Subtraction Imaging: Applications for Nonvascular Abdominal MRI

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OBJECTIVE. In this article we will illustrate the role of subtraction imaging for abdominal MRI applications.

CONCLUSION. Subtraction imaging has multiple applications for imaging the mediastinum, abdomen, and pelvis. Removing any preexisting signal of T1 unenhanced images causes contrast enhancement within a mass to become more conspicuous on subtracted sequences. This is helpful when evaluating a lesion with high signal on unenhanced T1-weighted sequences, where visual detection of enhancement can be difficult on conventional MRI.

Subtraction imaging is a readily available technique that is routinely used in MRI of the breast and in MR angiography. There have been reports of subtraction imaging in the solid organs of the abdomen [1–4], however it may be underused in routine body MRI applications, including but not limited to hepatic, renal, and adrenal imaging. This pictorial essay illustrates scenarios in which subtraction imaging can be valuable in characterizing a lesion and confidently arriving at a diagnosis. In particular, subtraction imaging can be helpful in evaluating for the presence of a neoplasm in hemorrhagic masses, complicated cysts, and other settings in which determining the presence or absence of enhancement is critical. Qualitative detection of enhancement within such lesions is often not a straightforward task due to hemorrhagic or proteinaceous contents making them hyperdense on CT or high signal on unenhanced T1-weighted MRI pulse sequences. Subtraction imaging can make evaluation of these lesions more straightforward.

Specific Applications

Simple Hemorrhage Versus Hemorrhagic Mass

In the setting of spontaneous hemorrhage within an intraabdominal organ, it is imperative to search for an underlying lesion responsible for the bleeding. Acute or subacute hemorrhage will be hyperdense on CT. On MRI, areas of high signal will be present on unenhanced T1-weighted sequences because of the presence of intracellular or extracellular met-hemoglobin. The presence of high density on CT or bright signal on unenhanced T1-weighted MRI sequences makes qualitative evaluation of enhancement difficult. However, any signal from blood products will be removed on subtraction images, making enhancement within a lesion much more conspicuous. Accordingly, a simple hematoma should appear as a signal void on subtraction images because it will not contain enhancing elements.

Within the liver, hepatocellular adenomas and carcinomas are the two neoplasms that are most likely to spontaneously bleed. Other causes of nontraumatic hepatic hemorrhage include HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome, coagulopathy, amyloidosis, and peliosis hepatis [5]. Acute flank pain secondary to spontaneous hemorrhage is a well-known presentation of renal cell carcinoma (Fig. 1). Nontraumatic adrenal hemorrhage is relatively common. This can be due to a hemorrhagic mass such as an adrenal cortical carcinoma, pheochromocytoma, myelolipoma, or metastasis or it can be secondary to nonneoplastic causes such as anticoagulation, bleeding diathesis (Fig. 2), sepsis, stress,
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or trauma [6]. In patients with an equivocal history of trauma, subtraction imaging can be used to characterize a complex splenic mass as either a hematoma or neoplasm (Fig. 3).

Other clinical settings in which subtraction images may be useful to distinguish hematoma from tumor are in the postoperative period (Fig. 4) and in patients receiving anticoagulation therapy.

Complex Cysts

Complex renal cysts often show high signal on unenhanced T1-weighted sequences due to the presence of either intracystic hemorrhage or proteinaceous debris. These cysts are hyperdense on CT. Subtraction imaging has been shown to be highly sensitive for detection of enhancement within these lesions and thus for accurate classification as either benign hemorrhagic cysts or cystic renal cell carcinomas [4] (Fig. 5). Subtraction imaging should be used for analysis of enhancement within this subset of cystic renal masses on MRI because the use of quantitative measurements (region of interest [ROI]) can result in false-negative results [4]. MRI is also not subject to pseudoenhancement artifact, which can limit evaluation of small intraparenchymal renal masses on CT because of a correction process that artifactually increases attenuation values [7] (Fig. 6).

Cirrhotic Nodules

In the cirrhotic liver, a nodule that exhibits enhancement greater than that of background liver on arterial-dominant gadolinium-enhanced images is presumed to be a hepatocellular carcinoma because this degree of enhancement is infrequently seen in dysplastic nodules and rarely seen in regenerative nodules [2]. However, regenerative and dysplastic nodules and hepatocellular carcinoma can all exhibit high signal on unenhanced T1-weighted sequences [2]. This can make qualitative analysis of the degree of enhancement within these lesions difficult. Subtraction imaging of dynamic gadolinium-enhanced sequences will remove any preexisting T1 signal and thus facilitate detection of lesion enhancement [2, 3].

Postablation Procedures

Radiofrequency ablation and cryoablation are being used with increased frequency for treatment of malignancies in the liver, kidneys, and other organs. The goal of either procedure is complete tumor necrosis. Postprocedural cross-sectional imaging is used to analyze the lesion for the presence of recurrent or residual neoplasm. This is a critical determination in the management of these patients, and subtraction imaging is ideally suited for such a role. Subtraction can make subtle enhancement within a tumor more conspicuous and can remove high T1 signal, which is often present because of coagulation necrosis (Fig. 7). It can also help differentiate the smooth, indistinct peritumoral enhancement seen in benign posttreatment hyperemia from the discontinuous nodular enhancement of viable tumor [4].

Other Applications

Subtraction imaging may also be useful for imaging the gallbladder in situations in which the differential diagnosis is between tumefactive sludge versus wall thickening from neoplasm. Whereas sonography using color or power Doppler or CT performed with and without contrast material can suggest the diagnosis of neoplasm by showing the presence of either blood flow or enhancement within the area in question, MRI with subtraction imaging can aid in making a more confident diagnosis. This is especially true in cases of early carcinoma (Fig. 8) when there is no detectable extramural disease.

Finally, a potentially important future indication for subtraction was recently described by Ajay et al. [8], who showed the utility of subtraction imaging in increasing sensitivity and decreasing readout time of dark-lumen MR colonography in a study of 20 patients in whom the lesions were confirmed on conventional endoscopy.

Pitfalls of Subtraction Imaging

An imperative technical principle of subtraction imaging is to keep all parameters constant on the unenhanced and contrast-enhanced images. This includes TR, TE, flip angle, slice thickness, matrix, and zero interpolation factor. It is also essential that the patient’s position remain unchanged within the magnet during the unenhanced and contrast-enhanced sequences. The patient should be able to maintain a breath-hold throughout the acquisition, and the breath-hold should be reproducible from sequence to sequence. Not fulfilling one or more of these criteria will result in misregistration artifact and image degradation on the subtraction series.

Imaging at end expiration may yield more consistent data sets than imaging at end inspiration [9]. Misregistration artifact can be identified by high signal intensity that outlines enhancing structures. If this occurs, subtracting individual images rather than entire data sets can be useful. The radiologist can select a single image from the unenhanced series and a single image from the gadolinium-enhanced series that corresponds to the identical anatomic level. The technologist can then subtract these selected images, which may reduce the degree of misregistration.

Conclusion

Subtraction MRI is an excellent technique for evaluating hemorrhagic masses or lesions with high signal intensity on unenhanced T1-weighted sequences, such as complicated cysts or hepatic nodules. Moreover, there are additional clinical scenarios in which it is essential to determine the presence or absence of enhancement within a mass. These include postablation therapy and evaluation for residual tumor versus postsurgical change. In these situations, the body imager should consider subtraction MRI as a useful problem-solving technique that can aid in arriving at a confident diagnosis.

References

Fig. 1—49-year-old woman with acute flank pain. 
A, Unenhanced axial CT scan at level of kidneys shows large acute subcapsular hematoma (arrows) in midpole of left kidney. 
B, Contrast-enhanced axial CT scan shows peripheral areas of high attenuation (arrows); however, differentiation of enhancement versus high-density blood is difficult. 
C, Axial T1-weighted spoiled gradient-recalled echo (SPGR) fat-suppressed image shows heterogeneous signal intensity (arrowheads) within area of hemorrhage. 
D, Axial T1-weighted SPGR contrast-enhanced image shows high signal intensity in periphery of hematoma (arrow) suggestive of enhancing tumor. 
E, Axial subtraction image confirms presence of enhancing peripheral mass (black arrows) and signal void hematoma (white arrow). Large hemorrhagic renal cell carcinoma was found at nephrectomy.

Fig. 2—74-year-old man with known history of right adrenal mass who presented for MRI for further characterization. 
A, Axial T1-weighted fat-suppressed spoiled gradient-recalled echo (SPGR) image shows 7-cm right adrenal mass with areas of high signal intensity suggestive of hemorrhage (arrow). LK = left kidney. 
(Fig. 2 continues on next page)
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Fig. 2 (continued)—74-year-old man with known history of right adrenal mass who presented for MRI for further characterization.

B, Axial T1-weighted fat-suppressed SPGR gadolinium-enhanced image again shows areas of high signal intensity (arrow). It is difficult to ascertain whether this is due to enhancement or hemorrhage. LK = left kidney.

C, Axial subtraction image shows lack of enhancement within this mass (arrow) consistent with simple hemorrhage. Because of high clinical suspicion for malignancy, patient underwent adrenalectomy. Pathology showed presence of hemorrhage without evidence of neoplasm. Patient was later found to have myelofibrosis. LK = left kidney.

Fig. 3—72-year-old man with hemorrhagic splenic mass on CT (not shown) and questionable history of trauma.

A, Axial T1-weighted fat-suppressed spoiled gradient-recalled echo (SPGR) unenhanced image through spleen shows large heterogeneous mass with areas of high signal intensity (arrowheads) and more central, focal hyperintense area (arrow). S = spleen.

B, Axial T1-weighted fat-suppressed SPGR contrast-enhanced image shows enhancement of normal splenic parenchyma (arrows). However, it is difficult to determine whether there is enhancement within mass. S = spleen.

C, Subtraction image shows definite areas of enhancement consistent with neoplasm (arrowheads). Areas of hematoma are signal void (arrow). Hemorrhagic lymphoma was found at splenectomy. S = spleen.
Fig. 4—25-year-old woman after attempted resection of pelvic sidewall mass. Initial pathology only showed hematoma. MRI was performed to determine presence of residual tumor.

A, Axial T1-weighted fat-suppressed spoiled gradient-recalled echo (SPGR) unenhanced image shows hyperintense mass (black arrow) in left perivesical space, displacing urinary bladder to right. Second mass (white arrow) of mixed signal intensity is identified posterior and inferior in relation to this mass with displacement of rectum and lower uterine segment to right (asterisk).

B, T1-weighted fat-suppressed SPGR gadolinium-enhanced image shows similar areas of high signal intensity in both lesions (arrows).

C, Axial subtraction image shows marked enhancement of deep left pelvic mass (black arrows) confirming presence of residual neoplasm. Left perivesical mass (white arrow) is now signal void, consistent with postoperative hematoma. Pathologic reanalysis showed desmoid tumor.

Fig. 5—45-year-old man presenting with hematuria.

A, Unenhanced CT scan shows indeterminate hyperdense, exophytic renal mass (arrow) in midpole of left kidney. MRI was performed to exclude underlying mass.

B, Axial T1-weighted spoiled gradient-recalled echo (SPGR) unenhanced MR image shows high signal intensity within renal mass (arrow).

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**Fig. 5 (continued)—**45-year-old man presenting with hematuria.

C, It is difficult to visually determine whether high signal within mass (arrow) is due to enhancement or to intrinsic T1 brightness from hemorrhage or protein.

D, Axial subtraction image shows complete lack of enhancement within lesion (arrow), consistent with benign cyst.

**Fig. 6—**36-year-old man with metastatic disease to ribs and spine, without known primary tumor.

A, Contrast-enhanced CT image shows indeterminate small left renal lesion (arrow).

B, Axial T1-weighted fat-suppressed spoiled gradient-recalled echo (SPGR) unenhanced image shows mildly hyperintense mass in upper pole of left kidney (arrow).

C, Axial T1-weighted fat-suppressed SPGR contrast-enhanced image. It is difficult to determine whether high signal intensity within mass (arrow) is due to enhancement or intrinsic high signal.

D, Axial subtraction image clearly shows nodular internal enhancement (arrow), consistent with small renal cell carcinoma. Biopsy of bone lesion showed carcinoma consistent with renal origin.
Fig. 7—65-year-old cirrhotic man after radiofrequency ablation for hepatocellular carcinoma.

A, Axial T1-weighted fat-suppressed spoiled gradient-recalled echo (SPGR) unenhanced image shows heterogeneous but mostly hyperintense mass (arrowheads).

B, Axial T1-weighted fat-suppressed SPGR contrast-enhanced image shows areas of high signal intensity (arrows) that could be compatible with either hemorrhagic necrosis or tumor recurrence. Arrowheads indicate mass.

C, Axial T1 subtraction image shows conspicuous area of nodular enhancement, consistent with tumor recurrence (arrow). Arrowheads indicate mass.
Fig. 8—67-year-old man with fever secondary to Escherichia coli bacteremia.

A, Contrast-enhanced axial CT image shows soft-tissue density along posterior wall of gallbladder (arrowheads). Differential diagnosis includes tumefactive sludge or gallbladder neoplasm.

B, Axial T1-weighted fat-suppressed spoiled gradient-recalled echo (SPGR) unenhanced image shows isointense polypoid lesion (arrow) along posterior wall of gallbladder.

C, Axial T1-weighted fat-suppressed SPGR contrast-enhanced image shows probable enhancement within mass (arrow).

D, Axial subtraction image shows avid enhancement of mass (arrow), highly suspicious for gallbladder neoplasm. Localized gallbladder cancer was found at cholecystectomy.