The utility of ADC values in the risk stratification of prostate cancer using a 1.5T MRI without ERC

Poster No.: C-2573
Congress: ECR 2015
Type: Scientific Exhibit
Authors: J. Lopes Dias, J. Magalhães Pina, N. Vasco Costa, S. Carmo, C. Leal, T. Bilhim, R. M. R. Mateus Marques, L. Campos Pinheiro; Lisbon/PT
Keywords: Genital / Reproductive system male, MR-Diffusion/Perfusion, Diagnostic procedure
DOI: 10.1594/ecr2015/C-2573

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR’s endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method ist strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys’ fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Aims and objectives

The use of multiparametric Magnetic Resonance Imaging (mp-MRI) has significantly changed the diagnostic approach and management of prostate cancer. It combines the conventional sequences, T1 and T2 weighted imaging (WI), with at least two functional studies which may include diffusion weighted imaging (DWI), dynamic contrast-enhanced (DCE) and spectroscopy (1,2).

Detection, staging, tumor aggressiveness assessment, and recurrence suspicion constitute its main indications. The adding of functional studies improved the accuracy of MRI and allowed the analysis of new parameters like tumor aggressiveness that inspires the use of mp-MRI in active surveillance. Both DWI and spectroscopy allow this assessment, the first by studying the effect of the increased cellular density on free water motion, and the second by analyzing changes on the concentration of some metabolites like choline, creatine and citrate (3-5).

This functional imaging technique assesses the random movement of water molecules in different physical media. It is possible through the application of diffusion-sensitizing gradients with distinct strengths, known as b values and measured in seconds per square millimeter (sec/mm$^2$). It means that with a b value of 0 sec/mm2, there is no gradient and the signal intensity is based on T2 weighting. At high b values, such as 1000 sec/mm2, the water molecules within a highly cellular tissue retain their high signal and persist bright on DWI, as may occur within a tumor. In contrast, tissues containing water moving freely, like the bladder, will lose their signal (6-9).

DWI allows a quantitative analysis through the calculus of the apparent diffusion coefficient (ADC), measured in square millimeters per second. This quantification is displayed parametrically in a gray-scale map, where areas of restricted diffusion appear with a darker shade of gray (lower ADC values) and tissues with freely moving water show lighter shades of gray (higher ADC values). Some studies have shown a significant negative correlation between the ADC values of prostate tumors and prostatectomy specimen Gleason scores. Moreover, ADC values appear to perform better than TRUS biopsy Gleason scores in the association with prostatectomy Gleason scores. ADC values may allow a risk stratification and correct guidance of low-risk patients towards active surveillance (6,10,11).

This scientific exhibit will focus on the role of DWI in evaluating tumor aggressiveness. The purpose of our study was to evaluate the relationship between mean ADCs and postsurgical Gleason scores, and to determine the diagnostic accuracy of mp-MRI on a 1.5 T magnet in distinguishing low, intermediate and high-risk prostate tumors.
Methods and materials

This is a retrospective institutional-review-board-approved, single-center study.

• Patients

Within a 2-year period (from January 2013 to December 2014), 198 patients underwent prostate mp-MRI for detection, staging and active surveillance purposes. Among these patients, 32 patients with biopsy-proven cancers underwent radical prostatectomies. Two patients were excluded from the study because of motion artifacts on MRI. The remaining 30 patients were included in the study (median age, 60 years, range, 50-74).

• MRI Protocol

Mp-MRI studies were performed on a 1.5 T body scanner (Magneton Avanto; Siemens) with a 33 mT/m maximum gradient capability using an eight channel pelvic phased array (PPA), without endorectal coil (ERC). Peristalsis was not suppressed. In order to avoid post-biopsy hemorrhage, mp-MRI was performed at least 6 weeks after biopsy.

The study of the pelvis included an axial turbo spin-eco T1WI imaging and an axial Blade T2WI with fat saturation. With regard to the prostate gland study, we performed a set of axial, coronal and sagittal high-resolution T2WI. An axial DWI with b values of 0, 50, 1000 and 1200 sec/mm2, and ADC maps were automatically generated by the imager software. DCE-MRI using an axial fat-saturated 3D Vibe T1W MR sequence after administration of gadoterate meglumine, with a dose of 0.2 mmol/kg of body weight as a bolus injection, was also performed.

• Imaging Analysis

Two radiologists with 3 years of experience in interpreting mp-MRI worked in consensus and reviewed all images on a workstation (Advantage, GE Healthcare). Using histological reports for guidance, the tumors were retrospectively localized in DWI and ADC maps, as bright and dark areas, respectively. Axial T2WI and DCE sequences were synchronized with the ones above for a better localization of the lesions and a clearer anatomic depiction. T1WI were also reviewed in order to exclude hemorrhage-related artifacts.

Six sextants were considered: left base, right base, left midgland, right midgland, left apex, and right apex. Each sextant was also divided into anterior, posterior, lateral,
and medial sections. When possible, each sextant was further divided into central and peripheral gland. All these divisions were considered and reported in order to precisely localize the tumors and achieve a better association with the histologic reports. Only tumors originating in the peripheral zone were included in our study.

Mean ADCs were measured and examined for correlation with Gleason scores. The radiologist was blinded to the Gleason scores. All measurements were performed through the application of a single slice region of interest (ROI) within the tumor in the ADC map, trying to avoid tumor edges. ROIs had the same size for all tumors (27 mm²). In multifocal tumors, the two largest foci were considered for ADC measurement. In large, heterogeneous tumors, ROIs were placed in the darkest area of the tumor. Due to limitations in spatial resolution, tumors smaller than 5 mm in bigger axis were not studied. Figure 1 shows an example of ROI placement. Among the 30 patients, 2 had multifocal pathology with volume enough to measure on the ADC map, so a total of 32 tumors were studied.

- **Histologic Examination**

All prostatectomies were performed within 15 days of mp-MRI, and no treatment was implemented between them. The pathologist was blinded to the MRI results.

- **Statistical Analysis**

Two variables were considered: ADC values, a numeric variable, and Gleason scores, an ordinal variable. In relation to the Gleason scores, eight different grade groups were identified according to the primary and secondary features present. Gleason score was discretized into two new binary variables (score 6 vs score higher than 6; scores 6, 7 vs scores 8, 9). An exploratory analysis was carried out for all variables. Continuous variables were presented as mean or median, standard deviation (SD) or inter-quartile range (25th percentile-75th percentile), as required.

The relationship between ADCs and ordinal Gleason score groups was firstly analyzed by applying Spearman's correlation coefficient. Data was also displayed in a scatterplot. Moreover, in order to study the diagnostic accuracy of the mean ADC, logistic regression models were fitted to the data considering the two previous defined binary variables as the outcome. Predictive and discriminative abilities of the models were assessed by the Hosmer-Lemeshow goodness of fit test and by the area under the Receiver Operating Characteristic curve (AUC), respectively. A model with good fit will have a lower observed Hosmer-Lemeshow chi-square statistic value and a non-significant p-value. A level of
significance $\alpha=0.05$ was considered. Statistical analyses were performed with software (SPSS, version 22.0.01).
Fig. 1: Example of ROI placement. Left peripheral prostate cancer in a 67-year-old man (PSA 9.5 ng/mL; Gleason Score of 8). (A) Axial T2-weighted MR image shows a left peripheral hypointense tumor (arrow). (B) ADC map reveals left suspicious hyposignal lesion and ROI placement (arrow).

© Serviço Imagiologia, Hospital de S. José - Lisbon/PT
Results

30 patients were included in the study, and a total of 32 tumors were considered to ADC measurement. 12 (37.5%), 13 (40.7%), and 7 (21.4%) had Gleason scores of 6, 7, and more than or equal to 8, respectively.

Mean ADC showed a significant negative correlation with Gleason ordinal scores. The Spearman p value for mean ADC was -0.594 (p<0.001). According to the scatterplot, some overlap is found between the ADCs measured in tumors with Gleason scores of 6 and 7 (Figure 1).

In the differentiation of tumors with a Gleason score of 6 from those with a Gleason score of at least 7, mean ADC yielded an AUC of 0.76 (95% confidence interval: 0.59, 0.93) (Figure 2). The p value of Hosmer-Lemeshow test was 0.789. For an ADC of 0.906 x 10^-3 m, sensitivity and specificity were 83.3% (95% confidence interval: 51.6%, 97.9%) and 70.0% (95% confidence interval: 45.7%, 88.1%), respectively.
Fig. 2: Scatterplot: relationship between Gleason scores and mean ADC.

© Serviço Imagioiologia, Hospital de S. José - Lisbon/PT
**Fig. 3:** ROC curves of mean ADC in the differentiation of tumors with Gleason score of 6 from those with Gleason score of at least 7 and tumors with Gleason score of 6 and 7 from those with Gleason score of at least 8.

© Serviço Imagiologia, Hospital de S. José - Lisbon/PT
Conclusion

Due to economical limitations, it is not possible to all institutions to acquire the most recent technology and accompany the evolution on technical protocols. So, it is essential to adapt these protocols and evaluate their diagnostic accuracy when applied in less stronger magnets. According to some authors, optimal mp-MRI on a 1.5 Tesla (T) magnet requires the use of an Endorectal Coil (ERC) combined with a Pelvic Phased-Array coil (PPA) in order to produce high Signal to Noise Ratios (SNR) and therefore improving the image resolution and acquisition speed. However, there is no entire consensus about this item and others suggest that the use of ERC might not be mandatory for tumor detection and localization. It may consequently save time and costs, and cause the patient less discomfort (2,12-15). Our results are concordant with the most recent studies with and without ERC. Therefore, we conclude that mp-MRI on a 1,5-T magnet without ERC is highly specific and sensible, and may be used for assessment of tumor aggressiveness.

A significant negative correlation between ADC values and Gleason scores was found. These results are consistent with other studies like those of Bittencourt et al (6) or Verma et al (16). An important overlap between ADCs on tumors with Gleason scores of 6 and 7 was noted. Moreover, our study shows that mp-MRI on a 1,5-T magnet without ERC allows a good discrimination between Gleason scores of 6 and more than 6, and an excellent discrimination between Gleason scores of 7 or lower and more than 7. We were able to provide cut offs with good sensitivity and specificity levels between different Gleason scores. It constitutes an indirect way of determining biologic aggressiveness of the tumor, with consequent treatment implications.

Patients with Gleason score of 6 are stratified as low risk patients. Depending on laboratorial findings, a protocol of active surveillance may be performed in these cases. Serum PSA (which should be less than 10) is the most important laboratorial feature, but PSA velocity and PSA density may also be considered. Since the randomized biopsy tends to underestimate the Gleason score, mp-MRI seems to have an important role in non-invasing aggressiveness assessment and, when combined to serum PSA, may be able to accurately estimate the risk. Many centers consider other features like the percentage or number of positive scores to estimate tumor volume and select patients for active surveillance (17,18). New studies should be developed in order to evaluate if mp-MRI findings better estimates tumor volume than these biopsy features.

Mp-MRI evaluation is also important on the follow-up of patients who underwent active surveillance. An important decrease on ADC is probably related to an increase on the histological aggressiveness and should be considered as tumor progression. In that situation, a new biopsy would be recommended. Other features should obviously be
evaluated, like the size, the existence of new foci, changes on post-gadolinium dynamic patterns, and signs of extra-prostatic extension.

According to our results, mp-MRI is able to exclude high-risk patients, which are those with Gleason scores of at least 8. The distinction between low and intermediate risk was not so good (sensitivity of 83%). This difference was already expected since an overlap between ADCs on Gleason scores of 6 and 7 had been apparent. So, in doubtful cases, a guided biopsy should be performed.

Our study had some limitations:

1. It was retrospective;
2. Our results may not apply to a large patient population, because we have only considered patients who underwent radical prostatectomy. Since most Gleason scores of 8 and 9 do not undergo prostatectomy, the majority of our patients had Gleason scores of 6 and 7;
3. These results may only apply to peripheral tumors. Considering central and transitional tumors show distinct behavior on DWI, a specific study should be performed;
4. Our ADCs were derived from single slice-based ROIs. Moreover, only a ROI was placed within each tumor foci (in the darkest area). So, we performed a visual, qualitative evaluation, and did not quantitatively study the entire foci;
5. The slice thicknesses of prostatectomy step-sections and ADC maps were not exactly the same.

Overall, our study shows results similar to other manuscripts. Nevertheless, it is important to emphasize that limitations in acquiring the most recent technology should not constraint protocol evolution and adaptation by each institution. Sustained analysis with internal technology should be performed in order to assess diagnostic accuracy and validate technical protocols.

In summary, our results show that mean ADC values are inversely correlated with prostatectomy Gleason scores of peripheral tumors. In combination with PSA levels, mean ADC values may allow a correct assessment of the patient risk for treatment and active surveillance purposes, on a 1,5 T magnet without ERC.
Personal information

**Acknowledgment:** We wish to thank Ana Luísa Papoila, PhD, and Marta Alves, MD, for guidance and help with statistical analysis.

**Disclosures of Conflicts of Interest:** No conflicts of interest to disclose.


