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SCIENTIFIC PAPER

An inter-centre statistical scale standardisation for quantitatively evaluating prostate tissue on T2-weighted MRI

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Abstract

Magnetic resonance images (MRI) require intensity standardisation if they are used for the purpose of quantitative analysis as inherent variations in image intensity levels between different image sets are manifest due to technical factors. One approach is to standardise the image intensity values using a statistically applied biological reference tissue. The aim of this study is to compare the performance of differing candidate biological reference tissues for standardising T2WI intensity distributions. Fifty-one prostate cancer patients across two centres with different scanners were evaluated using the percentage interpatient coefficient of variation (%interCV) for four different biological references; femoral bone marrow, ischioanal fossa, obturator-internus muscle and bladder urine. The tissue with the highest reproducibility (lowest %interCV) in both centres was used for intensity standardisation of prostate T2WI using three different statistical measures (mean, Z-score, median + Interquartile Range). The performance of different standardisation methods was evaluated from the assessment of image intensity histograms and the percentage normalised root mean square error (%NRSME) of the healthy peripheral zone tissue. Ischioanal fossa as a reference tissue demonstrated the highest reproducibility with %interCV of 18.9 for centre1 and 11.2 for centre2. Using ischioanal fossa for statistical intensity standardisation and the median + Interquartile Range method demonstrated the lowest %NRMSE across centres for healthy peripheral zone tissues. This study demonstrates ischioanal fossa as a preferred reference tissue for standardising intensity values from T2WI of the prostate. Subsequent image standardisation using the median + Interquartile Range intensity of the reference tissue demonstrated a robust and reliable standardisation method for quantitative image assessment.

Keywords Standardisation · MRI · T2WI · Quantitative imaging · Prostate cancer · CV · NRMSE

Introduction

MRI is widely used in prostate cancer diagnosis and clinical management due to its high tissue contrast compared with computed tomography (CT). MR T2-weighted images (T2WI) has become the primary imaging technique for demonstrating patient anatomy and pathology in prostate cancer [1, 2]. However MRI images are expressed in arbitrary units and the absolute values contained within those images can vary due to differences between: MRI scanners; scanning techniques or other technical influences resulting in variations between patients or for the same patient when rescanned at different time points [3–5]. Whilst generally not a problem for diagnostic interpretation, this variability compromises the ability to use T2WI in a quantitative manner such as when studying pathological changes over time or comparing or combining results from different MRI scanners. Furthermore, robust

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quantitative models can improve the reliability and objectivity of image interpretation by removing the influence of interpreter experience or improve automatic segmentation approaches for the identification of disease. Quantitative imaging is an approach in which absolute image values are applied to such things as machine learning and deep learning or for undertaking segmentation, co-registration and response to treatment evaluation [6–8]. A requirement for quantitative imaging is data consistency such that the image values are independent of technical influences and only dependent upon pathology.

To use T2WI quantitatively, however, requires a way of ensuring numerical consistency independent of non-pathological influences. One approach is to create T2 maps from multiple echo time acquisitions [9–12], however this requires additional sequences and cannot be applied retrospectively to standardly acquired T2WI.

Image standardisation is another approach in which the goal is to minimise the intensity variation for the same tissue type across different subjects or subjects scanned at different times [13]. One standardisation approach is based on histogram matching. This involves the mapping of a histogram for each subject onto a histogram template by matching the intensities of manually or automatically chosen landmarks [14]. Although this has been shown to produce reproducible results, reliable landmarks could be difficult to find, and in the case of disease, could result in the mismatching of tissue [10, 15, 16].

Statistically-based standardisation methods have been used to address these problems [17]. Examples of these methods include standardisation using the peripheral zone (PZ) pixels of the prostate T2WI using a Z-score [18]. The main drawback of the Z-score method using PZ pixels is that only 70% of prostate cancers are located in the peripheral zones. Another suggested approach is to standardise by dividing the image by the "median + Interquartile Range" [19]. These approaches however include pathology which are expected to differ between patients and may therefore influence the resulting image.

As an alternative, ratio based standardisation methods have been investigated using a reference tissue type such as bladder urine or obturator-internus muscle [20–24]. Statistical approaches have the advantage of being simple to implement and can be retrospectively applied to any image dataset; provided that a suitable reference tissue is available.

In this paper, four candidates for the reference tissue were evaluated; femoral bone marrow, ischioanal fossa, obturator-internus muscle and urine using T2WI data from two groups of patients from two different centres. The performance of the most reproducible reference tissue was then evaluated by using one of three previously reported intensity standardisation methods (mean, Z-score and median + Interquartile Range (median + IQR)).

Materials and methods

Our solution to image intensity standardisation is based on statistical intensity standardisation using a biological reference with high reproducibility in T2W Images. The process is demonstrated in the flow diagram of Fig. 1.

Data collection, image sequence and pre-processing

T2W images of the prostate images were acquired from two centres at the Calvary Mater Hospital (Centre 1) and Hunter Medical Research Institute (Centre 2), Australia. Images from Centre 1 were acquired from 30 transrectal ultrasound (TRUS)-guided biopsy proven prostate cancer patients (stages T2–T4) aged between 58 and 78 years (64.05 ± 14.74) and from Centre 2, 21 TRUS-guided biopsy proven prostate cancer patients (stages T2–T4) aged between 53 and 72 years (64.10 ± 6.34). Ethics approval for the study protocol was obtained from the local area heath ethics committee, and informed written consent was obtained from all patients for this retrospective study. The MRI images were performed with a 3T Skyra (Siemens Healthineers, Erlangen) scanner at Centre 1 and 3T Prisma scanner (Siemens Healthineers, Erlangen) at Centre 2, both using identical body phase array coils (Siemens Healthineers, Erlangen).

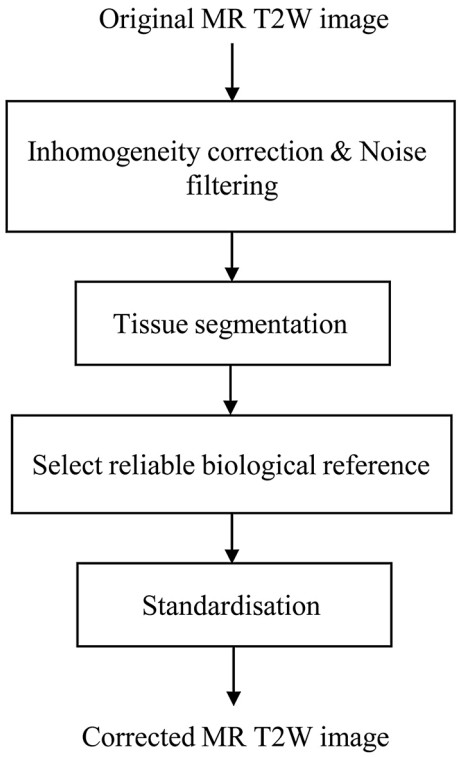


Fig. 1 Flow diagram of the intensity standardisation using biological references

All patients underwent contrast-free T2WI and DTI imaging at least 6 weeks after biopsy.

In both centres, two-dimensional turbo spin echo T2WI of the prostate (repetition time (TR): 1400 ms; echo time (TE): 96 ms; flip angle: 135°; slice thickness: 2 mm; field of view (FOV): 200 mm) were obtained in the axial plane. The T2WI were bias corrected using N4ITK bias correction method using [25] 3D Slicer software (http://www.Slicer.org) to eliminate intensity bias due to differing coil sensitivities [26]. The N4ITK algorithm is based on non-parametric nonuniform intensity normalisation (N3), with improvement in B-spline smoothing strategy. The N4ITK optimization parameters included: BSpline order of 3, BSpline grid resolution of (1,1,1), a shrinkage factor of 4, a maximum number of 100 iterations at each of the 3 resolution levels, and a convergence threshold of 0.001.

Noise reduction was then applied using a bilateral wavelet filter for Rician noise removal using Matlab2015.b software (The Math Works).

Biological reference selection

Four biological targets were considered for potential use as a reference for image standardisation: femoral bone marrow, ischioanal fossa, obturator-internus muscle and urine. These were selected as they all appear to meet the required criteria for a biological reference in that none were considered to be overtly affected by the disease pathology, were easily identifiable within the image and were of a size and uniformity to allow consistent sampling.

To determine the reference value, the femoral bone, ischioanal fossa, obturator-internus muscle and bladder were semi-automatically segmented (region growing variants algorithm) on axial 3D T2WI by a radiologist using Osirix software (http://www.osirix-viewer.com) (Fig. 2). In order to eliminate possible coil effects on the image intensity in different centres, the same anatomical location was selected after segmentation. The mean intensity of red bone marrow of the femur bone, ischioanal fossa, obturator-internus muscle and urine were measured and the potential of each as a reference evaluated.

Several different measures have been used for evaluating the reproducibility of tissue signal on MR images [27–29]. The most popular choice of intra-centre reproducibility evaluation among different tissues is the percent coefficient of variation (%CV) [28]. In this study, the biological reference reproducibility was assessed by inter-patient coefficient of variations (%interCV) in each centre, defined by

$$\%\text{interCV} = \frac{\sigma_t}{\mu_t} \times 100\% \tag{1}$$

where μ_t and σ_t are the mean and standard deviation of the biological reference across the patients. A smaller %interCV is an indication that intensity distributions are more similar and the biological reference is more reproducible. Therefore, the reference yielding the lowest %interCV was selected and used for statistical intensity standardisation.

Standardisation

The mean, standard deviation, median, and interquartile range intensity of the 3D biological reference were then determined. Three statistical standardisation methods; mean, Z-score and median + IQR were applied to the whole T2WI according to Eqs. (1–3), respectively:

$$S_i(v) = \frac{X_i(v)}{\mu_{iR}} \tag{2}$$

$$S_i(v) = \frac{X_i(v) - \mu_{iR}}{\sigma_{iR}} \tag{3}$$

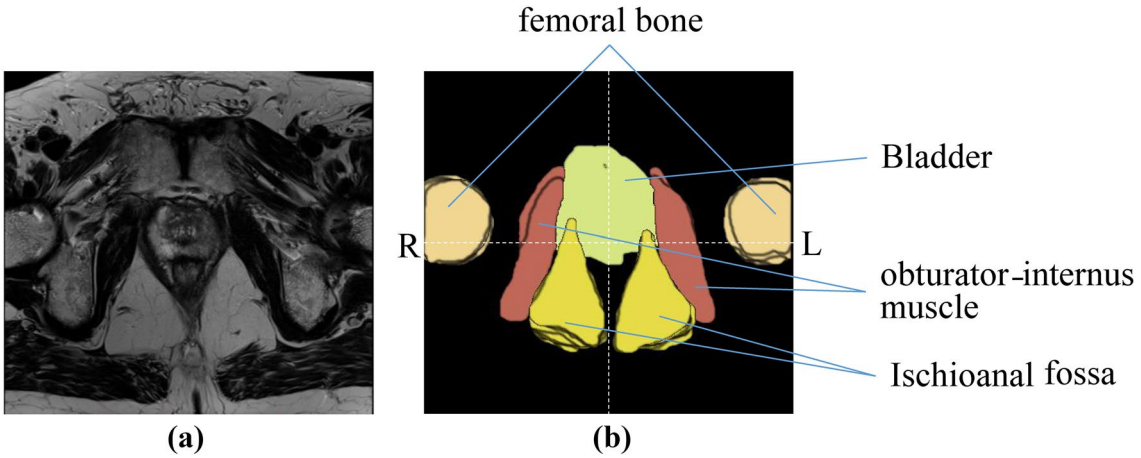


Fig. 2 Example of **a** axial T2WI form a prostate cancer patient, **b** 3D segmentation of femoral bone marrow, ischioanal fossa, obturator-interns muscle and bladder on axial T2WI

$$S_i(v) = \frac{X_i(v)}{m_{iR} + 2IQ_{iR}} \quad (4)$$

where $S_i(v)$ is the standardised image intensity at each voxel v for patient i,$X_i(v)$ is the image intensity at each voxel v for patient i, and μ_{iR}, σ_{iR}, m_{iR} and IQ_{iR} refers to the mean, standard deviation, median and interquartile range of the biological reference for patient i.

Evaluation of performance for standardisation

Pre- and post-standardised T2WI intensity histograms for each of the scans were calculated and plotted. For prostate tissue analysis, the prostate gland was manually segmented by an expert radiologist using OsiriX open-source medical imaging software (http://www.osirix-viewer.com). Then pre- and post-standardised intensity histograms for both the whole image and whole prostate for for all images from each centre were plotted and visually compared. Then the pre- and post-standardised mean histogram values for both the whole image and whole prostate for all images from each centre, were calculated and compared. The two tailed Student's t-test using IBM SPSS Statistics V 0.24 software (SPSS V.0.24.0, Chicago, IL, USA) was used to compare the difference between the mean histogram values of two centres and a p-value < 0.05 was regarded as statistically significant.

Then, the relative performance of the three statistical methods for image standardisation was assessed by evaluating the healthy PZ tissue. Healthy PZ was chosen since it is spatially close to prostate cancer pathology whilst unaffected by the cancer pathology, and hence should ideally be consistent between differing patient scans. To test for significant difference between the mean intensity of healthy PZ region before and after standardisation, a two tailed Student's t-test was used. Finally, to quantitatively evaluate the relative performance of statistical standardisation methods, the %NRMSE of intensity levels within healthy PZ tissue was used [30], defined by

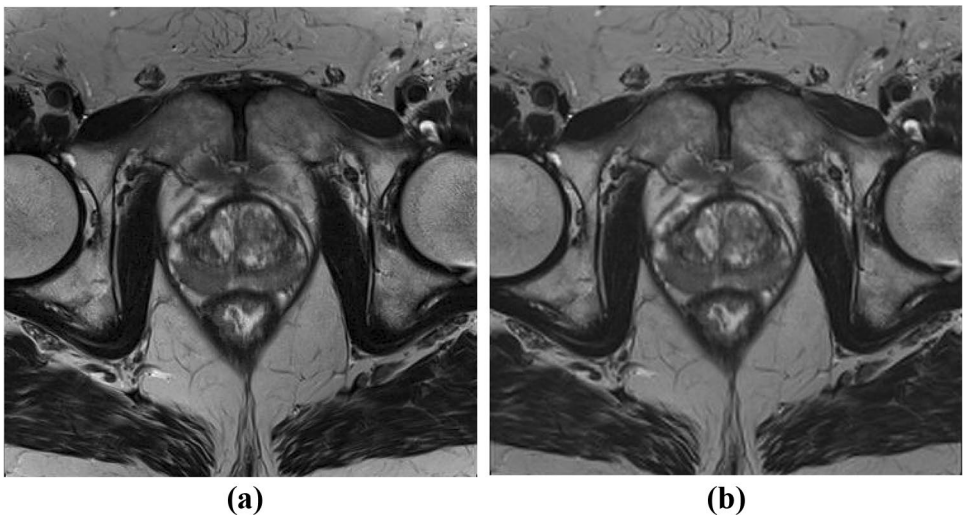
$$\%\text{NRMSE} = \frac{\sqrt{\frac{1}{2} \times \sum_{i=1}^{n} (x_i - \bar{x})^2}}{\max(x) - \min(x)} \quad (5)$$

where x_i is the mean intensity of healthy PZ tissue region for patient i and $\bar{x}$ is the mean intensity of healthy PZ tissue regions across patients. $Max(x)$ and $\min(x)$ are the maximum and minimum values of mean intensity of healthy PZ tissue regions over the patients. The %NRMSE facilities the comparison between of standardisation output with different scales.

Results

Filtering and bias correction

MR signal intensity measured from homogeneous tissue regions is seldom uniform due to different factors, such as radio frequency (RF) coil non-uniformity, statistic field inhomogeneity and gradient driven eddy currents and so on. These intensity variations significantly affect the performance of image registration, segmentation, machine learning and deep learning techniques. N4ITK bias correction and wavelet filter were used for inhomogeneity correction and noise filtering, respectively. A slice of a T2WI before and after correction is shown in Fig. 3. Figure 4 shows examples of five T2WI histograms from Centre 2 before (Fig. 4a) and after (Fig. 4b) bias correction and noise filtering.



(a) **(b)**

Fig. 3 **a** Raw slice of a prostate T2WI and **b** the corresponding slice after inhomogeneity correction and noise filtering

Biological reference tissue selection

To evaluate the biological references, the %interCV was measured in each centre. The urine demonstrated the least consistency between patients, while ischioanal fossa provided the best overall consistency considering interpatient variability (Table 1).

The intensity of femoral bone marrow, ischioanal fossa, obturator muscle and urine were scaled to 1 by dividing by its maximum value across the patients and used to create a boxplot as an overall comparison for the four biological references for each centre (Fig. 5). This boxplot shows the variation in the normalised intensity of the ischioanal fossa is lower that the normalised intensity of the other biological references in both centres.

Standardisation and performance evaluation

Using ischioanal fossa as the reference tissue, the performance of three statistical image standardisation methods

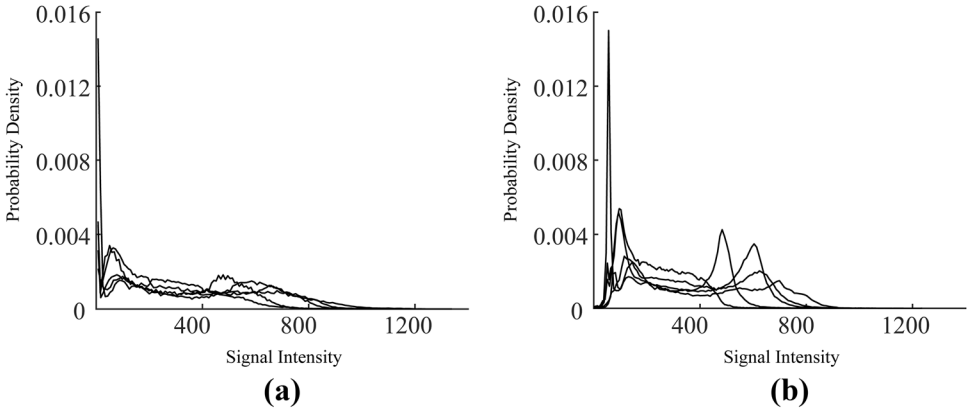


Fig. 4 Histograms of five prostate T2WI **a** before and **b** after noise filtering using bias correction using N4ITK and wavelet filter

Table 1 Interpatient coefficent of variation percentage (%interCV), standard devaiation (SD) and the 95% Confidence Interval (CI) of femoral bone marrow, Ischioanal fossa, obturator muscle and urine in Centre 1 and Centre 2

	Bone marrow	Ischioanal fossa	Obturator muscle	Urine
Centre 1 (N = 30)				
interCV	22.42	14.84	25.73	37.88
SD	21.39	22.182	6.69	88.21
CI (%95)	[87.75, 103.06]	[141.51, 157.39]	[23.92, 28.71]	[196.08, 261.96]
Centre 2 (N = 21)				
interCV	17.43	11.89	25.42	29.41
SD	77.34	57.60	14.44	13.66
CI (%95)	[410.42, 476.60]	[559.523, 608.79]	[50.63, 66.10]	[609.85, 804.23]

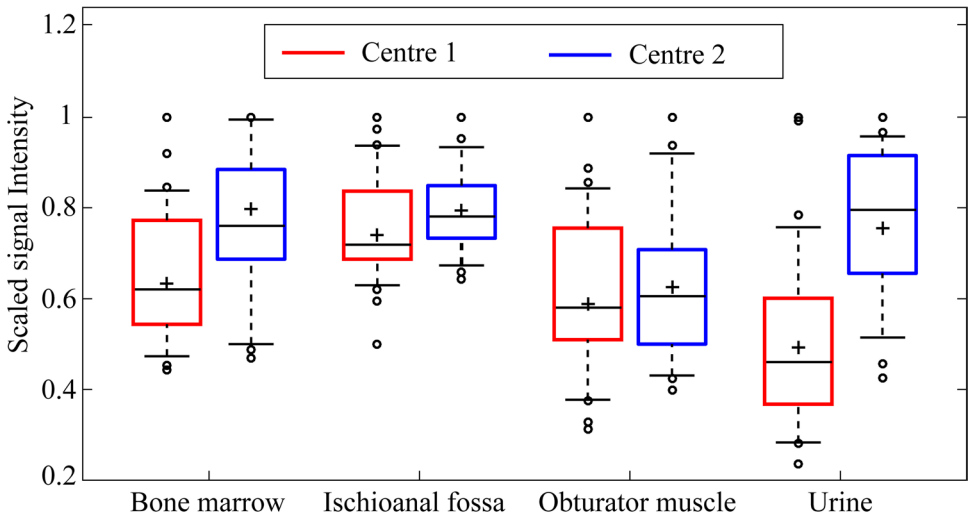


Fig. 5 The normalised mean intensity value of four different biological references derived from two centres using the same acquisition protocols. Ischioanal fossa yields lowest variability in both centres. For each centre, the intensity of femoral bone marrow, ischioanal fossa, obturator muscle and urine were scaled to 1 by dividing by its maximum value across the patients

have been assessed by comparing intensity histograms of T2WI from non-standardised and standardised images (Fig. 6). Non-standardised (Fig. 6a) histograms derived from two centres show significant variability as well as non-alignment. All three standardisation methods demonstrate a reduction in intensity variation with the greatest reduction observed with the mean and median + IQR methods (Fig. 6b, d).

A similar result was obtained when considering the whole prostate as can be seen in Fig. 7. As with the T2WI histogram results, visual inspection of the prostate histograms are more similar in distribution than before standardisation and in particular when using mean and median + IQR methods.

Following standardisation there was no significant difference in the mean histogram values of either the whole T2WI or the prostate gland between Centre 1 and Centre 2 (p-value > 0.05) (Figs. 8, 9).

Figure 10a, d show two slices from two different patients from two centres, acquired using the same protocol. The intensity range of the prostates before standardisation are quite different and these images are not appropriate for quantitative analysis. Figure 10c, f show the corresponding slices after bias correction and noise filtering and after bias correction, noise filtering and median + IQR based intensity standardisation using ischioanal fossa. These figures illustrate the improvements resulting from standardisation of prostate T2WI.

To evaluate the effect of standardisation on healthy PZ tissue, the mean intensity of each segmented healthy PZ region from each patient was calculated. There was a statistically significant difference between the mean intensity of non-standardised intensity of the healthy PZ between two centres (p-value < 0.001). No significant difference was observed between the mean intensity of pre- and post-standardised T2WI of the healthy PZ tissue using mean, Z-score and median + IQR methods with p-value = 0.254, 0.113 and 0.295, respectively. However, the %NRMSE of healthy PZ tissue across centres demonstrated a significant reduction following standardisation using ischioanal fossa for the mean and median + IQR standardisation methods (%NRMSE = 23.16 and %NRMSE = 20.35, respectively) compare to Z-score standardisation method (%NRMSE = 37.58). The mean intensity of the healthy PZ tissue and %interCV (Centre1–Centre2) results were summarised in Table 2. This result indicate that the performance of the median + IQR method is superior to other proposed methods.

Discussion

Standardisation of image intensity levels is a requirement when comparing results from images acquired from different patients or using different equipment. A number of statistical methods have been proposed in the literature to

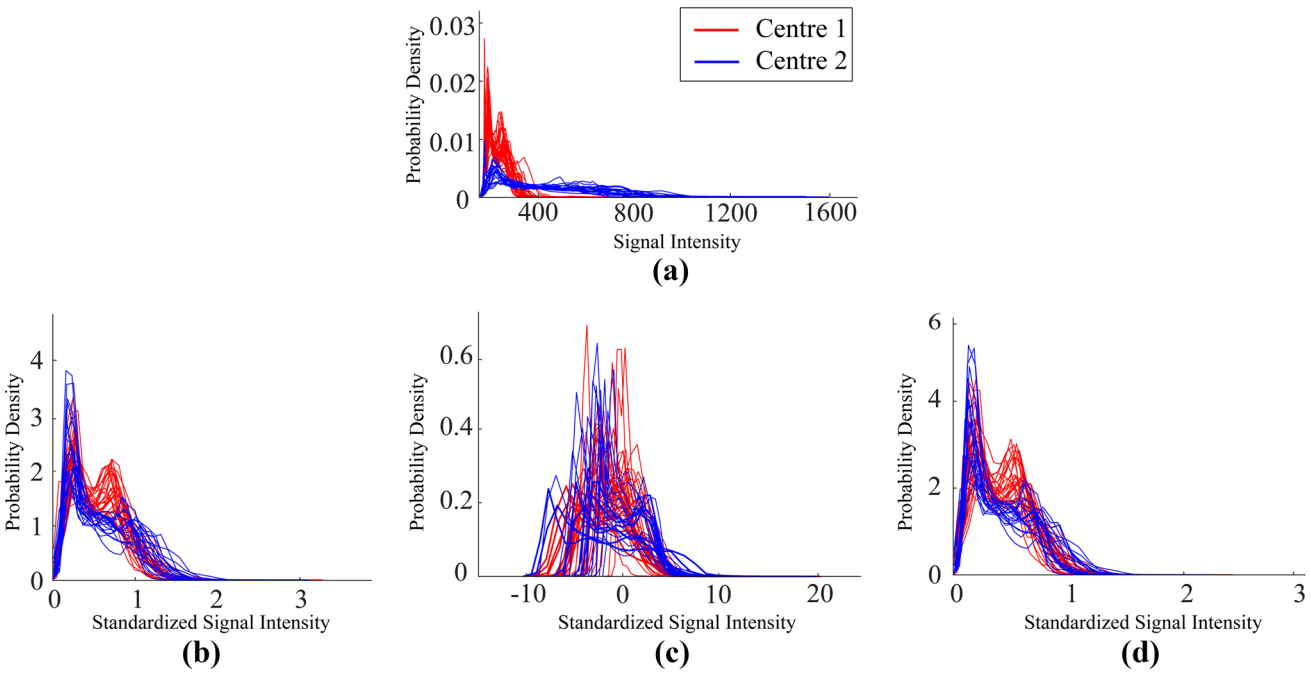


Fig. 6 Histograms of whole T2WI intensities: **a** before standardisation, and after standardisation using **b** mean, **c** Z-score and **d** median + IQR methods by ischioanal fossa tissue

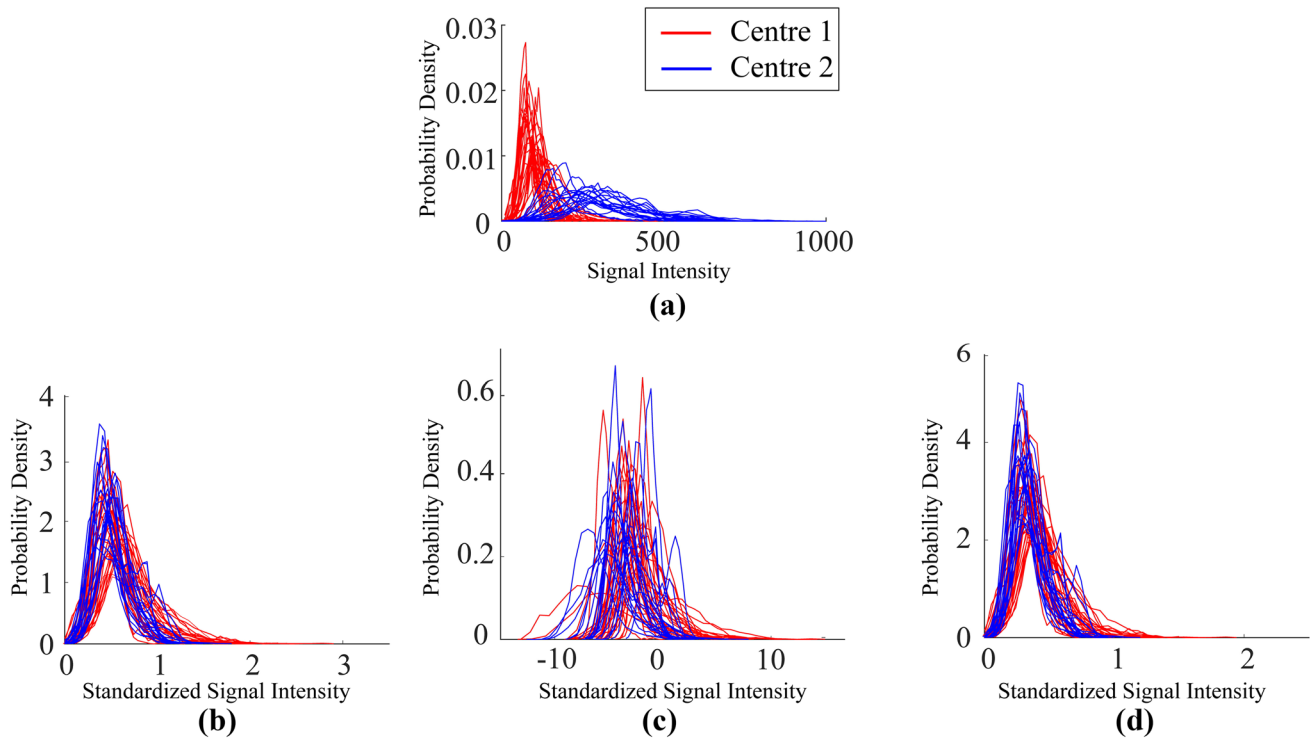


Fig. 7 Histograms of segmented prostate intensities on T2WI: **a** before standardisation, and after standardisation using **b** mean, **c** Z-score and **d** median + IQR methods by ischioanal fossa tissue

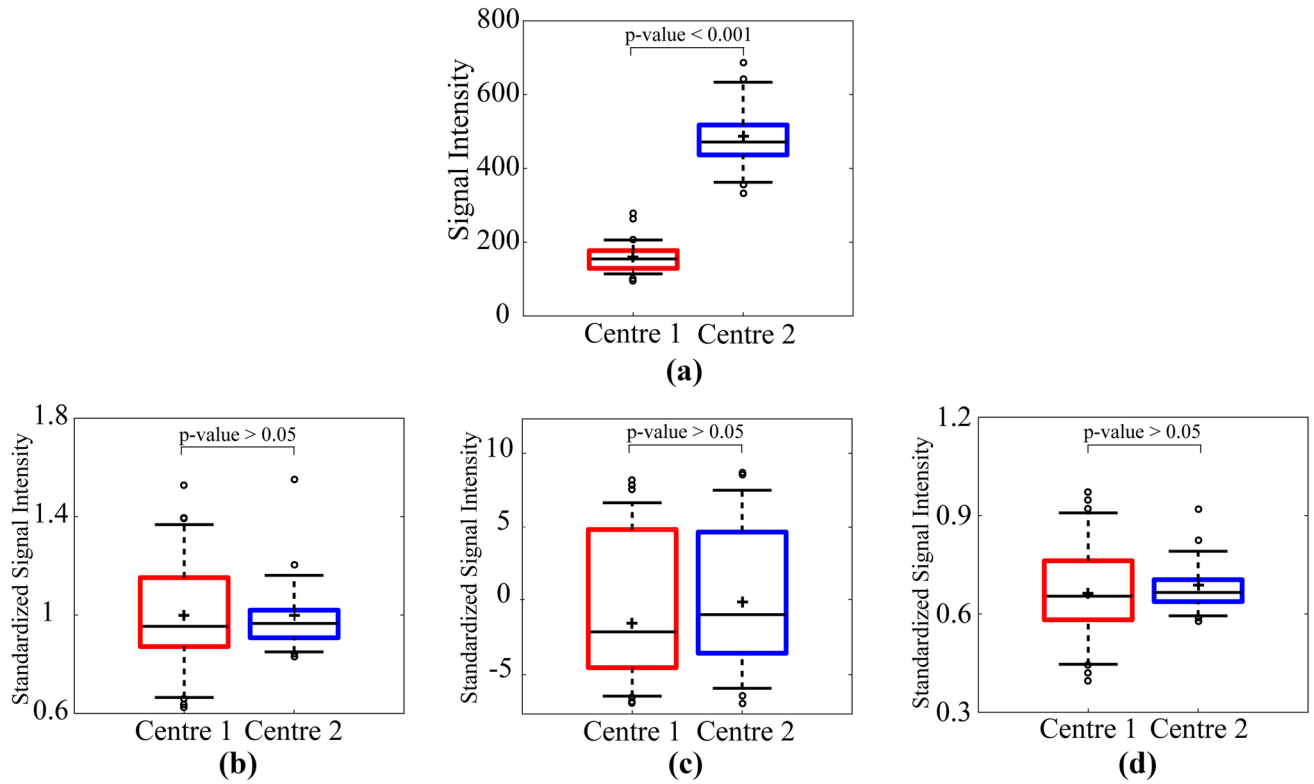


Fig. 8 The mean histogram values of whole T2WI: **a** before standardisation, and after standardisation using **b** mean, **c** Z-score and **d** median + IQR methods by ischioanal fossa tissue

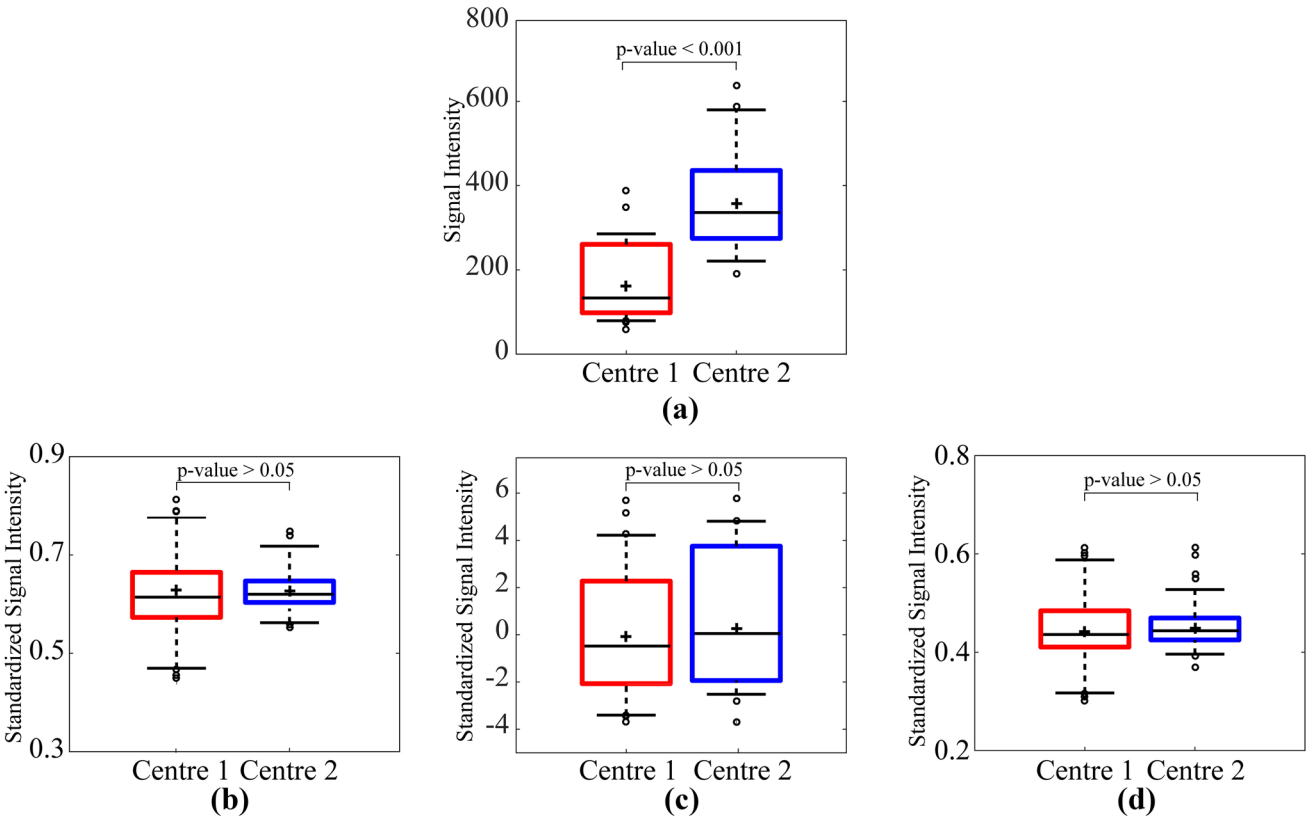


Fig. 9 The mean histogram values of prostate gland: **a** before standardisation, and after standardisation using **b** mean, **c** Z-score and **d** median + IQR methods by ischioanal fossa tissue

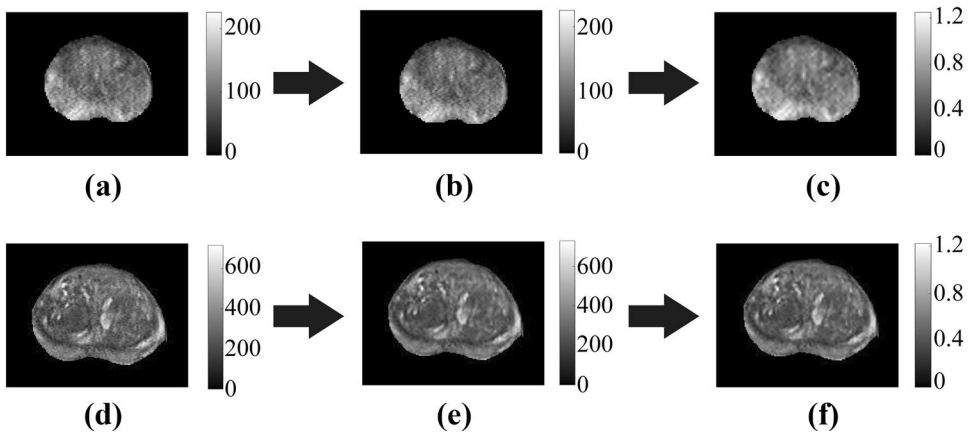


Fig. 10 An example of a segmented prostate on T2WI derived from Centre 1: **a** before, **b** after noise filtering and bias correction, and **c** after noise filtering, bias correction and standardisation. An example of a segmented prostate on T2WI obtained from Centre 2: **d** before, **e** after noise filtering and bias correction, **f** and after noise filtering, bias correction and standardisation

standardise prostate T2WI using different biological references. The choice of the actual reference for statistical intensity standardisation is an important consideration. In this paper, in order to find the best biological reference for statistical standardisation, we have assessed the reproducibility of femoral bone marrow, ischioanal fossa, obturator-internus muscle and urine using %interCV from images acquired at two different centres using magnets with same static magnetic fields, but different bore sizes (60 cm vs. 70 cm). Based on the results obtained from two centres, the ischioanal fossa demonstrated the lowest %interCV in both centres. In considering the choice of reference tissue, the normal femoral bone consists of a thin, sharply defined, low signal intensity cortex that surrounds a high signal intensity region consisting of red bone marrow and hematopoietic cells [31]. Ischemic necrosis and other abnormalities decrease the signal intensity of femoral bone marrow on MR images [32]. The

Table 2 Mean and standard deviation of signal intensity (SI) in healthy peripheral zone (PZ) tissue in Centre 1 and Centre 2 and the precentage of the normalized root-mean-square error (%NRMSE) of healthy PZ tissue intensity between centres before and after statistical standardisation

	Non-standardized	Mean	Z-score	Median + IQR
Centre 1 (N = 30)				
Mean SI ± SD	149.60 ± 41.05*	0.94 ± 0.27	− 0.38 ± 1.90	0.61 ± 0.11
Centre 2 (N = 21)				
Mean SI ± SD	495.98 ± 99.07*	1.03 ± 0.28	− 0.02 ± 2.05	0.65 ± 0.12
(Centre1–Centre 2)				
%NRMSE	69.98	23.16	37.58	20.35
SD	221.65	0.28	1.98	0.13
CI (%95)	[224.03, 341.96]	[0.90, 1.05]	[− 0.78, 0.30]	[0.65, 0.72]

*p-value < 0.05

Significant difference between the mean intensity of Centre 1 and Centre 2

obturator-internus muscle is one of the six deep pelvic muscles with medium signal intensity on T2WI. Muscle oedema, fatty infiltration, mass lesion and radiation therapy treatment might change the signal intensity on MRI images [33, 34]. Bladder urine is a fluid that gives a high and homogenous signal intensity on T2WI. In some cases, cystitis, stones, neoplasm or other abnormalities can cause haemorrhage or result in the presence of cells related to an inflammatory response, which can result in changes in the properties of bladder urine and thus can increase/decrease T2WI intensity variation as a consequence. In addition, the amount of bladder urine and the relative amounts of dissolved salts can change the proton density and thus the T2 intensity [35]. Although ex vivo MR spectroscopic studies of ischioanal fossa demonstrated altered chemical fat composition in patients with aggressive prostate cancer, there is no evidence of intensity variation of ischioanal fossa in MRI images taken from prostate cancer patients in vivo [36]. This study demonstrated that ischioanal fossa could be used as a reliable biological reference for intensity standardisation of T2WI.

This study demonstrates that normal femoral bone marrow, muscle and urine are not optimal biological references for standardisation due to their inherent signal variability. Ischioanal fossa signal is stable and thus confer a higher level of reproducibility when used a reference for intensity standardisation of prostate T2WI images, particularly when combined with a statistical methods of standardisation using the mean or median + IQR as the scaling factor. These results indicate good comparability across centres. These methods match the intensity without upsetting the natural and diagnostic balance of tissue intensities.

A limitation of this study is that there are no multiple repeats of a single patient to assess reproducibility. Another limitations are the small number of patients, the exclusion of healthy subjects and the lack of comparison of T2WI acquired at different static magnetic fields. Furthermore, artefacts from patient movement can affect segmentation, which could then also affect the standardisation.

Conclusion

Ischioanal fossa satisfies the requirement for a biological reference tissue for standardising prostate T2WI for different patients scanned at different times or on different scanners. Ischioanal fossa can be easily identified segmented on T2WI. Scaling the image intensity values according to the mean or median + IQR value of the ischioanal fossa demonstrated a significant reduction in intensity variations between different scanners.

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Author contributions The authors' responsibilities were as follows-Greer, Ramadan, Simpson: designed the research, protocol and project development, data acquisition and edited manuscript; Lau: prostate segmentation; Gholizadeh, Fuangrod, Ramadan: data analysis and wrote manuscript; Simpson: conducted the research and had primary responsibility for the final content of the manuscript.

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Compliance with ethical standards

Conflict of interest All authors read and approved the final manuscript. None of the authors had a conflict of interest.

Ethical approval Ethics approval for the study protocol was obtained from the local area heath ethics committee. This study was conducted under Hunter New England Imaging (HNEI) approval at Calvary Mater Newcastle, Australia.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Engelbrecht MR, Jager GJ, Laheij RJ, Verbeek AL, Van Lier H, Barentsz JO (2002) Local staging of prostate cancer using magnetic resonance imaging: a meta-analysis. Eur Radiol 12(9):2294–2302
2. Gupta RT, Spilseth B, Patel N, Brown AF, Yu J (2016) Multiparametric prostate MRI: focus on T2-weighted imaging and role in staging of prostate cancer. Abdom Radiol 41(5):831–843
3. Vovk U, Pernus F, Likar B (2007) A review of methods for correction of intensity inhomogeneity in MRI. IEEE Trans Med Imaging 26(3):405–421
4. Shah M, Xiao Y, Subbanna N, Francis S, Arnold DL, Collins DL, Arbel T (2011) Evaluating intensity normalization on MRIs of human brain with multiple sclerosis. Med Image Anal 15(2):267–282
5. Robitaille N, Mouiha A, Crépeault B, Valdivia F, Duchesne S (2012) Tissue-based MRI intensity standardization: application to multicentric datasets. J Biomed Imaging 2012:4
6. Doi K (2007) Computer-aided diagnosis in medical imaging: historical review, current status and future potential. Comput Med Imaging Graph 31(4):198–211
7. Avanzo M, Stancanello J, El Naqa I (2017) Beyond imaging: the promise of radiomics. Phys Med 38:122–139. https://doi.org/10.1016/j.ejmp.2017.05.071
8. Langer DL, van der Kwast TH, Evans AJ, Trachtenberg J, Wilson BC, Haider MA (2009) Prostate cancer detection with multiparametric MRI: logistic regression analysis of quantitative T2, diffusion-weighted imaging, and dynamic contrast-enhanced MRI. J Magn Reson Imaging 30(2):327–334
9. Liney GP, Knowles AJ, Manton DJ, Turnbull LW, Blackband SJ, Horsman A (1996) Comparison of conventional single echo and multi-echo sequences with a fast spin-echo sequence for quantitative T2 mapping: application to the prostate. J Magn Reson Imaging 6(4):603–607
10. Lemaître G, Rastgoo M, Massich J, Vilanova JC, Walker PM, Freixenet J, Meyer-Baese A, Mériaudeau F (2016) Martí R Normalization of t2w-mri prostate images using rician a priori. In: SPIE medical imaging. International Society for Optics and Photonics, pp 978529–978529–978527
11. Lewis S, Besa C, Rosen A, Rastinehad AR, Semaan S, Hectors S, Taouli B (2017) Multiparametric magnetic resonance imaging for transition zone prostate cancer: essential findings, limitations, and future directions. Abdom Radiol 42(11):2732–2744
12. Serai SD, Trout AT, Fleck RJ, Quinn CT, Dillman JR (2018) Measuring liver T2* and cardiac T2* in a single acquisition. Abdom Radiol. https://doi.org/10.1007/s00261-018-1477-4
13. Nyúl LG, Udupa JK (1999) On standardizing the MR image intensity scale. Magn Reson Med 42(6):1072–1081
14. Lv D, Guo X, Wang X, Zhang J, Fang J (2009) Computerized characterization of prostate cancer by fractal analysis in MR images. J Magn Reson Imaging 30(1):161–168
15. Madabhushi A, Udupa JK (2006) New methods of MR image intensity standardization via generalized scale. Med Phys 33(9):3426–3434
16. Shinohara RT, Sweeney EM, Goldsmith J, Shiee N, Mateen FJ, Calabresi PA, Jarso S, Pham DL, Reich DS, Crainiceanu CM (2014) Statistical normalization techniques for magnetic resonance imaging. NeuroImage 6:9–19
17. Wang S, Burtt K, Turkbey B, Choyke P, Summers RM (2014) Computer aided-diagnosis of prostate cancer on multiparametric MRI: a technical review of current research. BioMed Res Int. https://doi.org/10.1155/2014/789561
18. Artan Y, Haider MA, Langer DL, van der Kwast TH, Evans AJ, Yang Y, Wernick MN, Trachtenberg J, Yetik IS (2010) Prostate cancer localization with multispectral MRI using cost-sensitive support vector machines and conditional random fields. IEEE Trans Image Process 19(9):2444–2455
19. Kwak JT, Xu S, Wood BJ, Turkbey B, Choyke PL, Pinto PA, Wang S, Summers RM (2015) Automated prostate cancer detection using T2-weighted and high-b-value diffusion-weighted magnetic resonance imaging. Med Phys 42(5):2368–2378
20. Niaf E, Rouvière O, Mège-Lechevallier F, Bratan F, Lartizien C (2012) Computer-aided diagnosis of prostate cancer in the peripheral zone using multiparametric MRI. Phys Med Biol 57(12):3833
21. Niaf E, Rouvière O, Lartizien C (2011) Computer-aided diagnosis for prostate cancer detection in the peripheral zone via multisequence MRI. In: SPIE medical imaging. International Society for Optics and Photonics, pp 79633P–79633P–79638
22. Latifoltojar A, Dikaios N, Ridout A, Moore C, Illing R, Kirkham A, Taylor S, Halligan S, Atkinson D, Allen C (2015) Evolution of multi-parametric MRI quantitative parameters following transrectal ultrasound-guided biopsy of the prostate. Prostate Cancer Prostatic Dis 18(4):343
23. Giannini V, Mazzetti S, Vignati A, Russo F, Bollito E, Porpiglia F, Stasi M, Regge D (2015) A fully automatic computer aided diagnosis system for peripheral zone prostate cancer detection using multi-parametric magnetic resonance imaging. Comput Med Imaging Graph 46:219–226
24. Daffner R, Lupetin A, Dash N, Deeb Z, Sefczek R, Schapiro R (1986) MRI in the detection of malignant infiltration of bone marrow. Am J Roentgenol 146(2):353–358
25. Tustison N, Gee J (2009) N4ITK: Nick's N3 ITK implementation for MRI bias field correction. Insight J 9
26. Pieper S, Halle M, Kikinis R (2004) 3D Slicer. In: IEEE international symposium on biomedical imaging: nano to macro 2004. IEEE, pp 632–635
27. Westwood MA, Firmin DN, Gildo M, Renzo G, Stathis G, Markissia K, Vasili B, Pennell DJ (2005) Intercentre reproducibility of magnetic resonance T2* measurements of myocardial iron in Thalassaemia. Int J Cardiovasc Imaging 21(5):531–538. https://doi.org/10.1007/s10554-005-0651-2
28. Westwood MA, Anderson LJ, Firmin DN, Gatehouse PD, Lorenz CH, Wonke B, Pennell DJ (2003) Interscanner reproducibility of cardiovascular magnetic resonance T2* measurements of tissue iron in thalassemia. J Magn Reson Imaging 18(5):616–620
29. Byrum CE, MacFall JR, Charles HC, Chitilla VR, Boyko OB, Upchurch L, Smith JS, Rajagopalan P, Passe T, Kim D, Xanthakos S, Ranga K, Krishnan R (1996) Accuracy and reproducibility of brain and tissue volumes using a magnetic resonance segmentation method. Psychiatry Res 67(3):215–234
30. Patryla L, Galeriua D (2011) Statistical performances measures—models comparison. CEA, Paris
31. Totty WG, Murphy WA, Ganz WI, Kumar B, Daum WJ, Siegel BA (1984) Magnetic resonance imaging of the normal and ischemic femoral head. Am J Roentgenol 143(6):1273–1280
32. Mitchell DG, Kressel HY, Arger PH, Dalinka M, Spritzer CE, Steinberg ME (1986) Avascular necrosis of the femoral head: morphologic assessment by MR imaging, with CT correlation. Radiology 161(3):739–742. https://doi.org/10.1148/radiology.161.3.3786725
33. Ebner F, Kressel HY, Mintz MC, Carlson JA, Cohen EK, Schiebler M, Gefter W, Axel L (1988) Tumor recurrence versus fibrosis in the female pelvis: differentiation with MR imaging at 1.5 T. Radiology 166(2):333–340. https://doi.org/10.1148/radiology.166.2.3422025
34. Glazer H, Lee J, Levitt R, Heiken J, Ling D, Totty W, Balfe D, Emani B, Wasserman T, Murphy W (1985) Radiation fibrosis: differentiation from recurrent tumor by MR imaging. Radiology 156(3):721–726

35. Rosenkrantz AB, Bennett GL, Doshi A, Deng F-M, Babb JS, Taneja SS (2015) T2-weighted imaging of the prostate: Impact of the BLADE technique on image quality and tumor assessment. Abdom Imaging 40(3):552–559. https://doi.org/10.1007/s00261-014-0225-7
36. Iordanescu G, Brendler C, Crawford SE, Wyrwicz AM, Venkatasubramanian PN, Doll JA (2015) MRS measured fatty acid composition of periprostatic adipose tissue correlates with pathological measures of prostate cancer aggressiveness. J Magn Reson Imaging 42(3):651–657