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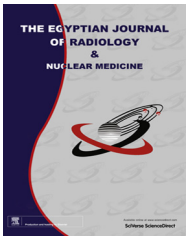

ORIGINAL ARTICLE

# Subtraction images: A really helpful tool in non-vascular MRI

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**KEYWORDS**

Magnetic resonance imaging (MRI);
Enhancement;
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**Abstract** *Background:* Subtraction imaging is a technique whereby an unenhanced T1-weighted sequence is digitally subtracted from the identical sequence performed after gadolinium administration.

*Aim of the work:* This study will highlight the role of subtraction imaging for non-vascular MRI applications.

*Subjects and methods:* The study included 40 patients presenting with lesions in different parts of the body, that are initially hyperintense on T1W sequences.

We used post-processing software (Osirix) to digitally subtract the pre-enhancement from the post enhancement sequences.

*Results:* Based on subtraction imaging findings 5 patients were diagnosed with intraocular melanomas, two patients were diagnosed with hemorrhagic cysts in the masseter muscle , two patients were diagnosed with hemorrhagic cysts in the parotid gland, two patients were diagnosed with dysplastic hepatic nodules, 5 patients were diagnosed with post-ablation necrosis following hepatocellular carcinoma (HCC) treatment, two patients showed recurrent HCC after chemoembolisation, 3 patients showed chemoembolised HCC without recurrence, 4 patients showed intraluminal gall bladder sludge, 4 patients showed hemorrhagic renal cysts, one patient showed solid papillary neoplasm of the pancreas, 6 patients showed chocolate ovarian cysts, two patient showed ovarian cystadenoma and two patients showed ovarian cystadenocarcinoma.

*Conclusion:* Subtraction MRI is very helpful tool in non-vascular MRI applications.



## 1. Introduction

Subtraction imaging is a readily available technique that is routinely used in MR angiography. It may be still underused in routine body MR applications. It is simply a technique whereby an unenhanced T1-weighted sequence is digitally subtracted from the identical sequence performed after gadolinium administration. By performing this operation, any native T1 signal is removed and the remaining signal on

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the subtracted images is due solely to enhancement. There are many potential applications for this technique including 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

**Table 1** Shows the distribution of the 40 patients included in this study according to the site of the lesion, pattern of enhancement and pathological diagnosis.

| Type of lesion | Enhancement | Number | % |
|---|---|---|---|
| Choroidal melanoma | Positive | 5 | 12.5 |
| Hemorrhagic masseter cyst | Absent | 2 | 5 |
| Hemorrhagic Parotid cyst | Absent | 2 | 5 |
| Dysplastic hepatic nodule | Absent | 2 | 5 |
| HCC (post-ablation necrosis) | Absent | 5 | 12.5 |
| HCC (recurrent after chemoembolization) | Positive | 2 | 5 |
| HCC (chemoembolized without recurrence) | Absent | 3 | 7.5 |
| Gall bladder sludge | Absent | 4 | 10 |
| Hemorrhagic renal cyst | Absent | 4 | 10 |
| Solid papillary neoplasm of pancreas | Tiny enhancing papilla | 1 | 2.5 |
| Ovarian chocolate cyst | Absent | 6 | 15 |
| Ovarian cystadenoma | Internal enhancing septations | 2 | 5 |
| Ovarian cystadenocarcinoma | Solid enhancing mural nodules | 2 | 5 |

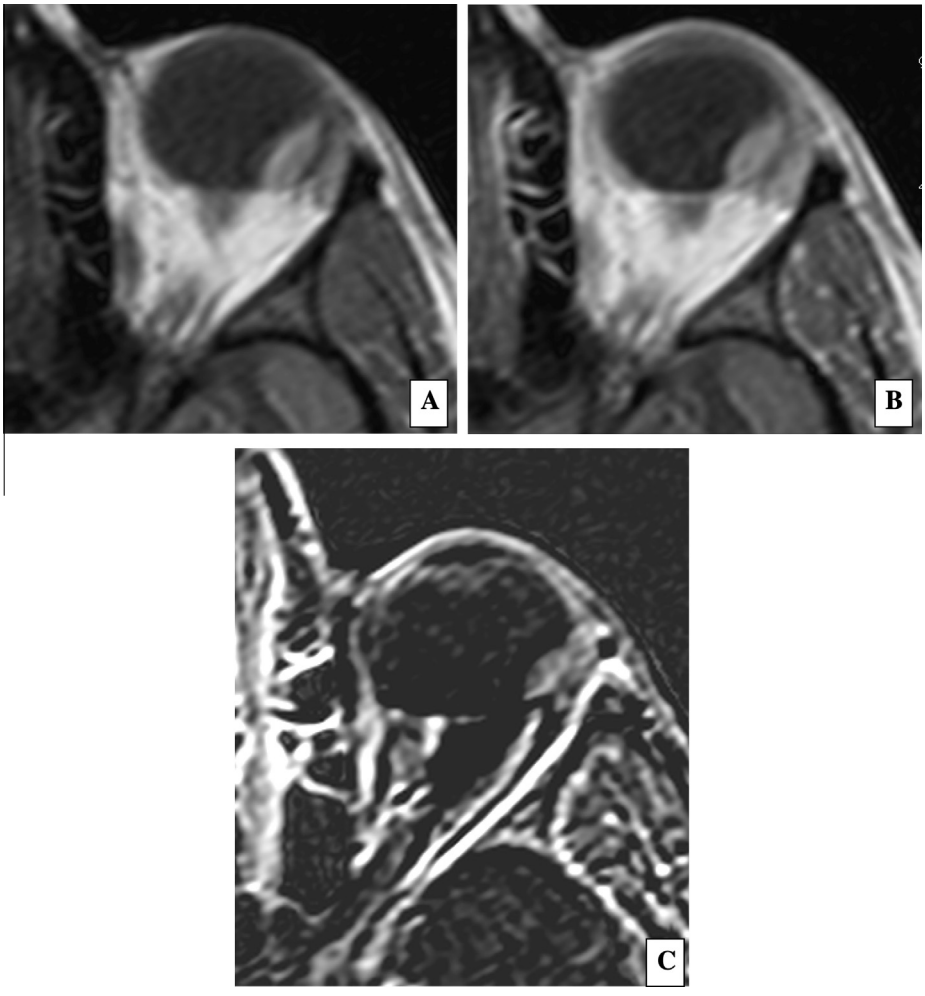


**Fig. 1** Pre and postcontrast enhanced T1W MRI images (A and B) of the left orbit showing an initially hyperintense intraocular lesion along the lateral aspect of the choroidal lining of the left globe. Subtraction image (C) shows positive enhancement of the lesion denoting its neoplastic nature. The lesion was histopathologically proven to be choroidal melanoma.

unenhanced T1-weighted MRI pulse sequences. Subtraction imaging can make evaluation of these lesions more straightforward. Its use in non vascular MRI applications has not been widely discussed in the radiological literature (1–4).

This study will highlight the role of subtraction imaging for non-vascular MRI applications.

## 2. Materials and methods

This retrospective study included 40 patients presenting with lesions in different parts of the body, that are initially hyperintense on T1W sequences, and in whom visual assessment of enhancement is difficult.

Different types of MRI exams were included (heterogeneous sample) to show the utility of the post-processing technique, irrespective of the body part under study. All the studies were performed on a 1.5 T closed magnet MRI machine (Avanto, Siemens, Erlangen, Germany). We used a set of 8-channel phased array coils dedicated to different body parts included in the study.

An integral step of the MRI technique is the exact similarity in all parameters (FOV, slice thickness, TR, TE, fat suppression …etc.) between both sequences to be subtracted, i.e. pre- and post Gadolinium sequences.

The data sets were then transferred to an offline post-processing workstation (Osirix: Version 4.1.2; www.osirix-viewer.com) to digitally subtract the pre-enhancement from the post enhancement sequences.

Objective visual assessment of the subtraction image was used to assess enhancement: If no enhancement is noted, there would be a signal void in the corresponding voxel. Any visually detectable signal on this image would thus represent enhancement.

The studies were viewed twice by both authors separately. In the first interpretation session, only the original dataset was shown, without the subtraction images. Each author was required to note whether the initially T1 hyperintense lesion was "enhancing", "not enhancing" or "indeterminate". Then after one month, and in a different randomized order, the cases where visualized again with the help of the subtraction images, and each author had again to classify the lesion as "enhancing", "not enhancing" or "indeterminate."

The final diagnosis was reached in all cases through histopathological/cytological evidence, either after surgical excision of the lesion, image-guided biopsy or FNAC of its fluid contents.

## 3. Results

This study included 40 patients presenting with lesions in different parts of the body all showing a hyperintense signal in the non contrast enhanced T1W scans. Subtraction images

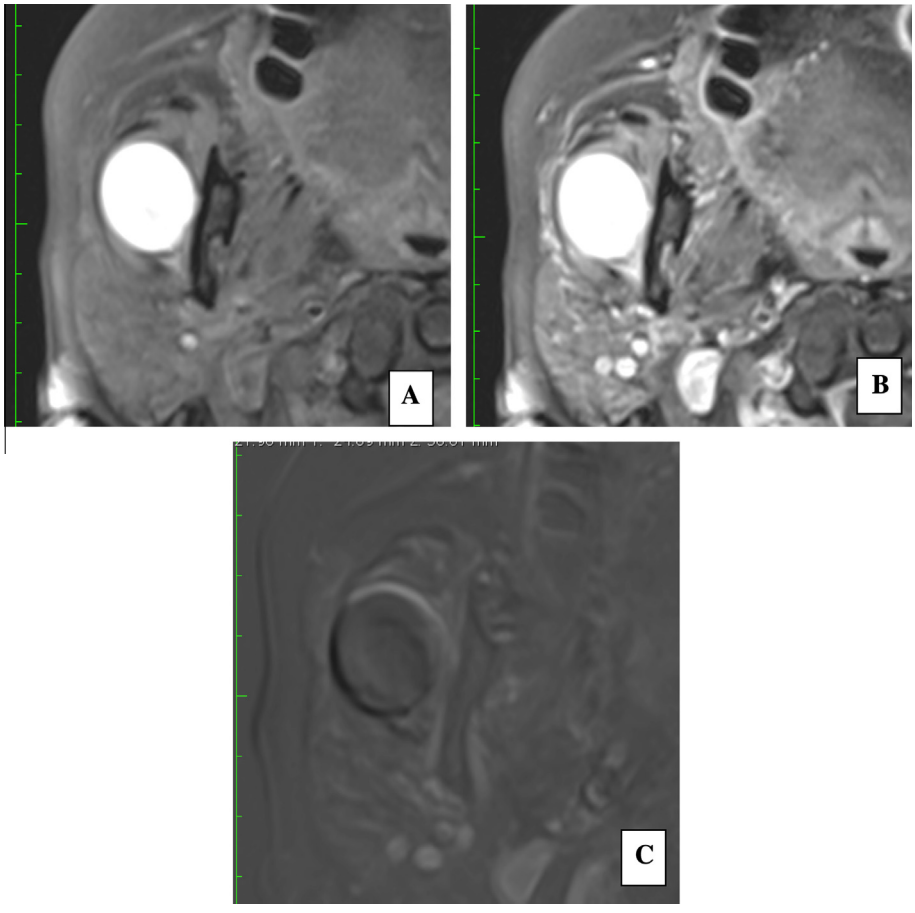


**Fig. 2** Pre and postcontrast enhanced T1W MRI images with fat suppression (A and B) of the face showing an initially hyperintense lesion in the right masseter muscle. Subtraction image (C) shows absence of enhancement within the lesion suggesting its hemorrhagic cystic nature. Diagnosis of hemorrhagic cyst was confirmed histopathologically.

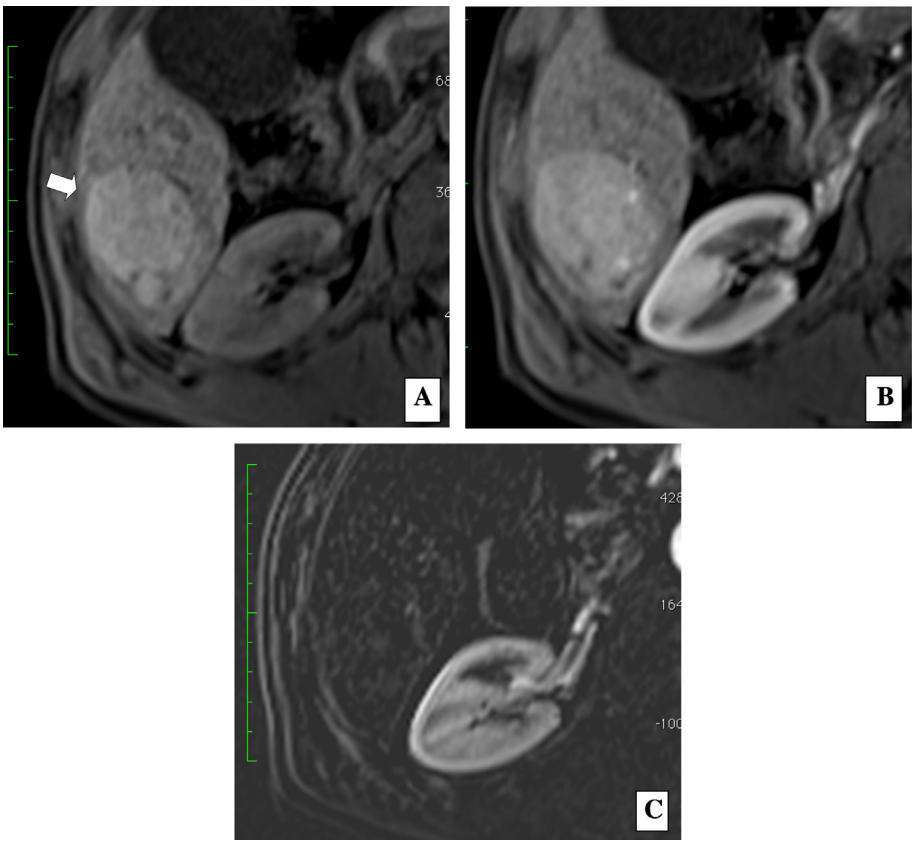


**Fig. 3** MRI images of the liver: precontrast T1W image with fat suppression (A) and postcontrast T1W image in the arterial phase of enhancement with fat suppression (B) showing an initially hyperintense large nodule in the right lobe of a cirrhotic liver (arrow). Subtraction image shows absence of enhancement within the lesion. The possibility of a large dysplastic nodule rather than hepatocellular carcinoma was suggested. Diagnosis was confirmed histopathologically via ultrasound guided biopsy.

were obtained after intravenous contrast injection to be able to assess the presence of enhancement for adequate detection of the nature of these lesions.

During the first session of interpretation, all lesions were categorized as ''indeterminate'' by both authors. With the help of subtraction data sets in the second interpretation session, they were easily categorized as either ''enhancing'' or ''not enhancing''. Any gray scale value in the lesion other than complete signal void on the post-processed subtraction image was considered as ''enhancement.''

Out of these 40 patients, 5 patients (12.5%) presented with intraocular lesions, two patients (5%) presented with lesions in the masseter muscle, two patients (5%) presented with lesions in the parotid gland, 12 patients (30%) presented with hepatic lesions, four patients (10%) presented with gall bladder lesions, four patients (10%) presented with renal lesions, one patient (2.5%) presented with pancreatic lesion and ten patients (25%) presented with ovarian lesions (Table 1).

Five patients presented with T1W hyperintense intraocular lesions all of which were located along the choroidal lining of the globe. Subtraction images confirmed the presence of enhancement within the lesions denoting their neoplastic nature and differentiating them from suprachoroidal hemorrhage. The diagnosis of choroidal melanoma was confirmed histopathologically in all of the five patients (Fig. 1).

Two patients presented with T1W hyperintense lesions in the masseter muscle. Subtraction images showed absence of enhancement within the lesions suggesting their hemorrhagic cystic nature. The diagnosis of hemorrhagic cysts was confirmed histopathologically in both patients (Fig. 2).

Two patients presented with T1W hyperintense lesions in the parotid gland. Subtraction images showed absence of enhancement within the lesions suggesting their hemorrhagic cystic nature. The diagnosis of hemorrhagic cysts was confirmed histopathologically in both patients.

Twelve patients presented with hepatic focal lesions all which on background of cirrhotic liver all showing a T1 hyperintense signal. Subtraction of non-contrast enhanced T1W images from post-contrast T1W images in the arterial phase was obtained in all patients. Two patients presented with T1 hyperintense large hepatic nodules with absence of enhancement in the arterial phase suggesting the possibility of regenerating/low grade dysplastic nodules (low grade dysplasia shows no enhancement, as opposed to high grade dysplastic nodules). This was confirmed via ultrasound guided biopsy in both patients (Fig. 3).

Five patients had lesions with previous diagnosis of hepatocellular carcinoma managed by radiofrequency ablation with absence of enhancement in the arterial phase as confirmed by the subtraction images suggesting the diagnosis of post-ablation necrosis (Fig. 4).

Five patients had lesions with previous diagnosis of hepatocellular carcinoma managed by chemoembolization showing retained T1 hyperintense lipidol particles out of which two

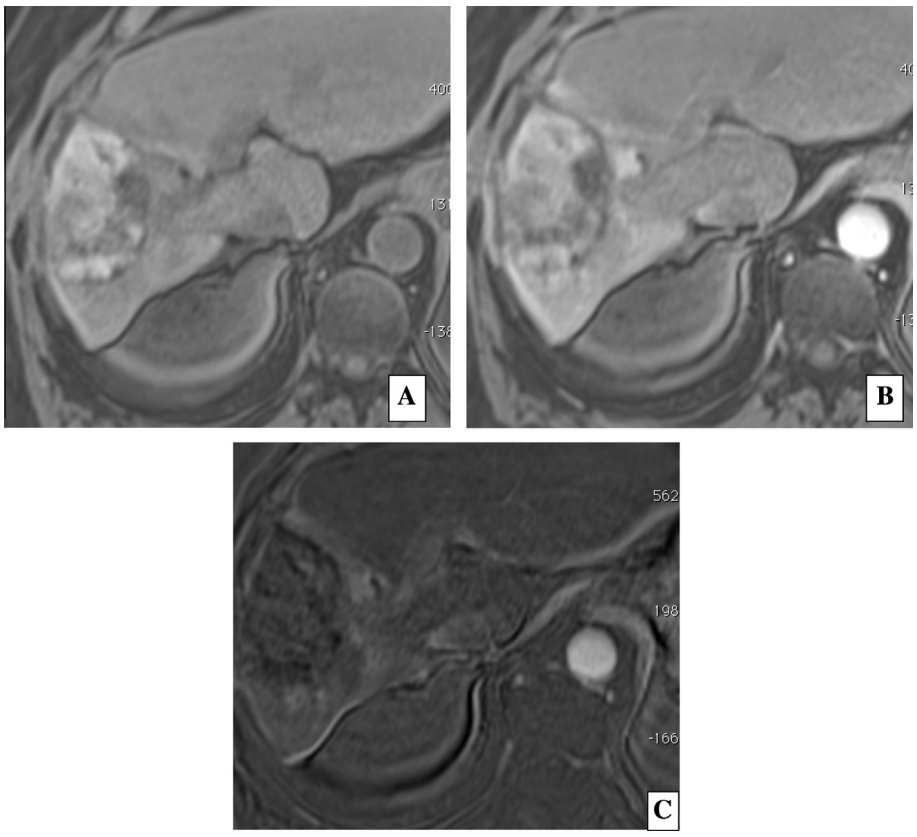


**Fig. 4** Patient with history of right hepatic lobe hepatocellular carcinoma managed by radiofrequency ablation. MRI images of the liver: precontrast T1W image with fat suppression (A) and postcontrast T1W image in the arterial phase of enhancement with fat suppression (B) showing the previously ablated mass exhibiting an initially hyperintense signal. Subtraction image (C) shows absence of enhancement within the mass confirming the diagnosis of post-ablation necrosis and excluding the possibility of recurrence.

patients showed positive enhancement of the lesions in the arterial phase denoting tumor recurrence (Fig. 5) and three patients had absent enhancement denoting absence of recurrent active tumor tissue (Fig. 6).

Four patients presented with T1W hyperintense lesions within the gall bladder lumen. In all of the four patients subtraction images showed absence of enhancement within the lesions confirming the diagnosis of intraluminal biliary sludge and excluding the presence of a neoplastic process (Fig. 7).

Four patients presented with T1W hyperintense renal cortical lesions. Subtraction images showed absence of enhancement within the lesions confirming the diagnosis of hemorrhagic cortical renal cysts (Fig. 8).

One patient presented with a lesion within the tail of pancreas exhibiting a T1W hyperintense signal denoting high proteinaceous content. Subtraction image confirmed absence of enhancement within the lesion apart from tiny enhancing papillary projections seen along its left lateral wall. The diagnosis of solid papillary neoplasm was confirmed histopathologically (Fig. 9).

Ten patients presented with T1W hyperintense ovarian cystic lesions including six patients with final pathological diagnosis of chocolate cysts, two patients with pathological diagnosis of mucinous cystadenoma and two patients with pathological diagnosis of mucinous cystadenocarcinoma. Subtraction images showed absent enhancement in the lesions in the six patients with diagnosis of chocolate cyst (Fig. 10).

The lesions in the two patients diagnosed with mucinous cystadenoma showed internal thin enhancing septations within the lesions with absent enhancing solid component (Fig. 11) while the lesions in the two patients diagnosed with mucinous cystadenocarcinoma showed multiple mural solid enhancing nodules seen along the walls of the lesions (Fig. 12).

## 4. Discussion

The study included 40 patients presenting with lesions in different parts of the body, that are initially hyperintense on T1W sequences, and in whom visual assessment of enhancement is difficult and is crucial for detection of nature of these lesions. Digital subtraction of T1W unenhanced images from similar contrast images was performed in all patients. Lee et al. (3) and Newatia et al. (4) found that subtraction technique is valuable in MR imaging and could adequately determine the degree of contrast enhancement on background of tissues which show a T1W hyperintense signal in the non contrast enhanced images like in hemorrhagic lesions or cystic lesions with mucinous or high proteinaceous contents. This agrees with the findings in our study in which such technique was able to provide adequate qualitative assessment of enhancement within all the lesions included within the study and was able to differentiate between non neoplastic cystic lesions with hemorrhagic or high proteinaceous contents with

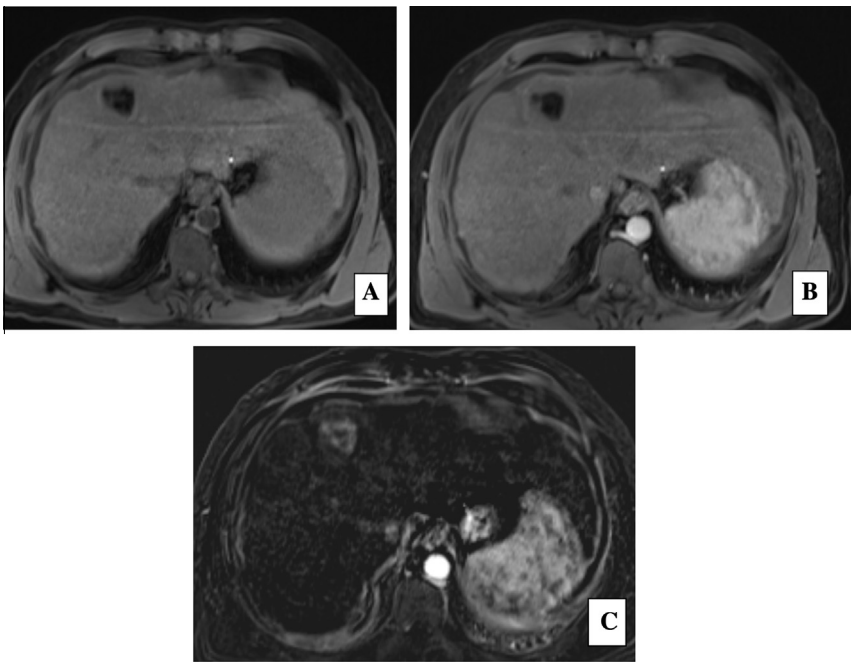


**Fig. 5** Patient with history of left hepatic lobe hepatocellular carcinoma managed by chemo-embolization. MRI images of the liver: precontrast T1W image with fat suppression (A) and postcontrast T1W image in the arterial phase of enhancement with fat suppression (B) showing a hyperintense signal within the lesion in both images. Subtraction image (C) shows positive enhancement within the lesion notably along its margins confirming tumor recurrence.

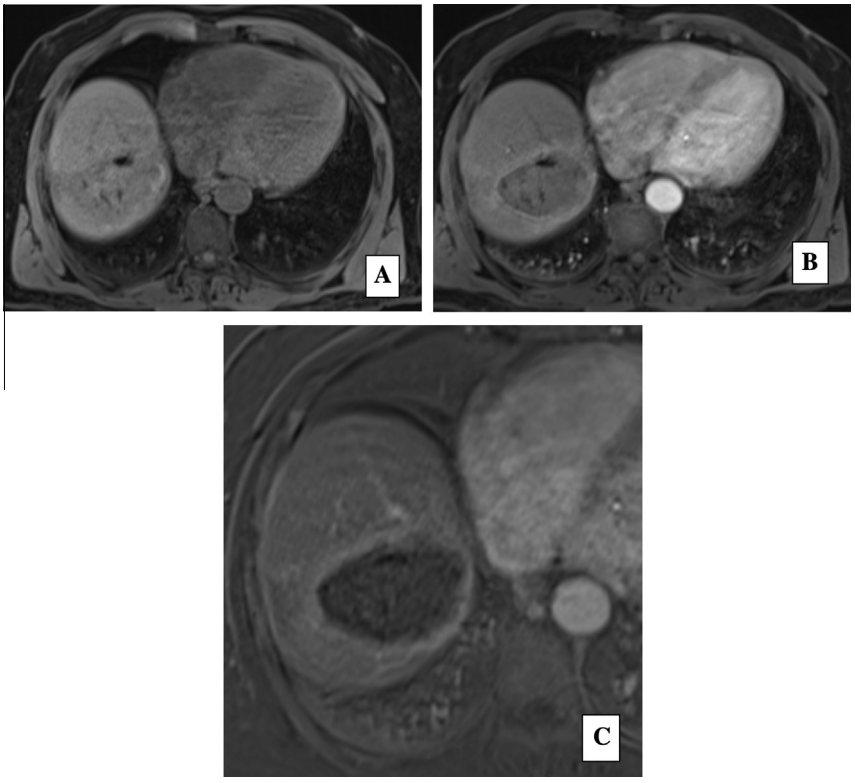


**Fig. 6** Patient with history of right hepatic lobe hepatocellular carcinoma managed by chemo-embolization. MRI images of the liver: precontrast T1W image with fat suppression (A) and postcontrast T1W image in arterial phase of enhancement with fat suppression (B) showing the previously managed mass exhibiting a heterogeneous signal with hyperintense foci in both images likely due to retained lipidol particles. Hypointense foci are also seen within the mass likely due to air. Subtraction image (C) shows absence of enhancement within the mass confirming the absence of recurrent active neoplastic tissue.

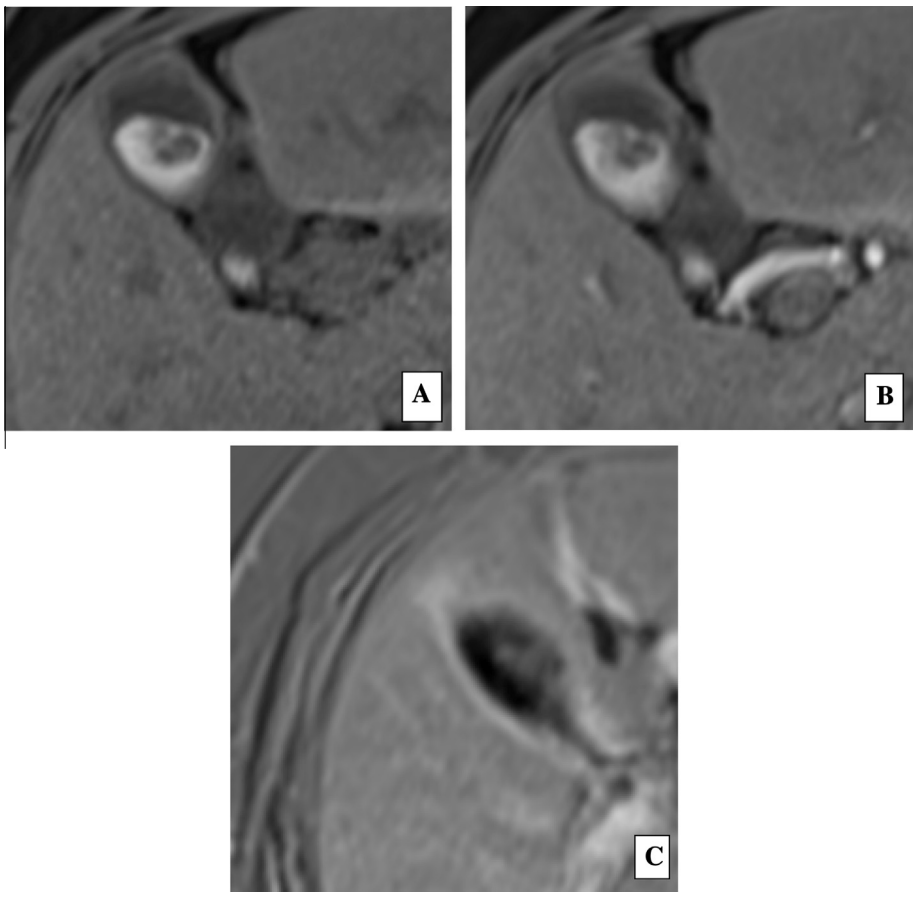


**Fig. 7** Patient with history of cholecystitis: MRI images of the gall bladder: precontrast T1W image with fat suppression (A) and postcontrast T1W image in the arterial phase of enhancement with fat suppression (B) showing a lesion within the gall bladder lumen exhibiting a hyperintense signal in both images. Subtraction image (C) shows absence of enhancement within the lesion confirming the diagnosis of intraluminal biliary sludge and excluding the presence of a neoplastic process.

absent enhancement and neoplastic lesions which showed solid enhancing components.

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. However, regenerative and dysplastic nodules and hepatocellular carcinoma can all exhibit a high signal on unenhanced T1-weighted sequences. 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 (5). Our study included two patients presenting with T1 hyperintense large hepatic nodules with absence enhancement in the arterial phase as confirmed by subtraction technique suggesting the possibility of dysplastic nodules which was confirmed via ultrasound guided biopsy in both patients.

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 a high T1 signal, which is often present because of coagulation necrosis. It can also help differentiate the smooth, indistinct peritumoral enhancement seen in benign post-treatment hyperemia from the discontinuous nodular enhancement of viable tumor (6,7). Our study included five patients having lesions with previous diagnosis of hepatocellular carcinoma managed by radiofrequency ablation with absence of enhancement in the arterial phase as confirmed by the subtraction images suggesting the diagnosis of post-ablation necrosis. Five patients had lesions with previous diagnosis of hepatocellular carcinoma managed by chemoembolization showing retained T1 hyperintense lipidol particles out of which two patients showed positive enhancement of the lesions in the arterial phase denoting tumor recurrence and three patients had absent enhancement denoting absence of recurrent active tumor tissue.

Complex renal cysts often show a 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. Subtraction imaging should be used for analysis of enhancement within this subset of cystic renal masses on MRI because the

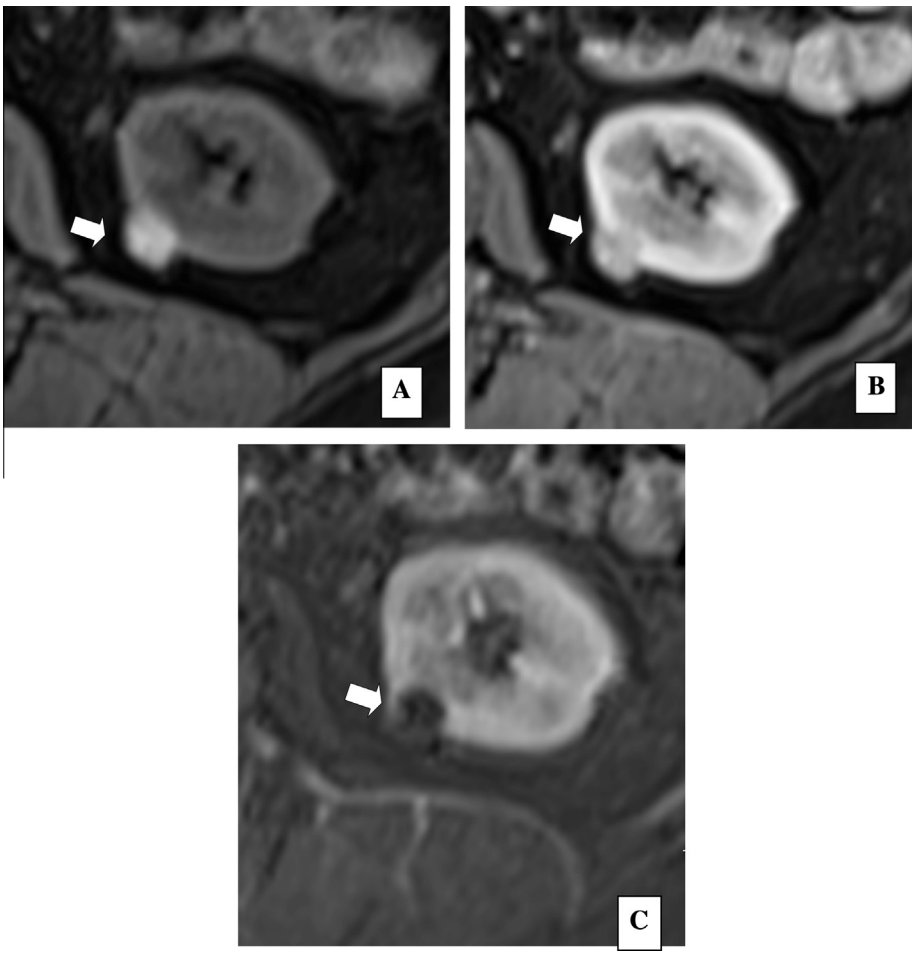


**Fig. 8** MRI images of the kidneys: precontrast T1W image with fat suppression (A) and postcontrast T1W image in the arterial phase of enhancement with fat suppression (B) showing a small cortical renal lesion (arrows) exhibiting a hyperintense signal in both images. Subtraction image shows absence of enhancement within the lesion confirming the diagnosis of hemorrhagic cortical renal cyst.

use of quantitative measurements (region of interest [ROI]) can result in false-negative results. 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 (1). Four patients in our study presented with T1W hyperintense renal cortical lesions. Subtraction images showed absence of enhancement within the lesions confirming the diagnosis of hemorrhagic cortical renal cysts.

Subtraction imaging may also be useful for imaging the gallbladder in situations in which the differential diagnosis is between tumefactive sludge and 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 when there is no detectable extramural disease (4). Four patients in our study presented with T1W hyperintense lesions within the gall bladder lumen. In all of the four patients subtraction images showed absence of enhancement within the lesions confirming the diagnosis of intraluminal biliary sludge and excluding the presence of a neoplastic process.

Subtraction of high-resolution images can aid in excluding features that suggest malignancy in complex cystic adnexal masses such as solid enhancing components like papillary projections and mural or septal nodules. In our study ten patients presented with T1W hyperintense ovarian cystic lesions (4). Subtraction images showed absent enhancement in the lesions in the six patients with diagnosis of chocolate cyst. The lesions in the two patients diagnosed with mucinous cystadenoma showed internal thin enhancing septations within the lesions with absent enhancing solid component while the lesions in the two patients diagnosed with mucinous cystadenocarcinoma showed multiple mural solid enhancing nodules seen along the walls of the lesions.

Lloyd et al. (8) concluded in a study performed on different T1W hyperintense lesions in the head and neck that subtraction technique is useful in evaluating the degree of enhancement in such lesions and in differentiating hemorrhagic cystic lesions from neoplastic masses likely choroidal melanoma which is characterized by short relaxation times and a high signal in the T1W sequence. This was matching with the findings in our study which included nine patients presenting with head and neck lesions. Five patients presented with T1W hyperintense intraocular lesions all of which were located along the choroidal lining of the globe. Subtraction images detected enhancement

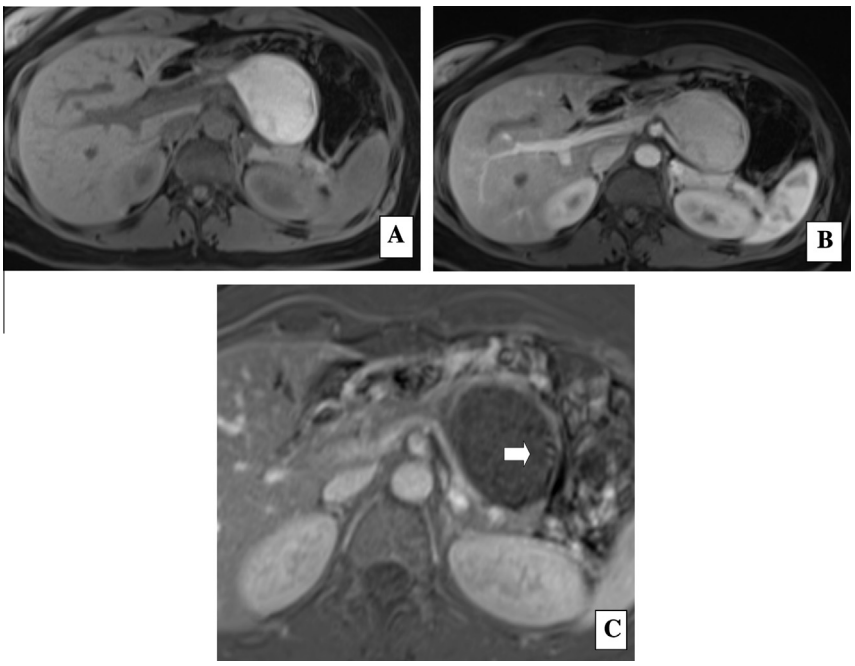


**Fig. 9** MRI images of the pancreas: precontrast T1W image with fat suppression (A) and postcontrast T1W image in the arterial phase of enhancement with fat suppression (B) showing a lesion within the tail of pancreas exhibiting a hyperintense signal in both images denoting high proteinaceous content within the lesion. Subtraction image shows absence of enhancement within the lesion apart from tiny enhancing papillary projections seen along its left lateral wall (arrow). The diagnosis of solid papillary neoplasm was confirmed histopathologically.

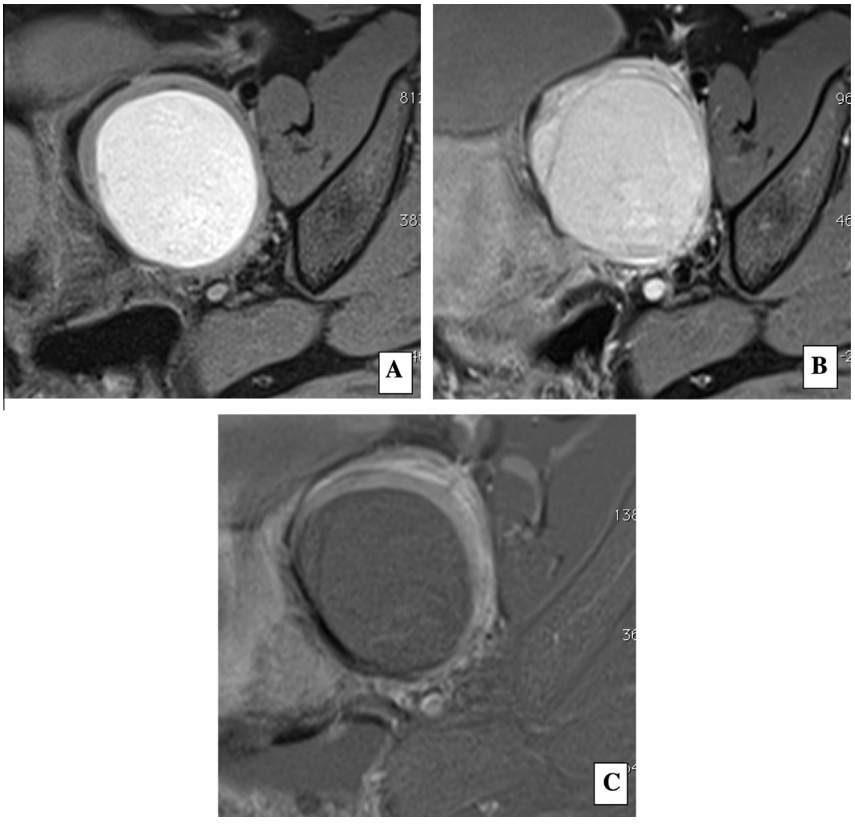


**Fig. 10** Pre and postcontrast enhanced T1W MRI images with fat suppression (A and B) of the pelvis in a female patient showing a large ovarian lesion exhibiting a hyperintense signal in both images. Subtraction image (C) shows absent enhancement within the lesion confirming its cystic nature and the possibility of an ovarian chocolate cyst was suggested and was confirmed histopathologically.

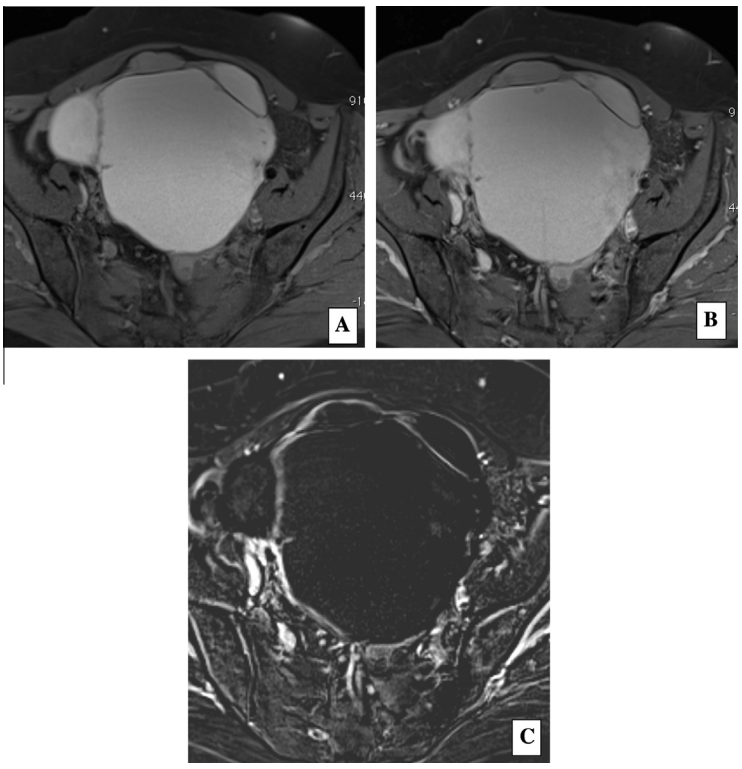


**Fig. 11** Pre and postcontrast enhanced T1W MRI images with fat suppression (A and B) of the pelvis in a female patient showing a large ovarian lesion exhibiting a hyperintense signal in both images. Subtraction image (C) shows internal thin enhancing septations within the lesion with absent enhancing solid component confirming its cystic nature. The possibility of a mucinous cystic neoplastic ovarian lesion of a benign nature was suggested. The diagnosis of ovarian mucinous cystadenoma was confirmed histopathologically.

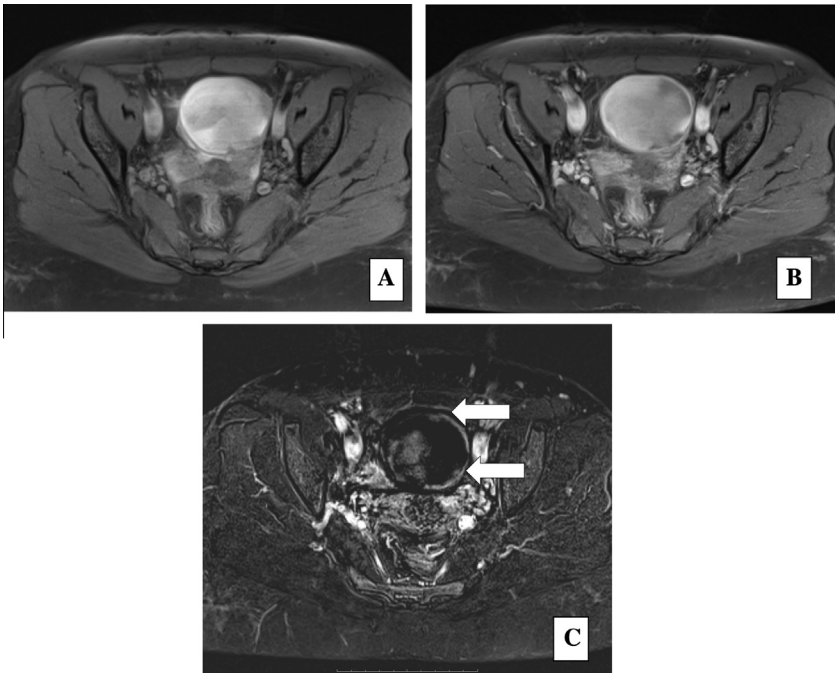


**Fig. 12** Pre and postcontrast enhanced T1W MRI images with fat suppression (A and B) of the pelvis in a female patient showing a large ovarian lesion exhibiting a hyperintense signal in both images. Subtraction image (C) shows multiple mural solid enhancing nodules seen along the wall of the lesion (arrows). The possibility of a mucinous ovarian cystic neoplasm probably of malignant nature was suggested and was confirmed histopathologically.

within the lesions confirming the diagnosis of choroidal melanoma and differentiating them from suprachoroidal hemorrhage. Four patients presented with non neoplastic hemorrhagic cysts with absent enhancement, two of which were located in the parotid gland and two in the masseter muscle.

In conclusion, Subtraction MRI, used since long time for MR angiography, is a still underused, though very helpful tool, in non-vascular MRI applications. It can unambiguously assess post Gadolinium enhancement in those lesions which show initial T1 hyperintensity, thus helping to characterize their nature.

## Conflict of interest

None declared.

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