Multi-parametric MRI at 3 Tesla for Prediction of Treatment Response in Rectal Cancer

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Introduction

Current functional MRI techniques have shown promising results for prediction and assessment of response to chemoradiotherapy (CRT) in rectal cancer [1,2], but lack sufficient accuracy for clinical use. There is a wide variation in performance of functional MRI in response prediction reported. Most studies describe single parameter values from either diffusion or perfusion MRI. Single parameter measurements, such as mean ADC or K^{trans}, do not adequately reflect tumor heterogeneity. Multi-parametric MRI using quantitative diffusion-weighted and dynamic contrast-enhanced imaging in combination can assess tumor heterogeneity and its response to treatment. This strategy has the potential to better reflect tumor heterogeneity and improve the accuracy of therapeutic response prediction and assessment in rectal cancer.

Since 2014 we have been conducting treatment response studies on our dedicated MRI system ('MR-Simulator' shown in Figure 1) which was installed in our Radiation Oncology Centre to provide MRI planning and guidance in various tumor sites. This report describes our results in rectal cancer.

Imaging details

Patients with locally advanced rectal cancer undergoing preoperative CRT prospectively underwent multi-parametric MRI on our 3T wide bore MAGNETOM Skyra (Siemens Healthcare, Erlangen, Germany) at 3 time-points: Pre-CRT, week 3 CRT, and post-CRT. The imaging protocol consisted of:

(i) T2-weighted image.

(ii) DWI using RESOLVE, which has been previously shown to be robust with respect to geometrical distortions [3]. Images were acquired with b-values 50 and 800 s/mm^2 and 1 & 3 averages. ADC maps and calculated b = 1400 s/mm^2 images were produced as part of protocol.

(iii) DCE consisted of pre-contrast VIBE scans with flip angles 2° and 15° in order to calculate native T1, followed by gadoversetamide (0.1 mM/kg) injection and 60 phases using TWIST with a 5 s temporal resolution. Buscopan was administered intravenously prior to the functional sequences to reduce rectal peristaltic motion.

1 The 3 Tesla MAGNETOM Skyra MR-Simulator at Liverpool Cancer Therapy Centre in Sydney, Australia.

Multi-parametric analysis and therapy monitoring

We developed a voxel-by-voxel multi-parametric histogram analysis strategy to assess tumor heterogeneity and its changes in response to combined chemotherapy and radiotherapy. A complete protocol and analysis strategy was developed which has utilized commercial, in-house developed and works-in-progress (Siemens' OncoTreat[1]) software. For DCE analysis, registration of the pre-contrast flip angle sequences to dynamic images was a crucial step in producing a pixel-by-pixel T1 map to ensure accurate voxel-by-voxel calculation of K^{trans}. Images were manually pre-registered in Siemens 3D fusion software and the headers of registered images were re-written with an in-house code to enable these images to be analyzed in

[1] The product is still under development and not commercially available yet. Its future availability cannot be ensured.

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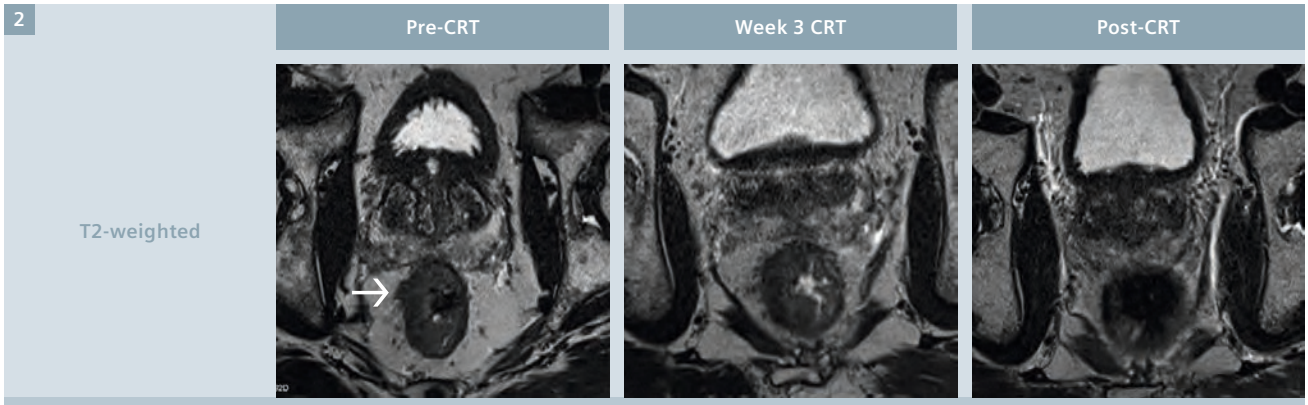

2 T2-weighted images for a rectal cancer patient at 3 time-points: pre-CRT, week 3 of CRT, and post-CRT. The rectal tumor (arrow) invades into the mesorectal fat. T2-weighted images alone cannot accurately assess treatment response, because of difficulty detecting residual tumor deposits within areas of radiation-induced necrosis or fibrosis.

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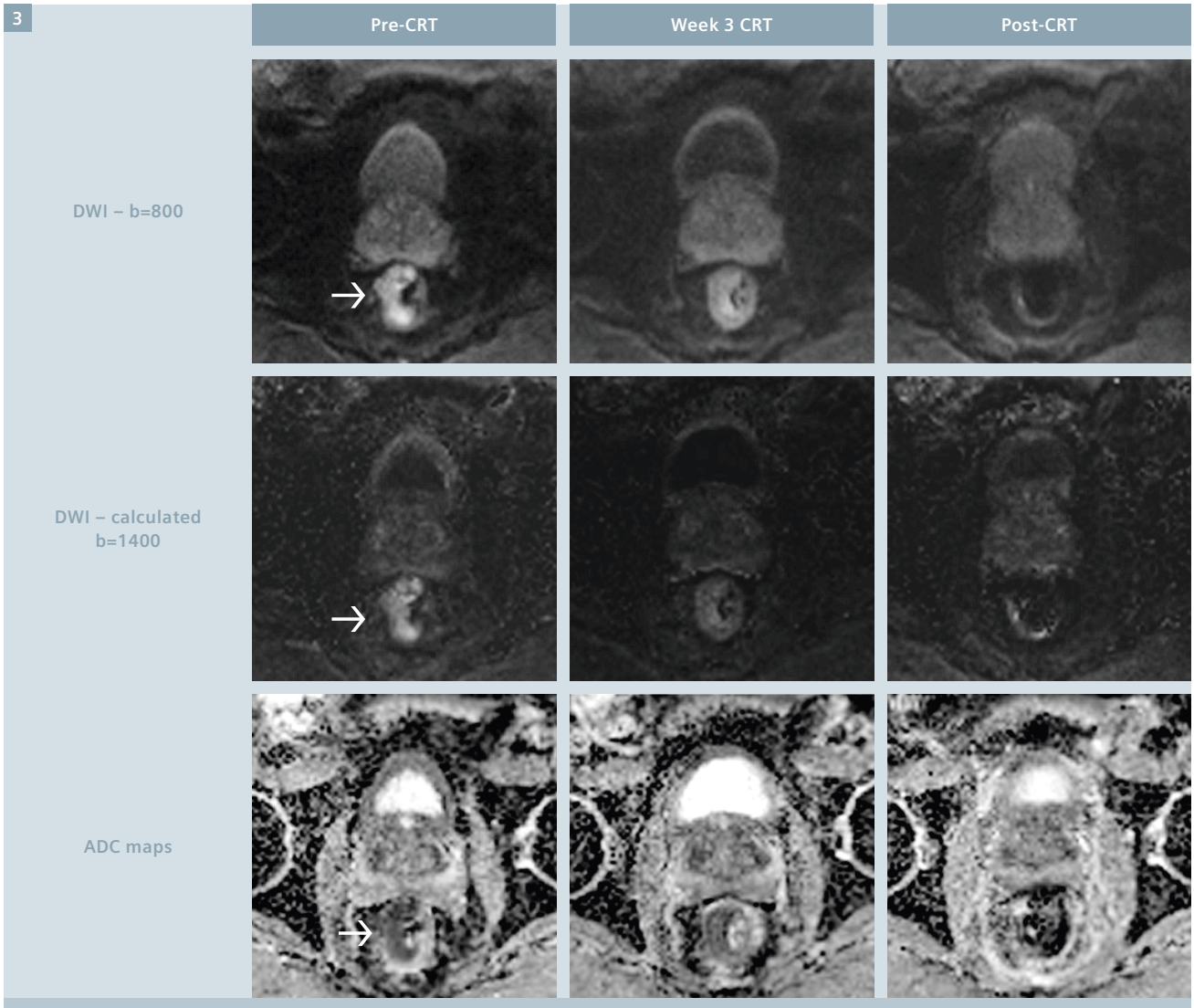

3 Diffusion-weighted RESOLVE images for the same rectal cancer patient at 3 time-points. The top panel shows the b = 800 s/mm^2 images, the middle panel shows the calculated b = 1400 s/mm^2 images and the bottom panel shows the ADC maps. Response to treatment can be seen on the diffusion images, with the level of tumor hyperintensity decreasing across the time-points. The histopathology demonstrated AJCC tumor regression grade 1 indicating a good response to preoperative CRT.

Tissue 4D. We have found this provides better results than using the available deformable registration. ADC and K^{trans} parameter maps were subsequently exported to OncoTreat where they were registered to T2-weighted images. Semi-automated segmentation was used to define the volume of interest from the hyperintense tumor on the calculated b-value = 1400 s/mm^2 images. We have found this dataset particularly useful – gaining both from the extra sensitivity and reduced noise of a calculated high b-value. A voxel-by-voxel technique was used to produce color-coded histograms of ADC and K^{trans}, as well as combined

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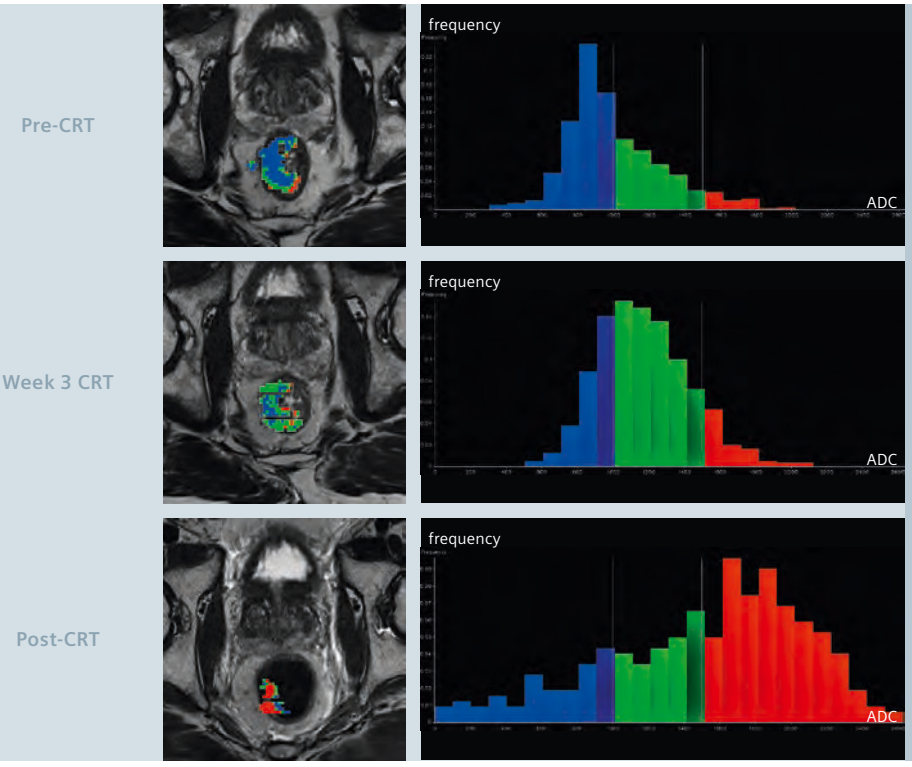

4 Example of the color-coded ADC maps and voxel-by-voxel histograms for a patient with good response to CRT. This patient had AJCC tumor regression grade 1 (moderate response, single cells or small groups of cancer cells) on histopathology. The histograms demonstrated an increase in the absolute ADC values of voxels over the time-points.

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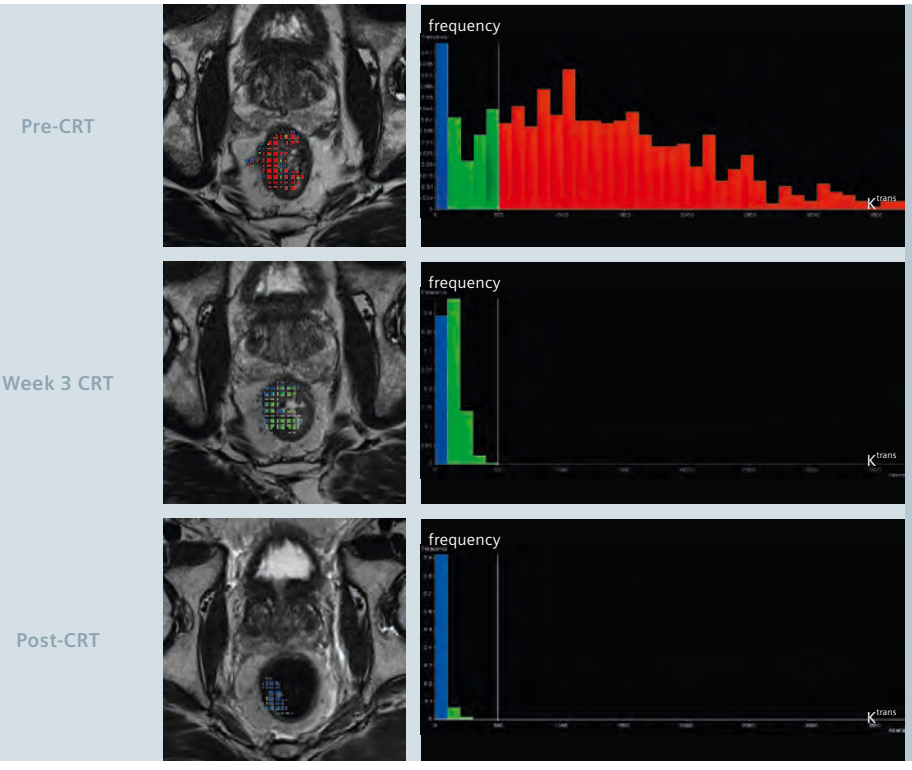

5 K^{trans} color-coded maps and voxel-by-voxel histograms for the same patient, who had a good response to CRT (AJCC TRG 1). The majority of K^{trans} voxel values were high (red) pre-CRT. A possible explanation for this is that the high K^{trans} is due to a well perfused oxic tumor, which is predictive of good radiotherapy response. By week 3-CRT the K^{trans} histogram demonstrated a marked reduction in the absolute K^{trans} values of voxels.

6 The scatterplots demonstrating changes in combined ADC and K^{trans} of voxels of segmented region over the time-points for a good responder with AJCC TRG 1 (top panel) and a poor responder with AJCC TRG2 (bottom panel). Percentages of voxels in each quadrant are shown. The scatterplots show different patterns of shift in the distribution of plots between the two patients. For Patient 1, the week 3 histograms and maps showed both a shift in distribution of ADC of voxels to higher values and K^{trans} of voxels to lower values compared to the pre-CRT histogram. In contrast, Patient 2 had low K^{trans} values pre-CRT, without much change in the values of voxels over the time-points. The low K^{trans} values in this patient may be due to poor perfusion representing a hypoxic tumor, which is predictive of a radio-resistant tumor and poor response to radiotherapy.

scatterplots for each time-point. CRT response was defined according to histopathology tumor regression grade (TRG) (AJCC 7th Edition) [4].

Conclusions

We have successfully integrated a multi-parametric MRI technique in our clinic to monitor response to treatment in patients with rectal cancer. This is a particularly challenging anatomy to image and provide robust functional datasets that can be examined in a serial manner. A voxel-by-voxel multi-parametric analysis strategy has been adopted and early results show this is important in quantitatively assessing heterogeneity within the entire tumor region, and the changes in response to CRT in rectal cancer.

Acknowledgement

This work was partially funded by the Royal Australian and New Zealand College of Radiologists (RANZCR) Withers and Peters Research Grant 2014.

References

1 van der Paardt et al. Patients who undergo preoperative chemoradiotherapy for locally advanced rectal cancer restaged by using diagnostic MR imaging: a systematic review and meta-analysis. Radiology. 2013;269:101-12.
2 Beets-Tan R and Beets G. MRI for assessing and predicting response to neoadjuvant treatment in rectal cancer. Nat Rev Gastroenterol Hepatol. 2014;11:480-88.
3 Liney G et al. Quantitative evaluation of diffusion-weighted imaging techniques for the purposes of radiotherapy planning in the prostate. Br J Radiol. 2015. DOI http://dx.doi.org/10.1259/bjr.20150034.
4 Edge S, Byrd D, Compt C et al (Eds). AJCC Cancer staging manual 7th edition. New York Springer 2010.

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