International Journal of Radiology Research
www.radiologyjournal.in
E-ISSN: 2663-4562, P-ISSN: 2663-4554
Received Date: 12-11-2018 Accepted Date: 16-12-2018; Published: 16-01-2019
Volume 1; Issue 1; 2019; Page No. 27-32

Development of an open source tool in magnetic resonance to evaluate knee cartilage lesions

Tiago Jornada[1], Luís Bueno[2] Regina Medeiros[3]
[1] Department of Diagnostic Imaging, Federal University of São Paulo, Paulista School of Medicine, São Paulo, São Paulo, Brazil
[2] Federal University of São Paulo, Institute of Science and Technology, Department of Science and Technology, Technology Park Unit São Paulo, São José dos Campos, Brazil
[3] Federal University of São Paulo, Paulista School of Medicine, São Paulo, São Paulo, Brazil

Abstract
T2 mapping is commonly used in the evaluation, progression and diagnosis of cartilaginous regions of the knee.
Objective: To develop a tool (open source free software) for the study of T2 relaxometry. Methods: We performed a pilot test through a knee image osssssf a volunteer using a 1.5 T MRI in order to developed a MATLAB program to generate the T2 maps. Results: We developed a software and named it Mapas T2. We obtained the T2 maps in the clinical routine of a group of three patients. In the comparison with the three free programs, no significant difference was found between the values of the T2 maps.
Conclusion: The developed software, now made available on the link https://mapast2.site123.me/, allows generating T2 maps of cartilaginous structures of the knee in an agile way and with usability features.

Keywords: cartilage, Relaxometry, T2 maps, MATLAB, Knee, Magnetic Resonance Imaging

Introduction

Degenerative joint disease is one of the most significant health problems in the elderly population [1]. Cartilaginous lesions usually progress slowly and clinical manifestations are observed when the articular cartilage is almost completely degenerated, making difficult the lesion detection through X-rays or CT exams [2].

One of the functionalities of Magnetic Resonance Imaging (MRI) is the study of cartilage diseases of the knee by means of T2 mapping. Therefore, T2 mapping is recommended for the evaluation of cartilaginous structures for providing a highly sensitive means to evaluate the water quantity, orientation and integrity of the collagen matrix [3].

This technique allows an indirect estimation of collagen content and does not require the use of contrast agents [4]. T2 mapping relates to the speed by which nuclei lose phase coherence following excitation [5]. Magnetisation loss allows estimating T2 or T2* relaxation times by adopting Equation 1 where S0 is the offset signal and Si is the signal obtained for TE (echo time) [6]. When articular cartilage is normal, collagen triggers the motion of water protons, which results in low signal intensity and consequently low T2 values. However, when articular cartilage is weakened, the mobility of cartilage water increases, thus increasing the values of T2 [7].

$$Si = S_0 e^{(-\frac{TE}{T2})} \tag{1}$$

Additionally, T2 mapping can be used as biomarkers to diagnose degenerative meniscus or as a repair indicator [8]. In this regard, Joseph *et al*. (2015) [9] conducted a study with 481 patients and created the first reference database of percentiles of T2 values associated with normal cartilage of the knee [9].

Kijowski *et al*. (2013) [10] implemented the addition of a T2 mapping sequence to a, routine MRI protocol at 3.0 T in the diagnosis of cartilage lesions within the knee joint. The addition of the sequence improved sensitivity in the detection of cartilage lesions from 74.6% to 88.9%, thus assisting in the identification of early cartilage degeneration [10].

Moreover, Andreisek and Weiger (2014) [11] carried out a descriptive review of the current literature on T2 mapping and concluded that the technique provides good results in the analysis of cartilage and that there is room for new studies and new clinical applications [11].

The ASPETAR is Orthopaedic and Sports Medicine Hospital accredited in 2009 as an International Federation of Association Football (FIFA) Medical Centre of Excellence published an article emphasising the use of T2 mapping in cartilage assessment. In the article, under the title Quantitative MRI of Cartilage: A Focus on T2 Mapping, the authors state that T2 mapping has shown to predict early degeneration cartilage and also monitor subtle changes due to therapy response after cartilage repair procedures [12].

The major difficulty in implementing T2 mapping in the clinical routine is the need for a standard multi-echo protocol specific to the MRI machine in use [13] as well as a software tool capable of performing the curve fittings or processing, automatically [14]. There is free software for the study of relaxometry, however with similar functions and tools.

In view of the above, the purpose of this paper is to develop an open source tool that allows obtaining T2 maps from magnetic resonance imaging of the knee with new tools that provide the radiologist with a new analysis possibility for T2 maps.

2. Materials and methods

The tool was written in Matlab version R 2015[b] ®. We programmed a code to obtain the T2 values, pixel per pixel, by means of Equation 2:

$$Si = S_0 e^{\left(-\frac{ET}{T2}\right)} + offset, \qquad (2)$$

where, S_o is the maximum sample signal, *offset* is the parameter to avoid convergence to zero, and S_i is the signal obtained for each Echo Time (ET).

For a given pixel and some echoes, parameters S_0, $offset$ and *T2* are calculated so that the measured signal values are as close as possible to the estimated values given by Equation 1. In our analysis, we used the Matlab's lsqcurvefit function, specifying the use of the Levenberg Marquardt method [15], and as an initial point we adopted the values obtained by classic linear approximation of the fitting given by Equation 2 with a null offset value.

Upon our request, Philips (the equipment manufacturer), furnished a multi-echo, similar-sequence protocol. This protocol was necessary as the equipment was unable to operate adequately using more than three echoes. Thus, the multi-echoes applied along with the technical parameters are described below.

In the present study, we used a 1.5 T Philips Achieva device with a dedicated 16-channel Sense Knee coil, adopting the following technical parameters: 180 x 142 Matrix (Freq X Phase), FOV 100 (mm), Retreat Time (RT) 2000 (ms), Echo Time (ET) 30-150 (ms), Time between Echoes 10 (ms), Echo Train 14, Pixel Bandwidth 263, Slice Thickness 3.5 (mm), Flip angle 90°, NEX 1, GAP 3.8 (mm) and scan time approximately 4min and 36s.

The equipment utilized was limited in resources necessary to reveal relaxometry T2 maps. Therefore, free software such as MRmap [16], Baum2D [17] and SPIN Lite [18] was implemented in the functionality study and was further used in the authentication of values obtained in the study reported.

The MRmap was published via GNU. a public platform (General PublicLicense), which was developed by Daniel Messroghli, MD. who is a member of the Cardiovascular Imaging Group of Congenital Heart Disease and Pediatric Cardiology at Deutsches Herzzentrum Berlin, a medical research center in Berlin? MRmap was programmed using IDL 7.0® (ITT Visual Information Solution, Boulder, CO, USA). The use of IDN requires a commercial license in order to be carried out ("IDL virtual machine"). As described in the work, the program was executed as follows: (1) The "File" tab was selected; (2) then the "Change directory" option was chosen; (3) subsequently, the folder was browsed to find solely DICOM images to be processed, as other image formats would report processing errors. Lastly, the Levenberg-Marquardt algorithm was implemented in order to adjust the curve appropriately.

Baum2D 1.14 was developed by Takashi Nishii, a staff member from the Innovative Imaging And Sensing Group from the Orthopedics Group at the University of Osaka. The MRI images were inserted via the following sequence: (1) the key labeled "DICOM" was selected and pressed; (2) the desired folder was picked; (3) afterward, the tool distinguished by a blue arrow was pointed and opted the study of T2 relaxometry. Finally, the key specified by the red arrow was clicked and the T2 Map was displayed.

SPIN Lite, a product developed by Magnetic Resonance Innovations, Inc, based in America, was used for image post-processing. Using the T2 / T2 * program tool, post-process images of the T2 maps were attainable.

The study of T2 relaxometry can be performed through a semiquantitative mode or an intensity scale. There are indiscernible differences when employing the MRmap program with respect to the apparent tones in the intensity scale; as a result, it makes the analysis quite complicated. However, it consisted of noteworthy characteristics: by placing the cursor over the region of interest, the application provided the T2 value as wells as the curve decay.

The SPIN Lite program consists of a T2 / T2 * function, where the intensity scale depicts only the maximum and minimum values; as a result, the task of assigning intermediate values to cartilage becomes difficult. There is an option to export processed DICOM format images through a viewer to observe the resolution. If the option is available to trace the Region of Interest (ROI), the values displayed would consist of T2 decay.

The Baun 2D program provides segmented values in the intensity scale. Thus, allowing the user to study the degree of cartilage involvement. The Baun 2D program provides the scale of the intensity with segmented intervals, allowing to deliberate about the degree of involvement of the cartilage.

As displayed in Figure 1, a program was developed consisting of characteristics unlike those analyzed in the present work, which was named T2 Maps.

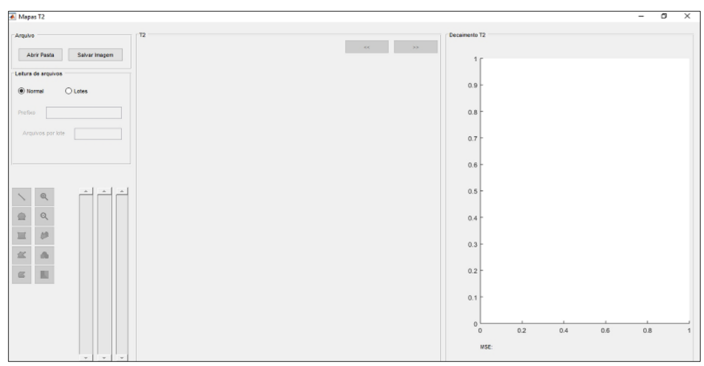

Fig 1

Fig 1 Maps T2 interface containing: tool to select folder with images in DICOM; to save images in different formats (JPEG, TIF, PNG and DICOM); option of the post-processing selection of the entire MRI series; space to enter the amount of echoes of the acquisition protocol, field to enter the prefix DICOM of the images; distance measurement tool; set of options to select different ROI formats; tools to increase and decrease the image magnification level; option to move the image within the preview area; option to switch the image between grayscale and color; scroll bar to modify lower and upper intensity scale value; tool to change the palette (or modify the LUT - Look Up Table); area for viewing post-processed image; intensity scale of T2 values; minimum and maximum intensity scale values; graph of the decay T2 with theMean Square Error (MSE).

The tools and functionalities of the proposed application were based on of Usability principles (International Organization for Standardization (ISO) [19], and the clinical needs of radiologists and academics.

We created a tool that allows the user to contour the anatomical areas in free format, thus obtaining the T2 value of the region of interest (ROI). This tool proves important if one considers that the irregular structures of the knee suggest the need to map the anatomical regions of the cartilage in segmented areas. One more function that was implemented allows delineating two or more structures and keeping ROI values visible in the interface, as shown in figure 2.

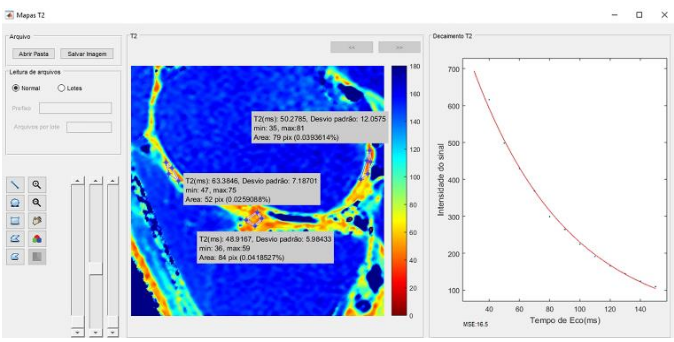

Fig 2: Simultaneous visualization of three ROIs on a single T2 map. Once the files containing the images are selected, the processed T2 map is displayed in the viewer and, after selection of an ROI, the decay curve is displayed.

We implemented the T2 map generator feature with all sequence images (batch processing mode). This function avoids the need to partition the exam, showing only echoes in an orderly manner in the regions of interest. For example, a protocol with 14 echoes may result in 210 images to cover the whole anatomy of the knee, and with the developed tool it is possible to order the images at every 15 echoes and obtain T2 maps of the entire anatomy. With the tool, one can visualize the decay curve of the region of interest with the value of the Mean Square Error (MSE). This information allows the user to deliberate on the fitting curve and whether the value of the error is within the degree of reliability adopted in the study.

The tool also allows obtaining a T2 map exclusively of the region under study while keeping the remainder of the image in grayscale. It tends to minimize errors of interpretation when the analysis of an ROI is carried out based on the scale of intensity. As presented, the T2 maps intensity scale is accessible to the user and is composed of 20 ms intervals. Thus, a more precise analysis of cartilage is able to be performed. The zoom function, coupled with the possibility of obtaining an ROI in free format, provides greater assertiveness in limiting the structure under analysis. There is also the possibility of post-processing all the images under examination, providing a broader and more precise view on the impairment degree of the cartilaginous structures of the knee.

In the post-processing and T2 mapping step, the script runs automatically and disregards the first echo of the sequence. Then, in a sequence with 10 echoes, only 9 will be used for the calculations. This particular function was implemented in order to minimize intrinsic errors in multi-echo imaging sequence and in T2 estimation [8] since some physical aspects in the first echo are not considered by the model described in Equation 1.

3. Results & Discussion

Initially, we performed a pilot test from which we obtained a series containing 280 MRI images in the axial plane of the knee of a healthy volunteer (male, 36 years old). In a folder, we separated 14 images of the medial portion and selected the normal processing mode to read the files, resulting in a single T2 map. Through the use of the Baun 2D software, no significant differences were observed when the results of the T2 values were compared between the medial patellar cartilage (MPC) and the lateral patellar cartilage (LPC). Based on the images, Figure 3, it can be assumed that the male patient volunteer regions with values above 60 ms, thus evidencing the cartilage injury.

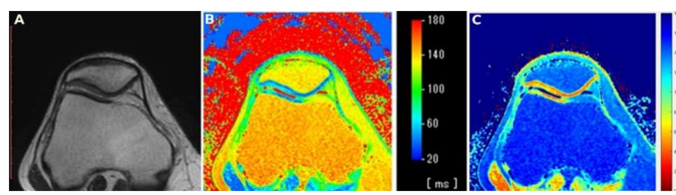

Fig 3: A) IRM of the volunteer, B) T2 map obtained with Mapas T2. C) T2 map obtained with Baun 2D.

The user can choose the batch processing mode, so the application will simultaneously provide 20 T2 maps of the sagittal plane of the volunteer, as shown in figure 4. A comparative study whit Baun 2D is apparently unfeasible, as the functionality is specific to the program developed.

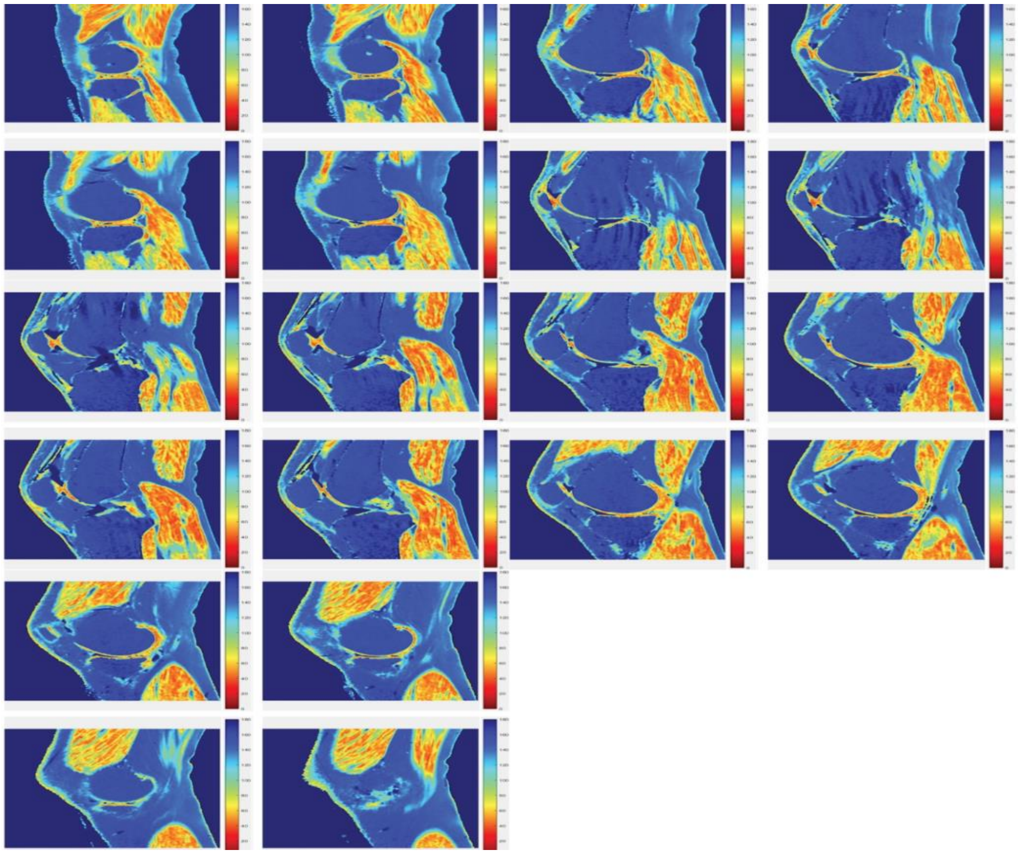

Fig 4: Simultaneous post-processing of the 280 MRI.

We obtained the T2 maps in the clinical routine by MRI of a group of three patients (N = 3), all of them referred to magnetic resonance examination of the right knee. In other words, there were no calls for patients or volunteers, and the study was approved by the Ethics and Research Committee of UNIFESP (CAAE: 16837213.1.0000.5505).

We adopted a simultaneous post-processing procedure and obtained T2 maps from the group of three patients, as shown in Figures 5, 6 and 7.

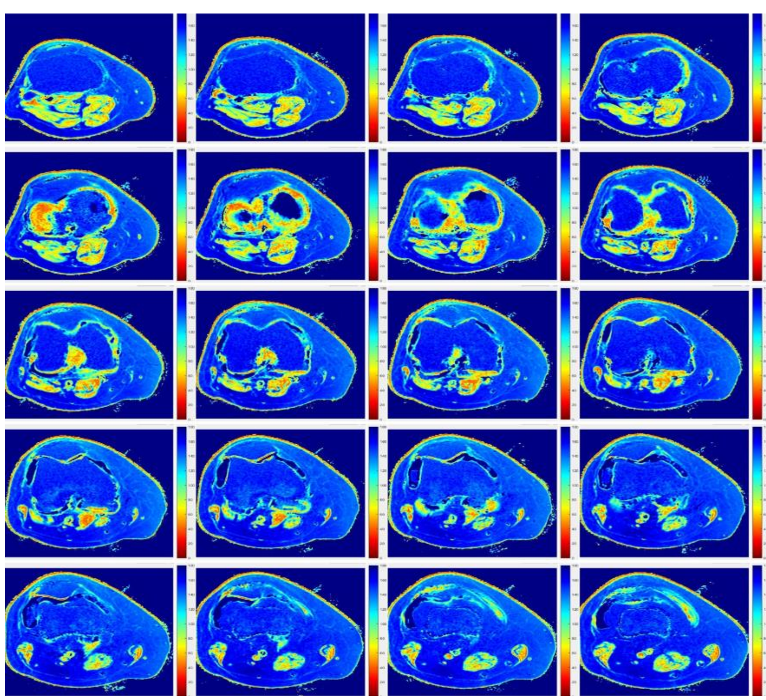

Fig 5: Exam of the 57-year-old female patient with a total of 280 images and an echo train of 14, therefore resulting in 20 T2 maps.

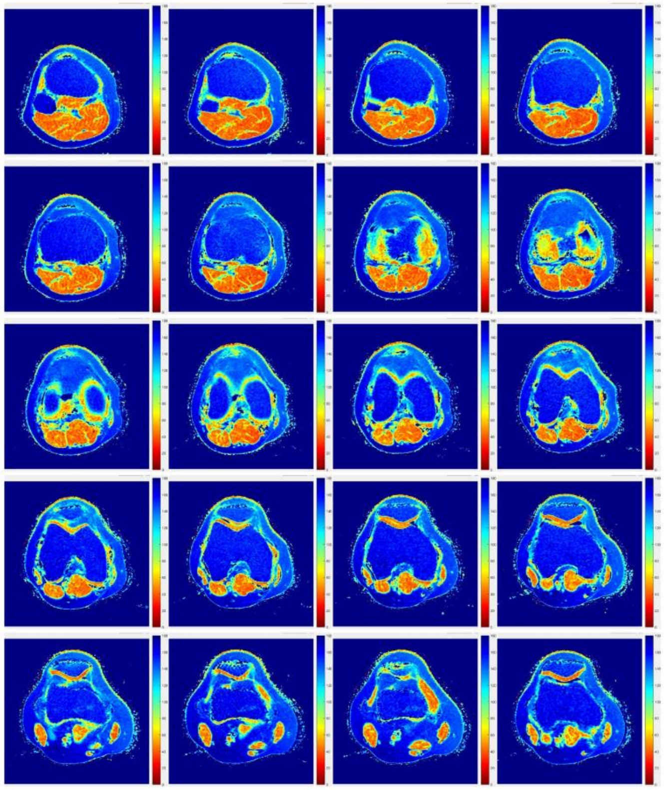

Fig 6: Exam of the 17-year-old female patient with a total of 280 images and an echo train of 14, therefore resulting in 20 T2 maps.

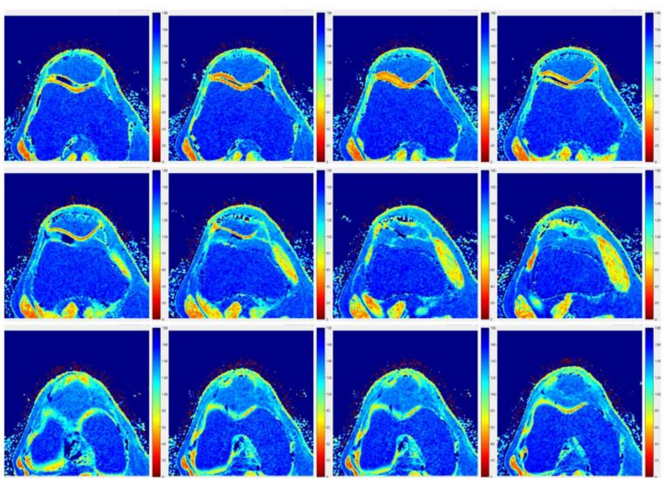

Fig 7: Exam of the 47-year-old female patient with a total of 168 images and an echo train of 14, therefore resulting in 12 T2 maps.

This function allows quantifying T2 values in different images, positions and regions of the organ under study allowing greater reliability in the evaluation of cartilage.

Normal processing methods were used in each patient, and the T2 values obtained from the medial patellar cartilage (MPC) and lateral patellar cartilage (LPC) via Baun 2D software were contrasted, as shown in Table 1.

No significant differences were observed in the T2 values within the software; however, a significant inconsistency in the standard deviation was noted. These differences arise due to the tracing difficulty concerning ROI with Baun 2D. This is resultant of a language barrier involved with Japanese. Hence, it was undefinable and uncertain whether the program contained a tool that allowed images to be enlarged in order to observe structure outlines.

Table 1: Values of T2 in clinical patients

Patient	Software	Value of T2 (ms)	
		Portion of Cartilagem	
		MCP	LPC
1	Mapas T2	74,46 ± 22	51,96 ± 10
	Baun 2D	73,45 ± 21	49,53 ± 11
2	Mapas T2	46,96 ± 6,2	44,67 ± 5,3
	Baun 2D	45,93 ± 7,2	43,89 ± 8,6
3	Mapas T2	63,70 ± 5,3	54,85 ± 8,2
	Baun 2D	62,22 ± 7,3	56,74 ± 6,9

For the T2 values between 30 ms and 40 ms, the tissue was preserved, and in the cases with values between 45 and 60 ms there are indications of cartilage injury [20].

In the female patient whit 57-year-old one is at an advanced stage of cartilage wear showing a very thin cartilage portion, which, even very thin, it was possible to zoom in the region and then quantify the T2 value, thus evincing a continuous process of degradation, with T2 values of about 70 ms in the portion MCP and about 50 ms in the portion LPC evincing stage of cartilage injury, Figure 5. In the 17-year-old female patient two, despite her young age and little cartilage wear, there is indication of cartilage injury, probably due to her practice of a high-impact sport namely soccer, as displayed, Figure 6. On the other hand the 47-year-old female patient is at an advanced stage of cartilage wear with T2 values of about 60 ms in the portion MPC and in the LPC s at an stage of cartilage injury with T2 values of about 55 ms, Figure 7.

8. Conclusions

The developed software, now made available to academic and professional environments, allows generating T2 maps of cartilaginous structures of the knee in an agile way and with usability features.

The zoom tool, coupled with the possibility of doing ROI in free format, provides greater assertiveness in the limitation of the structure under analysis. There is also the possibility of post-processing all the images of the examination, providing a broader and more precise view on the state of involvement of the cartilaginous structures of the knee.

The Mapas T2 application is an open source code and it is freely available (http://mapast2.site123.me) under the General Public License (GNU) for non-commercial use and open source development.

9. Acknowledgments

The authors are thankful to Dr. Henrique Manoel Lederman from the Support Group for Children and Adolescents with Cancer (GRAACC) for contributing to the conception and accomplishment of this paper. Special thanks are also addressed to the Radiation Physics and Hygiene Radiation team of the Diagnostic Imaging Department of the Paulista School of

Medicine - Federal University of São Paulo, and to the Coordination for the Improvement of Higher Education Personnel (CAPES) for the doctoral scholarships.

10. References

1. Thomas M. MRI of cartilage: pathological findings. Cartilage Imaging. Springer New York, 2011, 67-91.
2. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis. 1957; 16:494-502.
3. Braun HJ, Gold GE. Advanced MRI of articular cartilage. Imaging Med. 2011; 3(5):541-555. doi:10.2217/iim.11.43
4. Link TM. Cartilage Imaging: Significance, Techniques and New Developments, 2011, doi:10.1007/978-1-4419-8438-8
5. Plewes DB, Kucharczyk W. Physics of MRI: a primer. J Magn Reson Imaging. 2012; 35(5):1038-54.
6. Carneiro AAO, *et al*. MRI relaxometry: methods and applications. Brazilian Journal of Physics. 2006; 36.1A:9-15.
7. Dardzinski BJ, Mosher TJ, Li S, Van Slyke MA, Smith MB. Spatial variation of T2 in human articular cartilage. Radiology. 2014; 205(2):546-550. doi:10.1148/radiology.205.2.9356643
8. Potter HG, Foo LF. Magnetic resonance imaging of articular cartilage: Trauma, degeneration, and repair. Am J Sports Med. 2006; 34(4):661-677. doi:10.1177/0363546505281938
9. Joseph GB, McCulloch CE, Nevitt MC, *et al*. A reference database of cartilage 3T MRI T2 values in knees without diagnostic evidence of cartilage degeneration: Data from the osteoarthritis initiative. Osteoarthr Cartil. 2015; 23(6):897-905. doi:10.1016/j.joca.2015.02.006
10. Kijowski R, Blankenbaker DG, Munoz del Rio A, Baer GS, Graf BK. Evaluation of the Articular Cartilage of the Knee Joint: Value of Adding a T2 Mapping Sequence to a Routine MR Imaging Protocol. Radiology. 2013; 267(2):503-513. doi:10.1148/radiol.12121413
11. Andreisek G, Weiger M. Mapping of articular cartilage: current status of research and first clinical applications. Invest Radiol. 2014; 49(1):57-62. doi:10.1097/RLI.0b013e3182a574e1
12. Alizai H, Guermazi: A. Quantitative MRI of cartilage: a focus on T2 mapping. Aspetar Sports Medicine Journal, 2015; 4(1):152-157. http://www.aspetar.com/journal/upload/PDF/2015419132441.pdf. 01 july 2019.
13. Chavhan GB, Babyn PS, Thomas B, Shroff MM, Haacke EM. Principles, Techniques, and Applications of T2*-based MR Imaging and Its Special Applications. Radiographics. 2009; 29(5):1433-1449. doi:10.1148/rg.295095034
14. Fernandes JL. Perspectivas em ressonância cardíaca-mapa T1 e T2: fundamentos e utilidade clínica. Arq Bras Cardiol. 2015; 28(3):175-184.
15. Messroghli DR, Rudolph A, Abdel-Aty H, *et al*. An open-source software tool for the generation of relaxation time maps in magnetic resonance imaging. BMC Med Imaging, 2010, 10. doi:10.1186/1471-2342-10-16