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New MRI series for kidney evaluation: Saving time and money

1 **New Magnetic Resonance Imaging Series for Kidney Evaluation: Saving Time**

2 **and Money**

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4 Renzulli M[1], Brocchi S[1], Pettinari I[1], Biselli M[2], Clemente A[3], Corcioni B[1], Cappabianca S[3],

5 Gaudiano C[1], Golfieri R[1].

6

7 [1] Department of Diagnostic Medicine and Prevention Radiology Unit, Sant'Orsola Hospital,

8 University of Bologna, Via Albertoni , Bologna , Italy.

9 [2] Department of Medical and Surgical Sciences, Sant'Orsola Hospital, University of Bologna, Via

10 Albertoni , Bologna , Italy.

11 [3] Department of Precision Medicine Radiology and Radiotherapy Unit, University of Campania "L.

12 Vanvitelli", Piazza Miraglia , Naples , Italy.

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14 **Short Title:** New MRI series for kidney evaluation

15

Abstract

Objectives: This study investigates the diagnostic performance of a new T1 imaging series, generated by the digital subtraction of the opposed phase from in phase T1-weighted images, in magnetic resonance imaging (MRI) for renal angiomyolipoma (AML) evaluation.

Methods: This retrospective study involved 96 patients, sixty-three (65.6%) with at least one renal AML and 33 (34.4%) healthy patients. Two radiologists having different experience retrospectively reviewed two MR imaging series, starting with in and out-phase T1-weighted images and then the new subtracted T1 images, in which AML appeared white on black background. The presence, number, location, and dimensions of the AMLs, and reading time were collected separately for the two kidneys. Statistical analysis was carried out using the appropriate tests.

Results: The number of lesions identified and the evaluation of lesion dimension did not statistically differ between the different MR imaging series evaluated, without interobserver variability. Both percentage agreement of the total number of observations and the κ coefficient showed very good agreement between the radiologists. The median time for the diagnosis was statistically lower when using the subtracted T1 imaging series for both observers with a median gain from 6.5 to 15 seconds per identified lesion, resulting in a total time-saving of more than half (52.9%), in both patients with and without AMLs, and in patients with a single or with more than one AML ($P < 0.001$).

Conclusions: The new subtracted T1 imaging series proved to be reliable in identifying fat-containing renal lesions, by both expert and non-expert radiologists, resulting in a saving of both time and money. Moreover, this new subtracted T1 imaging series could be an effective tool in non-dedicated kidney examinations in which a faster reading is advisable.

41

42 **Advances in knowledge:** The opportunity of using a single set of MRI images in kidney evaluation

43 for identifying fat-containing lesions, considerably reducing reading time, resulting in cost-

44 effectiveness.

45

46 **Keywords**

47 Angiomyolipoma; Kidney Neoplasms; Magnetic Resonance Imaging; Chemical Shift Imaging;

48 Subtraction Technique.

49

50

Introduction

A renal Angiomyolipoma (AML) is a non-uncommonly found benign solid tumour[1] which represents the second most frequent pathology (28.7%) after oncocytoma (51.2%) in kidneys.[2] The vast majority of AMLs are incidentally identified because they are usually asymptomatic.[3] However, more rarely, AMLs can be associated with two hereditary symptomatic diseases: the tuberous sclerosis complex and sporadic lymphangioleiomyomatosis.[3] Incidental AMLs are smaller and usually unilateral as compared with AMLs in a tuberous sclerosis complex.[4] Solitary small AMLs (<20 mm) have a low risk of growth and, if asymptomatic, do not warrant follow-up.[5,6] Therefore, a correct imaging diagnosis is mandatory in order to avoid unnecessary follow-up or non-appropriate treatment. A classic AML is a benign, slow growing tumour composed of smooth muscle, adipose tissue and blood vessels.[3] The majority of AMLs contains fat that is clearly identifiable on imaging techniques, such as Magnetic Resonance Imaging (MRI), so these tumours can be diagnosed without biopsy or surgery. Approximately only 5% of renal AMLs have too little fat to be detected by imaging.[7] An AML is the only renal tumour which can be characterised based on its tissue composition in the vast majority of cases. In fact, its diagnosis depends on the detection of the macroscopic fat within the lesions. On MRI, the diagnosis of AMLs has traditionally been reached using T1-weighted sequences, comparing the images with and without frequency-selective fat suppression.[8] However, AMLs can be more accurately diagnosed using the chemical shift in MRI.[8-10] In fact, in chemical shift imaging, widely used to identify microscopic amounts (intravoxel or intracellular) of fat, minimal fat AML shows a significant signal-drop on opposed-phase images.[6,11,12] Chemical shift imaging is an artefact due to positional misregistration of the fat signal resulting from the different processional frequencies of fat and water protons, and manifests as alternating bands of bright and dark signals along the frequency-encoding direction at fat–water interfaces.[13] This artefact can be recognized on opposed-phase MR images as a characteristic sharp black line at fat–water (fat–muscle or fat–solid organ) interfaces.[14]

76 Because the majority of AMLs contain macroscopic fat, this artefact will appear at the interface of

77 the AML with the kidney, or at the interface of the fatty and non-fatty portions of the mass. In small

78 AMLs, the signal void phase suppression artefact occupies the entire lesion. Consequently, small

79 AMLs, which will appear as a signal void on out-of phase images, may simulate cysts. For this reason,

80 comparison of in-phase and opposed phase images, generated from the same sequence, is always

81 required to identify fat components in small renal lesions.[8]

82 Subtraction imaging is a readily available technique which is routinely used in MRI, for example in

83 breast and liver imaging or in MR angiography to improve enhancing detection after the use of

84 contrast media.[15,16] In fact, in liver MRI, the presence of arterial enhancement in some cases is not

85 easy to detect by visually comparing two image sets, such as those in arterial and unenhanced phases.

86 For example, some enhancing nodules can show the same relative signal intensity as the liver

87 parenchyma on arterial phase images and on unenhanced images, and this is also true for small

88 nodules. In these cases, dynamic subtraction of an unenhanced T1-weighted sequence from the

89 identical sequence carried out after gadolinium administration can be helpful.[17-20]

90 The accurate identification of the chemical shift imaging is crucial in diagnosing AMLs. This is also

91 true in all the examinations carried out with different indications but always involving kidneys in

92 their field of view since AMLs are usually incidentally found. Furthermore, it would be useful to have

93 a single set of images in order to be able to evaluate the chemical shift imaging since this could reduce

94 reading time as compared to that involved in evaluating the two sets of standard T1-weighted images

95 (in-phase vs. out-phase). The chemical shift imaging can be overcome by Dixon sequences which

96 however are not available on all MR machines. Therefore, we decided to generate a new imaging

97 series by the digital subtraction of the opposed phase from in phase T1-weighted images. In these

98 subtracted T1 images, the remaining signal is only the eventual presence of chemical shift artefacts,

99 which appear strongly hyperintense on a "dark background".

100 The purpose of this study was to investigate the diagnostic performance of our new subtracted T1

101 imaging series in kidney evaluation on MRI.

102

Methods and Materials

104 This single-centre retrospective study, carried out at our tertiary care centre, was approved by the

105 institutional review board, and the requirement for informed consent was waived.

106

107 *Study Patients*

108 The MRI database was reviewed from January 2012 to December 2017 to identify all patients in

109 which the word "Angiomyolipoma" was present in the final MRI report. The patients which satisfied

110 the following criteria were included in our study: (a) MRI performed in our Hospital, (b) good-quality

111 MRI examinations, in particular availability of opposed phase and in-phase T1-weighted images of

112 good quality and (c) a renal AML imaging diagnosis. During the study period, 64 consecutive patients

113 with at least one renal AML were identified. Only one patient was excluded due to inadequate

114 imaging examination (respiratory artefacts in the T1-weighted images), thus allowing analysis of 63

115 patients.

116 In order to evaluate the diagnostic performance of the new subtracted T1 imaging series, it was

117 decided to create an overall study population in which at least one third were healthy patients without

118 AML. In this way, the observer radiologists could analyse a patient population without knowing how

119 many patients were positive for AMLs. In the same study period (from January 2012 to December

120 2017), thirty-three healthy subjects with no renal AMLs were consecutively enrolled from the MRI

121 database by a radiologist who did not carried out the subsequent image analysis.

122 The final study population involved 96 patients, of whom thirty-three (34.4%) were healthy subjects

123 with no renal AMLs.

124

125 *MRI technique and image analysis*

In patients with AMLs, MRI examinations were performed following a previously described protocol.[21] In the healthy subjects, the MRI protocol was not dedicated to renal study in all cases and, sometimes, the protocol was that of a study of the upper abdomen. In this latter case, the MRI examination was performed following a previously described protocol.[22,23] In particular, in all these MRI examinations, the new imaging series was generated by the subtraction of the images obtained from a breath-hold T1-weighted gradient-echo dualecho "in and out of phase" sequence (TR/TE 150/4.6 ms and TR/TE 150/2.1 ms, respectively; 80° flip angle; 256 ×160 matrix; 62.50 Hz per pixel bandwidth; one signal acquired; and 20–25-second acquisition time). In detail, for each of the 96 examinations, the new imaging series (subtracted T1 images) was created by a technologist subtracting opposed phase T1-weighted images from in phase T1 weighted images using standard software called Add/Sub on an independent console (Advantage Workstation, Release 4.4 Software, General Electric Medical Systems, Milwaukee, WI, USA). This series generated a set of images with a black background except for fat–water (fat–muscle or fat–solid organ) interfaces which appeared white. Therefore, the chemical shift artefacts at the interface of the AML with the kidney, or at the interface of the fatty and non-fatty components of the lesion, appeared white on black background. All the images, standard T1 in phase and out of phase and subtracted T1 imaging series, were retrieved from and evaluated on our institutional picture archiving and communication system (Carestream PACS, version 1.4; Kodak, Rochester, NY).

The images were assessed by two radiologists, one senior radiologist with more than 10 years of experience in abdominal MRI, and one junior with <3 years' experience in abdominal MRI. They were blinded to all of the information, including clinical history and imaging reports, especially those concerning the presence of renal AMLs. The two observers independently reviewed all images, starting with in and out of phase T1-weighted images, to evaluate the following features separately for the two kidneys: presence, number, anatomic location and dimensions of the AMLs. The reading time, in seconds, was also recorded beginning when the reader started to view the images and ending once reaching the diagnosis (presence and number of AMLs), separately for each kidney. Reading

152 time did not include the time needed to measure and locate the lesion, since this time is the same

153 independent of the different images used. All data were collected in a dedicated database for this

154 series, one for each observer.

155 After at least 2 weeks, each observer independently evaluated the subtracted T1 imaging series of the

156 entire study population. For this new imaging series, the two observers also independently reviewed

157 all the radiologic images to evaluate the same features as for the standard T1 sequence, separately for

158 the two kidneys. All data were collected by each observer in a new dedicated database, different from

159 the first one.

160

161 *Statistical Analysis*

162 The distribution asymmetry of the quantitative data was assessed using the Skewness test. The

163 quantitative variables were expressed as mean ± standard deviation, or median and interquartile range,

164 as appropriate.

165 The systematic difference between the intra-observer and inter-observer results obtained from each

166 MR images (T1 or subtracted T1 imaging series) was assessed using the Wilcoxon signed-rank test

167 or the Mann-Whitney test, as appropriate. A statistically significant result showed that there was

168 evidence of a systematic difference between the proportions of "positive" responses from the two

169 MRI imaging series. The absence of a systematic difference implied that there was no bias. The

170 degree of agreement between the observers was measured by both percentage agreement of the total

171 number of observations, considering the total number of times in which the observers agreed which

172 was divided by the total number of readings/classifications made, and by calculating Cohen's kappa

173 (κ) coefficient. Perfect agreement was evident when Cohen's kappa equalled 1; a value of Cohen's

174 kappa equal to zero suggested that the agreement was no better than that which would be obtained by

175 chance alone. A *P* value of less than 0.05 was considered statistically significant. All the analyses

176 were carried out using SPSS 20.0 software (SPSS Inc., Chicago, IL, USA).

178 **Results**

179 The overall study population consisted of 96 patients evaluated by MRI from January 2012 to

180 December 2017. Mean age was 59 ± 9 years; 37.5% of the patients were male. Sixty-three patients

181 (65.6%) had at least one renal AML.

182 The number and dimensions of the lesions identified by the two observers using the T1 sequence as

183 a standard method and subtracted T1 images as an alternative method are shown in Table 1.

184 The overall number of lesions identified with the two imaging series by each observer did not

185 statistically differ. Moreover, a statistically significant difference between the observers in terms of

186 the number of lesions identified in both kidneys was not observed. When the size of the lesions was

187 considered, there were no significant differences between the imaging series (for either observer) and

188 between the observers (Table 1).

189 T1 subtracted imaging series showed good sensitivity and specificity for both the observers. In

190 particular, for the observer 1 the sensitivity and specificity in the evaluation of both the kidneys were

191 respectively 100% and 99.1% (CI95% 96.2-99.9%) [right kidney: sensitivity and specificity 100%;

192 left kidney: sensitivity 100% and specificity 98.2% (CI95% 92.4-99.8%)]. For the observer 2 the

193 sensitivity and specificity in the evaluation of both the kidneys were respectively 97.4% (CI95% 93.6-

194 99%) and 100% [right kidney: sensitivity 94.7% (CI95% 87.5-98.1%) and specificity 100%; left

195 kidney: sensitivity and specificity 100%].

196 The degree of agreement between the two observers is reported in Table 2. Both percentage

197 agreement of the total number of observations and the κ coefficient showed very good agreement

198 between the observers for each of the imaging series (Table 2).

199 The time needed by the two observers for kidney evaluation using both the standard T1 and the

200 subtracted T1 imaging series, are shown in Table 3. The median time for the diagnosis was

201 statistically lower in both observers, with a median gain of from 6.5 to 15 seconds per identified

202 lesion when using the subtracted T1 imaging series (Table 3). In both the patients with AMLs (Figure

203 1) and in those without AMLs (Figure 2), it was observed that the subtracted T1 imaging series

204 obtained a significant median time gain for the diagnosis for both observers (Table 3). Moreover, the

205 subtracted T1imaging series allowed obtaining a significant median time gain in reaching a diagnosis

206 for both radiologists, even in the case of patients with a single AML or in those with more than one

207 lesion (Table 4). It is to note that regarding observer 1, when T1 sequence was utilized for right

208 kidney, only 3 out of 10 patients, who were identified by observer 2 with multiple lesions, were

209 detected. On the contrary, utilizing both T1 sequence in the left kidney and subtracted T1 imaging

210 series in both of kidneys, no substantial differences were detected between the two observers (right

211 kidney evaluated by T1 subtracted series: observer 1 six cases vs observer 2 eight cases; left kidney

212 evaluated by T1 sequence: observer 1 eight cases vs observer 2 eight cases; T1 subtracted series:

213 observer 1 ten cases vs observer 2 eleven cases).

214

215

216 **Discussion**

217 Solitary small AMLs (<20 mm) have a low risk of growth and, thus, do not require follow-up if

218 asymptomatic.[5] Therefore, a correct imaging diagnosis is mandatory in order to carry out correct

219 management, such as the abstention from follow-up. An AML can be characterised based on its tissue

220 composition and depends on the detection of the fat within the lesions. On MRI, the diagnosis of

221 AMLs can be accurately carried out using chemical shift imaging which is also able to identify

222 microscopic amounts of fat as in case of a minimal fat AML.[6,8-12]

223 Historically, MRI has an advantage as compared to Computed Tomography: the possibility of

224 carrying out image subtraction. For example, dynamic subtraction of an unenhanced T1-weighted

225 sequence from the identical sequence performed after gadolinium administration is helpful in liver

226 imaging,[8,17,19,20] and it has become an integral part of radiological clinical practice. In fact, the

227 accurate detection of arterial enhancement is important for diagnosing small single HCCs,[24] and

228 enables more effective treatment.[25] Dynamic subtraction in MRI allows more accurate detection of

229 arterial enhancement leading to an earlier diagnosis of hepatocellular carcinoma.[17] However, the

230 limits of this subtracted image series are well known in clinical practice. In fact, the subtraction is

231 obtained from two different acquisitions, the arterial phase and the unenhanced phase, which are

232 performed in two different breath-hold periods. Therefore, in case of different breaths, the subtracted

233 series results blurred due to the subtraction of images in different spatial levels. This problem, known

234 as misregistration artefact,[17] is particularly relevant in cirrhotic patients with poor clinical condition

235 in whom the need to utilise these subtracted images exists.

236 In this study, the subtracted T1 imaging series is digitally generated in post-processing from two

237 identical imaging sets resulting from the same sequence, the dual T1-weighted in-phase and opposed-

238 phase sequences. This method allows having exact subtracted images acquired during the same

239 breath-hold period. Therefore, this is a "true" subtracted imaging series, different from subtraction

240 technique commonly used in the evaluation of contrast enhancement in which the unenhanced images

241 are subtracted from those performed after contrast injection, therefore in different breath-hold. Our

242 T1 subtracted imaging series is characterised by a black background on which the chemical shift

243 artefacts appear white.

244 In the present study, the new subtracted T1 imaging series for kidney evaluation was tested, in

245 particular for the identification of AMLs.

246 There is no evidence in the literature regarding this new imaging series, thus it is difficult to compare

247 these results to others. Therefore, the data of this study are critically discussed to highlight the

248 diagnostic utility of the new subtracted T1 images in kidney evaluation.

249 No significant differences were observed in the evaluation of the dimensions and number of AMLs

250 in either kidney when using the subtracted T1 imaging series with respect to the standard T1-weighted

251 sequence, with a good result in terms of sensitivity and specificity. Furthermore, there were no

252 differences in the evaluation of the dimensions and number of AMLs between the two observers,

11

253 even if, utilizing T1 sequence, observer 1 identified a lower number of patients with multiple lesions

254 in the right kidney. In particular, there was very good agreement between the two observers, despite

255 their different radiological skills.

256 This study was designed to calculate the time needed to evaluate the kidneys using the two different

257 imaging series, the standard T1-weighted and the subtracted T1 images. In the entire study

258 population, the reading times were markedly and statistically reduced using the new subtracted T1

259 imaging series for both observers, regardless of their different radiological skills. When evaluating

260 the total time spent on image reading by the two radiologists, the time saved is more than half (52.9%)

261 by using the new subtracted T1 images. This time saving was also achieved by dividing the study

262 population into different subgroups. In fact, in both patients with AMLs and in those without AMLs,

263 time saving was globally greater than 50% when using the subtracted T1 images, regardless of the

264 different experience of the two observers. A saving of more than 50% using the subtracted T1 imaging

265 series was also obtained when it was used in both patients with a single AML and in those with more

266 than one AML. Finally, the possibility of shortening reading times by analysing a single series rather

267 than two different sets of images yields very important saving in terms of time. This reduction in MRI

268 reading time is becoming increasingly important due to an increasing demand for cost-effectiveness

269 and efficiency in hospitals. Benjamin Franklin said: "time is money". Nevertheless, time is more

270 valuable than money: you can get more money, but you can't get more time.[26] This is not true when

271 using our new subtracted T1 imaging series which does not cost anything and is time saving.

272 More sophisticated 2D and 3D Dixon sequences are commercially available, which allow to obtain

273 qualitatively superior images by the use of techniques for phase correction and reduction of borders

274 artifact in chemical shift imaging.[27-29] Unfortunately, the Dixon technique cannot be performed by all

275 MR machines; however, many recent papers were published without performing the Dixon

276 technique[20,21,30] Therefore, in absence of Dixon sequence, our new subtracted T1 imaging series could

277 be an alternative tool to quickly and reliably detect renal fat-containing lesion because this imaging

278 series can be generated on any MR machine, regardless of the brand and technology.

279 The present study had a number of limitations, the first being its retrospective design. Another

280 limitation is that it is a single-centre study, which is a strong factor in interobserver coherence.

281 In conclusion, this new subtracted T1 imaging series not only proved to be reliable in the

282 identification of fat containing renal lesions but was also found to have zero cost. These advantages

283 were obtained by expert and non-expert radiologists. This new subtracted T1 imaging series could be

284 an effective tool in non-dedicated kidney examinations in which a faster reading is advisable.

285 Therefore, if our results are confirmed, the subtracted T1 imaging series could be used in radiological

286 practice in all hospitals and by all radiologists.

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362

363   **TABLES**

364

365   **Table 1** The dimensions and number of lesions identified by two observers using the standard T1

366   sequence and the new subtracted T1 imaging series in abdominal MRI in patients with

367   angiomyolipoma.

	Observer 1		*P*	Observer 2		*P*	Comparison Interobservers (*P*)	
	T1	Subtracted		T1	Subtracted		T1	Subtracted
Dimensions (mm)								
Right Kidney	7 (8.5)	7 (8)	.688	7 (8)	7 (7)	.676	.619	.64
Left Kidney	6.5 (6.5)	6 (7)	.816	8 (7.5)	8 (7)	.077	.188	.077
Number of lesions (N)								
Right Kidney	41	44	.87	51	47	.713	.598	.987
Left Kidney	54	60	.802	50	55	.862	.885	.824

368   Note: Values are expressed as medians (interquartile range) or numbers.

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373 **Table 2** Degree of agreement between the two observers concerning the two MR imaging series

374 (T1 sequence or subtracted T1 imaging series).

Agreement	Right Kidney		Left Kidney	
	T1	**Subtracted**	**T1**	**Subtracted**
Percentage agreement (%)	88.5	92.7	88.5	87.5
Cohen's kappa (κ) **coefficient**	.759	.845	.762	.741

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378   **Table 3** Time needed for the diagnosis of an angiomyolipoma using a standard T1 sequence or the

379   alternative subtracted T1 imaging series.

	Observer 1		*P*	Observer 2		*P*
All Patients	**T1**	**Subtractive**		**T1**	**Subtractive**	
Time (seconds)						
Right Kidney	15 (7)	7 (2)	<0.001	25 (13)	10 (3)	<0.001
Left Kidney	14.5 (9)	8 (4)	<0.001	23 (11)	10 (3)	<0.001
Patients *with* angiomyolipoma						
Time (seconds)						
Right Kidney	17 (11)	7 (4)	<0.001	25 (16)	10 (3)	<0.001
Left Kidney	15 (9)	9 (3)	<0.001	20.5 (10)	10 (3)	<0.001
Patients *without* angiomyolipoma						
Time (seconds)						
Right Kidney	15 (5)	7 (1)	<0.001	26.5 (12)	9 (3)	<0.001
Left Kidney	14 (7)	7 (3)	<0.001	25 (13)	9 (3)	<0.001

380   Note: Values are expressed as medians (interquartile range).

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384 **Table 4** Time needed for the diagnosis of an angiomyolipoma using a T1 sequence or the alternative

385 subtracted T1 imaging series in patients with a single angiomyolipoma and in those with more than

386 one lesion.

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	Observer 1		*P*	Observer 2		*P*
Patients *with* a Single Lesion	T1	Subtracted		T1	Subtracted	
Time (seconds)						
Right Kidney	16.5 (11)	7 (5)	<0.001	25 (18)	10 (4)	<0.001
Left Kidney	14 (7)	8 (3)	<0.001	20.5 (9)	10 (4)	<0.001
Patients *with more than one* Lesion						
Time (seconds)						
Right Kidney	18 (*)	9 (3)	.118	23 (7)	11.5 (3)	.002
Left Kidney	18 (11)	10 (3)	.016	21 (12)	11 (3)	<0.001

388 Note: Values are expressed as medians (interquartile range). *not computable because only 3 patients were detected with

389 multiple lesions.

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Figure Legends

Figure 1. Magnetic resonance images in 64-year-old woman with renal angiomyolipoma. Axial T1 in phase image **(a)** shows a renal lesion with slightly hyperintense components (white arrow). In T1 out of phase image **(b)** is visible a loss of their signal intensity (white arrow). In the subtracted T1 image **(c)**, the intralesional fat appears strongly hyperintense (black arrow) in a dark background.

Figure 2. Axial magnetic resonance images in a healthy man, without angiomyolipoma. In and out of phase T1-weighted images **(a, b)** do not show any signal intensity abnormality and the renal parenchyma appears homogeneously black in the subtracted T1 sequence **(c)**.