodality imaging data into therapeutic decision making. In fact, multimodality combination imaging suites and hybrid operating rooms are being installed, where intraoperative MRI or CT imaging can be performed during the procedure and overlaid with fluoroscopy. So far, such multimodality imaging suites have has been shown to add value during chemoembolization or radioembolization of liver tumors under near-simultaneous CT and fluoroscopy guidance as well as cardiac catheterization and interventional procedures performed under interventional MRI guidance.[50]

SUMMARY

Multimodal imaging, particularly recent MR imaging techniques, has shown promising results for disease characterization and can potentially guide future interventional therapies for venous occlusive diseases. Current imaging systems provide preliminary solutions for enhancing fluoroscopy with information from preoperative CT or MRI datasets to provide guidance during complex interventions. However, seamless real-time intraoperative image guidance may be helpful for improving safety and for optimizing therapeutic decisions. This highlights the need for an integrated platform for multimodality image acquisition and image guidance during complex venous interventions.

Conflict of Interest Disclosure:
Dr. Chinnadurai is a full-time senior staff scientist for Advanced Therapies, Siemens Medical Solutions USA, Inc.

Keywords:
image fusion, MRI venous imaging, cone-beam CT imaging, intraoperative imaging, multimodality image guidance

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