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Research Article

MRI Quantitative Mapping Sequences of Renal Masses: Preliminary Results and its Potential Usefulness

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Abstract

Purpose: The goal of this monocentric prospective study consisted in recording T1 (T1m) and T2 (T2m) mapping relaxation times of common renal masses to evaluate the potential usefulness of such biomarkers to discriminate between several types of renal masses.

Materials and Methods: We recorded the T1m and T2m values of 62 patients with renal masses on a clinical 3T MR unit using the consensus-based technical recommendations. For the quantitative evaluation, measurements were performed by carefully delineating Regions of Interest (ROIs). Interobserver agreement for the qualitative analysis of image quality was assessed using quadratic Cohen's weighted kappa statistics (k). Student's paired t-test was used to compare pairs of datasets in terms of T1m and T2m values. Data from our three subgroups with renal masses were compared using a non-parametric Kruskal-Wallis test.

Results: For renal masses, mean T1m and T2m values were 1,727±97ms and 125±18ms; 1,621±96ms and 117±6ms, and 1,453±75ms and 95±10ms for renal cell carcinomas, angiomyolipomas, and oncocytomas, respectively. For T1m values, there was no significant difference (p=0.42) among the three types of renal masses. However, we have found a statistically significant difference for the T2m value (p=0.001).

Conclusion: T1 and T2 mapping are promising sequences, which are not time-consuming and have a rather good interobserver agreement.

Moreover, despite a small cohort, those sequences could play a role in the differential diagnosis between benign and malignant renal tumoral masses. This needs to be confirmed by further studies.

Keywords: Biomarkers; Kidney; MRI; Renal masses; T1 and T2 mapping techniques

Introduction

Magnetic Resonance Imaging (MRI) plays an important role in routine clinical practice for evaluating renal masses and certain chronic kidney diseases. This MR examination uses a multiparametric approach with conventional T1- and T2-weighted sequences for a visual image interpretation based on signal intensity, in addition to diffusion and contrast-enhanced sequences providing rough tissue analysis.

Therefore, there is a need for a non-invasive imaging marker to get more precise quantitative information on the tissue. Mapping is a non-invasive MRI technique enabling tissue characterization based on the measurement of the native longitudinal T1 (T1m) and transverse T2 (T2m) relaxation times in milliseconds without any contrast agent. Mapping technique has been initially developed in the context of cardiac imaging and is used in the clinical setting for quantification of infiltrative myocardial diseases and fibrosis, but can be applied to other organs such as the liver, brain, and kidneys [1]. There are few recent clinical studies [2-4] which promoted the potential usefulness of mapping sequences as a promising tool to

evaluate and predict the outcomes in the context of various chronic renal diseases, including kidney transplant. To our knowledge, normal T1 and T2 values have been sporadically reported, with a wide range of technical parameters at different magnetic fields based on small cohorts of volunteers with a normal renal function. Recently, consensus-based technical recommendations for clinical renal MRI with T1 and T2 mapping have been published [5]. To the best of our knowledge, in the context of renal masses, only two papers published by the same research team studied T1 and T2 mapping in malignant kidney tumor processes [6,7]. This study performed with a clinical high-field magnet (3T) using the technical sequences recommended by consensus on a large cohort of normal patients. We evaluated the potential usefulness of such biomarkers to differentiate malignant from benign lesions in the context of renal masses.

Materials and Methods

Study Population

Our monocentric prospective study was approved by our local Institutional Review Board, which waived the need for written informed consent. All patients recorded were orally informed about the purpose of the study and agreed to participate. During a period of 9 months (between February 2023 and November 2023), a cohort of 72 patients (over 18 years old) examined for renal masses was enrolled. Exclusion criteria were: inability to complete the MRI examination due to claustrophobia (three cases), motion artefacts on MR images with insufficient image quality (three cases), any history of renal surgery or medical kidney disease (four cases). Finally, we recorded 62 patients with 62 renal masses.Participants were considered as having a good renal function with the estimated glomerular filtration rate (eGFR) normal (eGFR≥100mL/min/1.73m^2) or mildly impaired (80mL/min/1.73m^2≤eGFR<99mL/min/1.73m^2) (Figure 1). We did not record simple or complicated cysts.

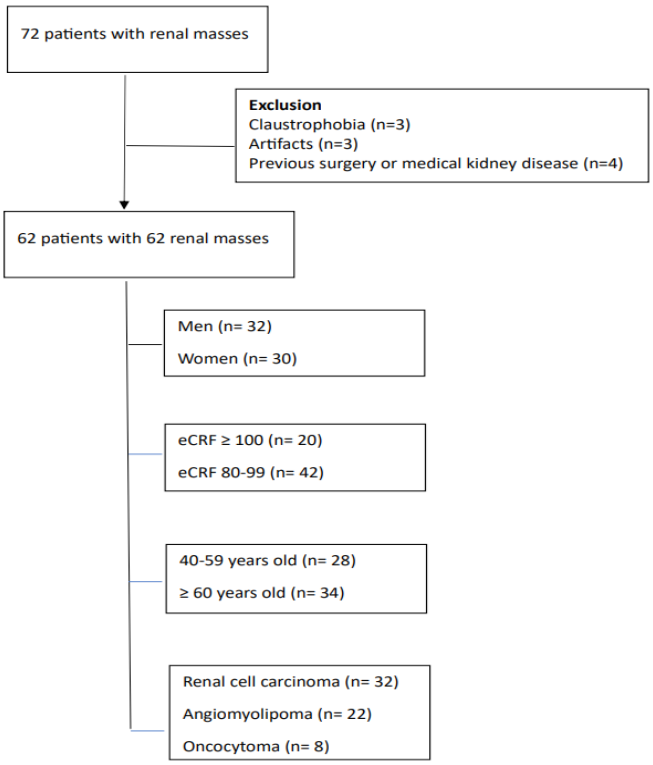

Figure 1: Flowchart of the cohort of patients with renal masses. It shows the reasons for exclusion and the different types of renal masses.

MR Protocol

MR examinations were performed using a clinical 3T MR unit (Ingenia CX, Philips Medical Systems, Best, the Netherlands) and a standard 32-channel torso phased-array coil. Patients were scanned with normal hydration status, no fluid intake restriction,

and no fasting. These mapping sequences were implemented on our MR device. The T1 and T2 mapping sequences were performed before gadolinium injection, in addition to our routine protocol for clinical purpose. We followed the consensus-based technical recommendations for clinical renal MRI with T1 and T2 mapping [5]. For T1 measurement, we used the modified Look-Locker inversion recovery sequence, called MOLLI, with the most recent 5(3)3 scheme according to a b-TFE (Turbo Field Echo) acquisition basis, and a low flip angle in order to save time and be compatible with individual breath-hold. The sequence was synchronized with the heart rhythm via a pulse oximetry at the end of the diastole, allowing a single shot-image to be obtained at different inversion times (TI), always at the same time of the cardiac cycle. This sequence followed a pattern of eight heartbeats: after a first 180° tilt, a first block of five inversions for five images was made, then after a pause of 3 seconds, three new inversions were performed to obtain three new images. The total acquisition time was 11 seconds in apnea and allowed to obtain eight images. Image parameters were: repetition time/echo time (TR/TE) of 1.99/0.90ms, field of view (FOV) of 300x300mm, matrix size of 256x256, one single coronal section passing through the long axis of both kidneys (normal cohort), one single coronal section passing through the tumoral process (renal mass cohort), section thickness of 10mm, TFE factor of 3, voxel size of 1.97x1.99x10mm, 20° tilt angle, SENSE factor 2, as well as TI with a minimum of 155ms, a maximum of 350ms, and TI increment of 24s.

T2 mapping was obtained using a multi-echo Gradient-Spin-Echo (GRASE) sequence [5], with a TR focused on the detection of the end of diastole. This sequence was performed in a single breath-hold. Nine echoes were performed using a TE of 8.9 to 80ms. Total acquisition time was 13 seconds in a single apnea, resulting in 11 images. Image parameters were: TR/TE of 741/9.3ms, FOV of 300x300mm, matrix size of 256x256, one single coronal section passing through the long axis of both kidneys (normal cohort), one single coronal section passing through the tumoral process (renal mass cohort), section thickness of 10mm, voxel size of 1.97x2.03x10mm, 90° tilt angle, and a SENSE factor of 2. The T1 and T2 maps were automatically generated by the supplier's post-processing software integrated into the dedicated workstation (Philips IntelliSpace Portal PACS 8.0, Philips Medical Systems, Netherland B.V).

Quantitative Evaluation

Measurements were recorded by a fellow radiologist (x) with 4 years of MRI experience and independently checked by a senior radiologist (xx) with 10 years of experience in abdominal imaging. Both were blinded to the biological data, gender, age, side, and final tumor type of the lesion. In cases of disagreement, data were reviewed and checked by consensus with a third expert (xxx) with more than 20 years of experience in uroradiology. Readers had previously been trained on this dedicated software for this purpose. For kidney masses, a circular freehand ROI of 1.0 to 3.0cm^2 encompassing the homogeneous solid portion of the lesion was drawn based on the visual evaluation of conventional sequences. It was thoroughly delineated to avoid the necrotic or cystic areas or the fatty tissue component. Measurements were repeated twice in the tumoral tissue (Figure 2). The mean value was recorded for each location. Care was taken to avoid any part of the medulla and perirenal fatty tissue. Average T1m and T2m values recorded in milliseconds (ms) with standard deviations (SDs) were collected.

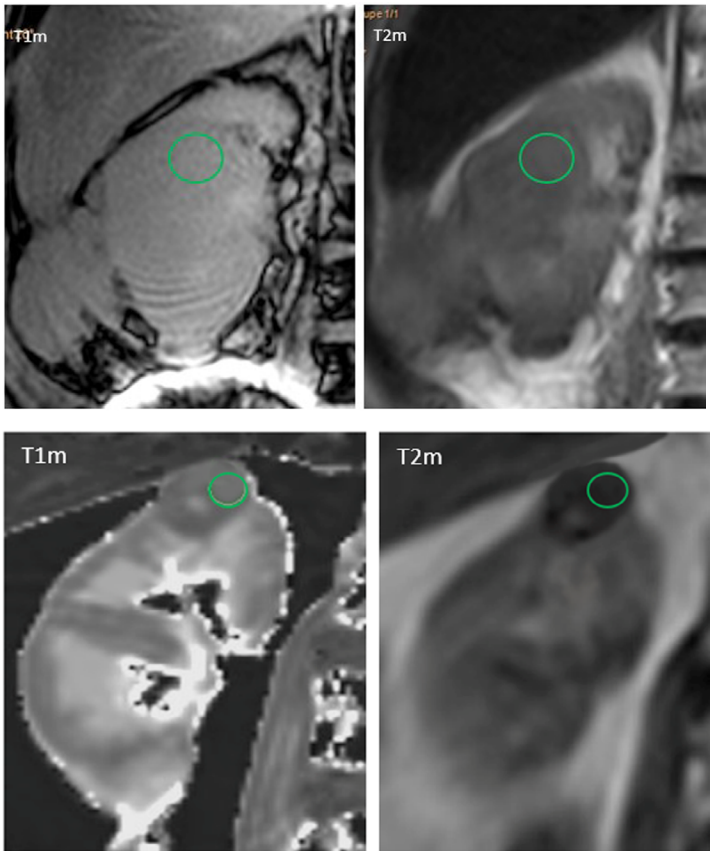

Figure 2: Examples of T1 and T2 mapping in the renal mass cohorts with region of interest (ROI) delineation.

2A: Native T1 mapping (left) and T2 mapping (right) coronal image of a huge ccRCC of the right kidney. The freehand circular ROI in the tissular part of the tumor was set at 1.5cm^2.

2B: Native T1 mapping (left) and T2 mapping (right) coronal image of an oncocytoma of the upper pole of the right kidney (maximum diameter: 3cm). A freehand circular ROI in the tissue part of the mass was set at 1.0cm^2.

Qualitative Analysis

Image quality was evaluated by the two readers (x) (xx), blinded to patient data and sequence type. They were asked to subjectively

and independently rate the overall image quality in terms of cortex recognition and artifact presence using a five-point scale ranging from 1 to 5: 1 = very poor image quality with no anatomical information, 2 = low image quality reducing the confidence in delineating anatomical information or lesion, 3 = moderate image quality sufficient to delineate kidney structures and lesion, 4 = good image quality clearly demonstrating anatomical structures and lesion, and 5 = excellent image quality enabling excellent differentiation of even small anatomical structures. Disagreements were resolved by consensus with the third reader (xxx).

Statistical Analyses

Statistical analyses were performed using the XLSTAT statistical software (Addinsoft, for Microsoft excel version 2019). Interobserver agreement for the qualitative analysis of image quality was assessed using quadratic Cohen's weighted kappa statistics (k). Kappa statistics were calculated using 95% confidence intervals. Kappa values <0 indicated no agreement, 0.00-0.20 poor agreement, 0.21-0.40 fair agreement, 0.41-0.60 moderate agreement, 0.61-0.80 substantial agreement, and 0.81-1.00 excellent agreement. Student's paired t- test was used to compare pairs of datasets in terms of T1m and T2m values. Our three subgroups of patients with renal masses were compared using a non-parametric Kruskal-Wallis test. A p-value <0.05 was considered to be statistically significant.

Results

Study Population

Our final cohort of patients (Figure 1) with renal masses included 62 lesions distributed between 303 women (mean age: 62±15.7 years old) and 32 42 men (mean age: 68±8.2 years old). The pathological diagnosis was done by biopsy or surgery in 32 cases of clear cell renal cell carcinomas (ccRCCs). For benign lesions, the indication for MR examination was follow-up of previously diagnosed masses (22 cases of angiomyolipomas and 8 cases of oncocytomas). Maximum diameter ranged between 4.2 and 9.5cm, between 2.5 and 3.5cm, and between 2.5 and 4cm for ccRCCs, angiomyolipomas, and oncocytomas, respectively. Concerning the pathological correlation, 20 ccRCC cases were International Society of Urological Pathology (ISUP) Grade 2 and 12 were ISUP Grade 3. We did not evaluate the potential correlation between the T1 and T2m with tumor grade.

Image Quality

Image quality scores were calculated at 3.51±0.52 and 2.95±0.42 for T1m and at 3.94±0.72 and 3.12±0.55 for T2m by reader (x) and reader (xx), respectively. The interobserver concordance for Likert score using Cohen's weighted kappa were considered as substantial, calculated at 0.81 (95% CI [0.71-0.85]) and 0.75 (95% CI [0.68-0.85]). Those two values indicated a rather suitable reliability.

Quantitative Analysis (Figure 3)

For renal masses, our results were for mean T1m and T2m: 1,727±97ms and 125±18ms; 1,621±96ms and 117±6ms, and 1,453±75ms and 95±10ms for renal cell carcinomas, angiomyolipomas, and oncocytomas, respectively. For T1m values, there was no significant difference (p=0.42) among the three types of renal masses. However, we have found a statistically significant difference for the T2m values (p=0.001). In pair comparisons, only T2m values were clearly statistically significant for each combination (Figure 3B): RCC versus angiomyolipoma (p=0.012), RCC versus oncocytoma (p=0.0002), and oncocytoma versus angiomyolipoma (p=0.003).

Fig 3A

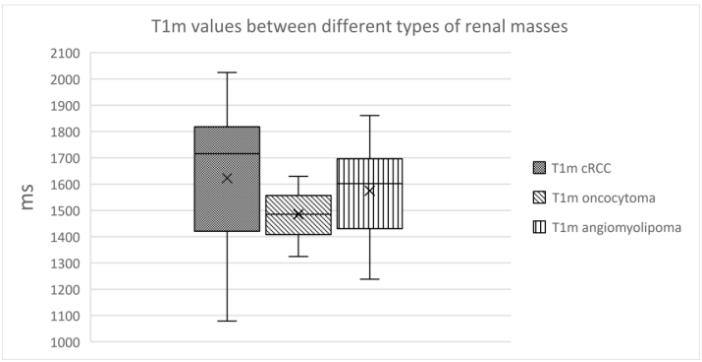

Fig 3B

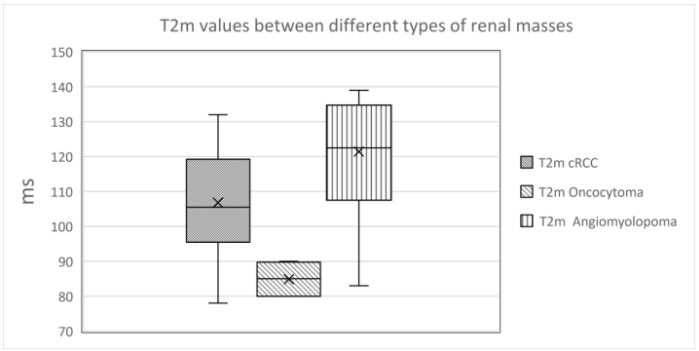

Figure 3: Box plots of T1m and T2m values of normal kidneys and different types of renal masses. There was no significant difference for T1m values among subgroups. In contrast, there was a clearly significant difference for T2 values between ccRCCs and benign masses, especially for oncocytomas. ccRCC: clear cell renal cell carcinoma.

Discussion

In the literature, a small number of papers with small cohorts reported unequal T1 and T2m values due to the heterogeneity of the acquisition protocols performed at different field strengths. Thus, no widely accepted references values are published, which limits their application [8]. There are inevitable variations of mapping values

caused by the increase of B0 from 1.5 to 3T, such as an increase in T1 accompanied by a decrease in T2. However, we think that for such advanced sequences, a clinical high-field magnet at 3T offers a better option than a low-field magnet. As those sequences have a short acquisition time, there is no real additional time to get more information on the tissue. Moreover, as those sequences were implemented in our MR unit for routine clinical cardiac practice, it was easy to use them for another organ. Our study was conducted on the renal masses which is a part we considered independent of the hydration status. We are aware that the T1 mapping value of the cortex is partially affected by the perfusion status, but none of our patients suffered from known impaired perfusion such as vascular disease or hypertension. Data were collected via manual placement of small-sized−circular ROIs, but the reviewers were very attentive to carefully delineate the surface, avoiding any part of the medulla, external fatty tissue or necrotic part. Our rather good interobserver agreement supports the reliability of our results. These findings are in agreement with the literature [1,8] concerning normal values and indicate that the native T1 mapping using the MOLLI 5(3)3 sequence is a reproducible and robust technique. It could be used as a reliable and consistent measurement of renal tissue composition. In previous papers conducted at 3 Tesla, a significant increased mean cortical T1m in patients with chronic kidney disease and pathological abnormalities such as fibrosis was reported. Consequently, our results could indicate that a patient with a normal T1m value and an eCRF between 60 and 79mL/min has no renal fibrosis [3,4,9,10].

Surprisingly, human *in vivo* measurements of renal T2m are relatively scarce. To our knowledge, there are only two papers that have studied cortical normal T2 values in humans at 3 Tesla, which were 76±7ms in the study by Bazelaire et al. [11] and 78±4ms; 85±16ms in the study by Adam et al. [6,10]. However, these studies included only six and 16 to 27 healthy patients, respectively. There is no explanation for this lack of data in the literature concerning the kidney parenchyma T2 mapping approach, especially as it does not require complex mathematical modeling and should be easily implemented in the clinical setting. Even if the image quality of the T2 mapping is always inferior to that of the T1m, it was always possible to record a value. For oncologic imaging, the potential usefulness of T2 mapping has been previously studied in a wide range of different malignancies such as gynecological tumors [12], brain tumors [13], prostate carcinoma [14], breast tumors [15] and lung tumors [16]. To our knowledge, only two papers have demonstrated on a 1.5T the potential usefulness of native T1 and T2 mapping for the distinction between lower and higher grades of ccRCC and suggested that it could be a helpful addition to multiparametric imaging. Low-grade ccRCC (ISUP 1, 2) showed significantly lower T1 values and higher T2 values compared with high-grade ccRCC (ISUP grades 3, 4), supporting the potential of T1 and T2 mapping as a non-invasive marker of ccRCC grade [6,7].

The explanation could be the pathological status of ccRCCs. Low-grade ccRCCs are associated with small nucleoli and low nuclear-to-cytoplasmic ratios, while high-grade ccRCCs are characterized by nuclear polymorphism, higher cellularity and nuclear-to-cytoplasmic ratios, suggesting that extracellular fluid is subsequently reduced. The hypothesis is that quantitative T2 mapping could be used to distinguish between lower and higher grade ccRCCs by visualizing differences in tissue composition, e.g., extracellular liquid. On the other hand, it has been also postulated that T1 values were significantly associated with the amount of collagen inside the tumor. Differentiating benign from malignant renal tumors is essential for patient management. To our knowledge, no data were found in the literature concerning this topic. We have found that only the T2m value displayed a statistically significant difference between benign and malignant processes. This was particularly significant when comparing ccRCCs and oncocytomas, as the latter presented a clear decrease in T2m value. We can suggest that it reflects the homogenous pattern of oncocytomas with a compact cell pattern, low extracellular liquid, and no necrotic part.

There were several limitations to this study. First, this was a monocentric study with a rather limited number of renal masses, however to our knowledge this is the largest cohort available in the literature. of renal masses. despite a large cohort of normal patients. Concerning renal masses, mapping values were only measured in one representative coronal plane, not in the whole tumor. Multicenter studies with a larger sample size of renal masses should be further conducted to validate our results. Second, we have used the MOLLI sequence optimized for cardiac T1 mapping, which was implemented and commonly used in our unit for cardiac application. An optimization for measuring renal T1 values could have been suitable.

Conclusion

T1 and T2 mapping are promising sequences, which are not time-consuming and displayed rather good interobserver agreement. Thus, they could be used in the near future to improve the potential of MR imaging as a non-invasive diagnostic tool. Moreover, despite the small sample size, those sequences can play a role in the differential diagnosis between benign and malignant renal tumoral masses. This need to be confirmed by further studies.

Ethical Guidelines

This study was approved by our local Institutional Review Board, which waived the need for written informed consent. All explored patients were orally informed about the purpose of the study and agreed to participate.

Conflict of Interest

All authors confirm the fact that they have no conflict of interest, no relationship and no financial support from the industry or personal relationships with other people or organizations that could inappropriately influence their work. There is no use of any type of

AI or AI-assisted technologies in the writing process of the manuscript

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