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New Magnetic Resonance Imaging Series for Kidney Evaluation: Saving Time and Money

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Short Title: New MRI series for kidney evaluation

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.

Advances in knowledge: The opportunity of using a single set of MRI images in kidney evaluation for identifying fat-containing lesions, considerably reducing reading time, resulting in cost-effectiveness.

Keywords

Angiomyolipoma; Kidney Neoplasms; Magnetic Resonance Imaging; Chemical Shift Imaging; Subtraction Technique.

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]

Because the majority of AMLs contain macroscopic fat, this artefact will appear at the interface of the AML with the kidney, or at the interface of the fatty and non-fatty portions of the mass. In small AMLs, the signal void phase suppression artefact occupies the entire lesion. Consequently, small AMLs, which will appear as a signal void on out-of phase images, may simulate cysts. For this reason, comparison of in-phase and opposed phase images, generated from the same sequence, is always required to identify fat components in small renal lesions.[8]

Subtraction imaging is a readily available technique which is routinely used in MRI, for example in breast and liver imaging or in MR angiography to improve enhancing detection after the use of contrast media.[15,16] In fact, in liver MRI, the presence of arterial enhancement in some cases is not easy to detect by visually comparing two image sets, such as those in arterial and unenhanced phases. For example, some enhancing nodules can show the same relative signal intensity as the liver parenchyma on arterial phase images and on unenhanced images, and this is also true for small nodules. In these cases, dynamic subtraction of an unenhanced T1-weighted sequence from the identical sequence carried out after gadolinium administration can be helpful.[17-20]

The accurate identification of the chemical shift imaging is crucial in diagnosing AMLs. This is also true in all the examinations carried out with different indications but always involving kidneys in their field of view since AMLs are usually incidentally found. Furthermore, it would be useful to have a single set of images in order to be able to evaluate the chemical shift imaging since this could reduce reading time as compared to that involved in evaluating the two sets of standard T1-weighted images (in-phase vs. out-phase). The chemical shift imaging can be overcome by Dixon sequences which however are not available on all MR machines. Therefore, we decided to generate a new imaging series by the digital subtraction of the opposed phase from in phase T1-weighted images. In these subtracted T1 images, the remaining signal is only the eventual presence of chemical shift artefacts, which appear strongly hyperintense on a "dark background".

The purpose of this study was to investigate the diagnostic performance of our new subtracted T1 imaging series in kidney evaluation on MRI.

Methods and Materials

This single-centre retrospective study, carried out at our tertiary care centre, was approved by the institutional review board, and the requirement for informed consent was waived.

Study Patients

The MRI database was reviewed from January 2012 to December 2017 to identify all patients in which the word "Angiomyolipoma" was present in the final MRI report. The patients which satisfied the following criteria were included in our study: (a) MRI performed in our Hospital, (b) good-quality MRI examinations, in particular availability of opposed phase and in-phase T1-weighted images of good quality and (c) a renal AML imaging diagnosis. During the study period, 64 consecutive patients with at least one renal AML were identified. Only one patient was excluded due to inadequate imaging examination (respiratory artefacts in the T1-weighted images), thus allowing analysis of 63 patients.

In order to evaluate the diagnostic performance of the new subtracted T1 imaging series, it was decided to create an overall study population in which at least one third were healthy patients without AML. In this way, the observer radiologists could analyse a patient population without knowing how many patients were positive for AMLs. In the same study period (from January 2012 to December 2017), thirty-three healthy subjects with no renal AMLs were consecutively enrolled from the MRI database by a radiologist who did not carried out the subsequent image analysis.

The final study population involved 96 patients, of whom thirty-three (34.4%) were healthy subjects with no renal AMLs.

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 time did not include the time needed to measure and locate the lesion, since this time is the same independent of the different images used. All data were collected in a dedicated database for this series, one for each observer.

After at least 2 weeks, each observer independently evaluated the subtracted T1 imaging series of the entire study population. For this new imaging series, the two observers also independently reviewed all the radiologic images to evaluate the same features as for the standard T1 sequence, separately for the two kidneys. All data were collected by each observer in a new dedicated database, different from the first one.

Statistical Analysis

The distribution asymmetry of the quantitative data was assessed using the Skewness test. The quantitative variables were expressed as mean ± standard deviation, or median and interquartile range, as appropriate.

The systematic difference between the intra-observer and inter-observer results obtained from each MR images (T1 or subtracted T1 imaging series) was assessed using the Wilcoxon signed-rank test or the Mann-Whitney test, as appropriate. A statistically significant result showed that there was evidence of a systematic difference between the proportions of "positive" responses from the two MRI imaging series. The absence of a systematic difference implied that there was no bias. The degree of agreement between the observers was measured by both percentage agreement of the total number of observations, considering the total number of times in which the observers agreed which was divided by the total number of readings/classifications made, and by calculating Cohen's kappa (κ) coefficient. Perfect agreement was evident when Cohen's kappa equalled 1; a value of Cohen's kappa equal to zero suggested that the agreement was no better than that which would be obtained by chance alone. A *P* value of less than 0.05 was considered statistically significant. All the analyses were carried out using SPSS 20.0 software (SPSS Inc., Chicago, IL, USA).

Results

The overall study population consisted of 96 patients evaluated by MRI from January 2012 to December 2017. Mean age was 59 ± 9 years; 37.5% of the patients were male. Sixty-three patients (65.6%) had at least one renal AML.

The number and dimensions of the lesions identified by the two observers using the T1 sequence as a standard method and subtracted T1 images as an alternative method are shown in Table 1.

The overall number of lesions identified with the two imaging series by each observer did not statistically differ. Moreover, a statistically significant difference between the observers in terms of the number of lesions identified in both kidneys was not observed. When the size of the lesions was considered, there were no significant differences between the imaging series (for either observer) and between the observers (Table 1).

T1 subtracted imaging series showed good sensitivity and specificity for both the observers. In particular, for the observer 1 the sensitivity and specificity in the evaluation of both the kidneys were respectively 100% and 99.1% (CI95% 96.2-99.9%) [right kidney: sensitivity and specificity 100%; left kidney: sensitivity 100% and specificity 98.2% (CI95% 92.4-99.8%)]. For the observer 2 the sensitivity and specificity in the evaluation of both the kidneys were respectively 97.4% (CI95% 93.6-99%) and 100% [right kidney: sensitivity 94.7% (CI95% 87.5-98.1%) and specificity 100%; left kidney: sensitivity and specificity 100%].

The degree of agreement between the two observers is reported in Table 2. Both percentage agreement of the total number of observations and the κ coefficient showed very good agreement between the observers for each of the imaging series (Table 2).

The time needed by the two observers for kidney evaluation using both the standard T1 and the subtracted T1 imaging series, are shown in Table 3. The median time for the diagnosis was statistically lower in both observers, with a median gain of from 6.5 to 15 seconds per identified lesion when using the subtracted T1 imaging series (Table 3). In both the patients with AMLs (Figure 1) and in those without AMLs (Figure 2), it was observed that the subtracted T1 imaging series obtained a significant median time gain for the diagnosis for both observers (Table 3). Moreover, the subtracted T1imaging series allowed obtaining a significant median time gain in reaching a diagnosis for both radiologists, even in the case of patients with a single AML or in those with more than one lesion (Table 4). It is to note that regarding observer 1, when T1 sequence was utilized for right kidney, only 3 out of 10 patients, who were identified by observer 2 with multiple lesions, were detected. On the contrary, utilizing both T1 sequence in the left kidney and subtracted T1 imaging series in both of kidneys, no substantial differences were detected between the two observers (right kidney evaluated by T1 subtracted series: observer 1 six cases vs observer 2 eight cases; left kidney evaluated by T1 sequence: observer 1 eight cases vs observer 2 eight cases; T1 subtracted series: observer 1 ten cases vs observer 2 eleven cases).

Discussion

Solitary small AMLs (<20 mm) have a low risk of growth and, thus, do not require follow-up if asymptomatic.[5] Therefore, a correct imaging diagnosis is mandatory in order to carry out correct management, such as the abstention from follow-up. An AML can be characterised based on its tissue composition and depends on the detection of the fat within the lesions. On MRI, the diagnosis of AMLs can be accurately carried out using chemical shift imaging which is also able to identify microscopic amounts of fat as in case of a minimal fat AML.[6,8-12]

Historically, MRI has an advantage as compared to Computed Tomography: the possibility of carrying out image subtraction. For example, dynamic subtraction of an unenhanced T1-weighted sequence from the identical sequence performed after gadolinium administration is helpful in liver imaging,[8,17,19,20] and it has become an integral part of radiological clinical practice. In fact, the accurate detection of arterial enhancement is important for diagnosing small single HCCs,[24] and enables more effective treatment.[25] Dynamic subtraction in MRI allows more accurate detection of arterial enhancement leading to an earlier diagnosis of hepatocellular carcinoma.[17] However, the limits of this subtracted image series are well known in clinical practice. In fact, the subtraction is obtained from two different acquisitions, the arterial phase and the unenhanced phase, which are performed in two different breath-hold periods. Therefore, in case of different breaths, the subtracted series results blurred due to the subtraction of images in different spatial levels. This problem, known as misregistration artefact,[17] is particularly relevant in cirrhotic patients with poor clinical condition in whom the need to utilise these subtracted images exists.

In this study, the subtracted T1 imaging series is digitally generated in post-processing from two identical imaging sets resulting from the same sequence, the dual T1-weighted in-phase and opposed-phase sequences. This method allows having exact subtracted images acquired during the same breath-hold period. Therefore, this is a “true” subtracted imaging series, different from subtraction technique commonly used in the evaluation of contrast enhancement in which the unenhanced images are subtracted from those performed after contrast injection, therefore in different breath-hold. Our T1 subtracted imaging series is characterised by a black background on which the chemical shift artefacts appear white.

In the present study, the new subtracted T1 imaging series for kidney evaluation was tested, in particular for the identification of AMLs.

There is no evidence in the literature regarding this new imaging series, thus it is difficult to compare these results to others. Therefore, the data of this study are critically discussed to highlight the diagnostic utility of the new subtracted T1 images in kidney evaluation.

No significant differences were observed in the evaluation of the dimensions and number of AMLs in either kidney when using the subtracted T1 imaging series with respect to the standard T1-weighted sequence, with a good result in terms of sensitivity and specificity. Furthermore, there were no differences in the evaluation of the dimensions and number of AMLs between the two observers, even if, utilizing T1 sequence, observer 1 identified a lower number of patients with multiple lesions in the right kidney. In particular, there was very good agreement between the two observers, despite their different radiological skills.

This study was designed to calculate the time needed to evaluate the kidneys using the two different imaging series, the standard T1-weighted and the subtracted T1 images. In the entire study population, the reading times were markedly and statistically reduced using the new subtracted T1 imaging series for both observers, regardless of their different radiological skills. When evaluating the total time spent on image reading by the two radiologists, the time saved is more than half (52.9%) by using the new subtracted T1 images. This time saving was also achieved by dividing the study population into different subgroups. In fact, in both patients with AMLs and in those without AMLs, time saving was globally greater than 50% when using the subtracted T1 images, regardless of the different experience of the two observers. A saving of more than 50% using the subtracted T1 imaging series was also obtained when it was used in both patients with a single AML and in those with more than one AML. Finally, the possibility of shortening reading times by analysing a single series rather than two different sets of images yields very important saving in terms of time. This reduction in MRI reading time is becoming increasingly important due to an increasing demand for cost-effectiveness and efficiency in hospitals. Benjamin Franklin said: "time is money". Nevertheless, time is more valuable than money: you can get more money, but you can’t get more time.[26] This is not true when using our new subtracted T1 imaging series which does not cost anything and is time saving.

More sophisticated 2D and 3D Dixon sequences are commercially available, which allow to obtain qualitatively superior images by the use of techniques for phase correction and reduction of borders artifact in chemical shift imaging.[27-29] Unfortunately, the Dixon technique cannot be performed by all MR machines; however, many recent papers were published without performing the Dixon technique[20,21,30] Therefore, in absence of Dixon sequence, our new subtracted T1 imaging series could be an alternative tool to quickly and reliably detect renal fat-containing lesion because this imaging series can be generated on any MR machine, regardless of the brand and technology.

The present study had a number of limitations, the first being its retrospective design. Another limitation is that it is a single-centre study, which is a strong factor in interobserver coherence.

In conclusion, this new subtracted T1 imaging series not only proved to be reliable in the identification of fat containing renal lesions but was also found to have zero cost. These advantages were obtained by expert and non-expert radiologists. This new subtracted T1 imaging series could be an effective tool in non-dedicated kidney examinations in which a faster reading is advisable. Therefore, if our results are confirmed, the subtracted T1 imaging series could be used in radiological practice in all hospitals and by all radiologists.

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TABLES

Table 1 The dimensions and number of lesions identified by two observers using the standard T1 sequence and the new subtracted T1 imaging series in abdominal MRI in patients with 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

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

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

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

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

Table 4 Time needed for the diagnosis of an angiomyolipoma using a T1 sequence or the alternative subtracted T1 imaging series in patients with a single angiomyolipoma and in those with more than one lesion.

	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

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

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)**.