## Can diffusion-weighted MRI predict pathological complete response after neoadjuvant chemoradiation therapy in rectal cancer patients?

Giuseppe Petralia<sup>1</sup>, Josep Garcia-Bennett<sup>2</sup>, Luke Bonello<sup>3</sup>, Stefano Viotti<sup>3</sup>, Paul Summers<sup>1</sup>, Maria Giulia Zampino<sup>1</sup>, Maria Cristina Leonardi<sup>1</sup>, and Massimo Bellomi<sup>1,3</sup>

<sup>1</sup>European Institute of Oncology, Milan, Italy, <sup>2</sup>Hospital St Joan de Reus, Reus, Spain, <sup>3</sup>University of Milan School of Radiology, Milan, Italy

BACKGROUND: Up to 24% of rectal tumours show pathologic complete response (pCR) after neoadjuvant chemoradiation therapy (NACRT) [1]. For these patients there is increasing evidence that minimalist approaches (transanal excision or observation alone) might be reasonable alternatives, with equivalent outcomes, to the standard of care (radical surgery) [2]. Conventional magnetic resonance imaging (MRI) has proven to be inaccurate in differentiating viable residual tumour from radiotherapy-induced fibrosis [3]. Diffusion weighted MRI (DW-MRI) is able to detect abnormalities in cellular tissue structure and there is preliminary evidence that it can differentiate viable rectal tumour from fibrosis induced by NACRT [4,5]. The purpose of this study was to evaluate the potential of DW-MRI to predict pCR after NACRT in patients with rectal cancer.

METHODS AND MATERIALS: The study was approved by our institutional ethics committee; written informed consent was obtained from all participants before entry into the study. Fifty-nine patients (mean age 63, range 40-82; 24F, 35 M) with locally advanced non-mucinous rectal adenocarcinoma (T stage ≥ T3, or N1-2) underwent conventional MRI along with DW-MRI before (n=57) and after (n=51) NACRT, prior to surgery. All exams were performed on a 1.5T scanner (Avanto, Siemens Medical Systems). The parameters for the DW-MRI were TR /TE: 6000/68 ms; field of view/slice thickness/gap: 420x290/5/1 mm; matrix 128x64; at 5 b-values (0, 50, 250, 500, 900 s/mm²). Regions of interest (ROIs) were drawn manually on b-value images by a radiologist tracing along the inner boundary of the lesion for all sections where tumour was visible using the T2 weighted images acquired in the same plane as reference. The volumetric ROIs, corresponding to solid lesions, were drawn using ImageJ (ImageJ 1.43u, National Institutes of Health, Bethesda, USA), saved, and then processed with scripts developed in our department based on the FMRIB Software Library (FSL) (fsl 4.1.8, Analysis Group, Oxford Centre for Functional MRI of the Brain (FMRIB), University of Oxford, UK) to obtain mean, median and standard deviation of the apparent diffusion coefficient (ADC) values for each volume. According to the pathologic stage on the surgical specimen, patients were categorized into those who achieved a pCR (ypT0ypN0) and those who had residual disease (rD) after surgery (including local downstaging, no local downstaging or increase in local stage). Differences in mean pre-therapy and post-therapy ADC values and their change in groups of patients with pCR and rD were assessed using Students t-tests.

**RESULTS:** T2 weighted images, DW images at b-value of 900 s/mm<sup>2</sup> and ADC maps before and after NACRT treatment for a patient with pCR are seen in Figures 1 a, b, c and Figure 1 d, e, f, respectively. Nine out of the 59 patients included in the study (15%) presented pCR at final histology. No differences were observed in ADC values before therapy (p=0.46) between patients who achieved pCR and those who had rD (Table 1). Similarly, the ADC values after NACRT (p=0.35), as well as the absolute and the percentage changes of ADC values over the course of NACRT were not different (p=0.36 and 0.24, respectively) between the patient groups (Table 1).

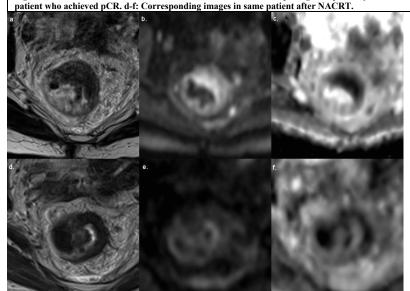


Figure 1.a-c: Pre-NACRT T2-wtd, b-value 900s/mm2, and ADC map images respectively for a

abie	1 Summa	ry or mean	ADC V	aiues at	amerent	umepoints

Mean ADC (x10-6 mm2/s)		р	
pCR	rD	1	
1214	1222	0.46	
1534	1505	0.35	
+320	+287	0.36	
32	26	0.24	
	(x10-6 pCR 1214 1534 +320	(x10-6 mm2/s)  pCR rD  1214 1222  1534 1505  +320 +287	

(pCR: pathological complete response, rD: residual disease)

CONCLUSIONS: In our study, ADC values before and after NACRT, as well as their changes related to treatment, did not predict pCR after NACRT in patients with rectal cancer.

## REFERENCES:

- [1] O'Neill BD, Brown G, Heald RJ, et al: Non-operative treatment after neoadjuvant chemoradiotherapy for rectal cancer. Lancet Oncol 8:625-633, 2007
- [2] Smith FM, Waldron D, Winter DC. Rectum-conserving surgery in the era of chemoradiotherapy. Br J Surg. 2010 Sep 15.
- [3] Barbaro B, Fiorucci C, Tebala C, et al: Locally advanced rectal cancer: MR imaging in prediction of response after preoperative chemotherapy and radiation therapy. Radiology 250:730-739, 2009
- [4] Kim SH, Lee JM, Hong SH, et al: Locally advanced rectal cancer: Added value of diffusion-weighted MR imaging in the evaluation of tumor response to neoadjuvant chemo- and radiation therapy. Radiology 253: 116-125, 2009
- [5] Lambregts DM, Vandecaveye V, Barbaro B, et al: Diffusion-weighted MRI for selection of complete responders after chemoradiation for locally advanced rectal cancer: a multicenter study. Ann Surg Oncol. 2011 Aug;18(8):2224-31