Combined use of DWI, DCE-MRI, and PET/CT in treatment response for preoperative chemoradiation in primary rectal adenocarcinoma

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Introduction: Rectal cancer is potentially curable condition but usually carries a poor prognosis because of local recurrence or distant metastasis. Neoadjuvant chemoradiation therapy (CRT) is often used for patients who have increased risk of circumferential resection margin involvement at surgery. Non-invasively methods for monitoring tumor response to preoperative CRT are mainly imaging based. New functional imaging techniques can potentially improve accuracy including diffusion-weighted imaging (DWI), dynamic contrast-enhanced MRI (DCE-MRI) and ^{18}F-fluorodeoxyglucose (^{18}F-FDG) PET/CT. An increase of apparent diffusion coefficient (ADC), a quantitative parameter measured on DWI, suggests treatment-induced cell lysis and necrosis during the course of CRT[(1)]. However, increase in ADC can also result from change in vessel permeability due to radiation therapy. For this, DCE-MRI may provide useful information regarding vascular permeability. On the other hand, late decrease in ADC is usually considered result of tissue compaction and fibrosis[(1)]. But presence of residual active disease can also decrease ADC. Therefore, DWI alone might not distinguish between residual active disease and treatment-induced tumor fibrosis, which can be differentiated using PET/CT. The aim of this study was to investigate DWI, DCE-MRI and PET/CT for response assessment over a course of pre-operative combined CRT for primary rectal adenocarcinoma, to see if the combination of different techniques can best predict biological behavior and clinical outcome.

Materials and Methods: 8 consecutive patients (6 men, 2 women, 54-73 years) suffering from rectal cancer of stage T3 or above were included in this study. Each patient received neoadjuvant chemoradiation preoperatively with 1.8Gy/fr daily 5fr/wk up to 50.4Gy. They underwent both MRI and PET/CT scans at three time points: baseline (before CRT), early mid treatment (2-week after start of CRT), and post-treatment (6-week after conclusion of CRT). All MRI and PET/CT were performed within one week interval (mean time interval: 2±1 days) at each time point. Total mesorectal excision (TME) was performed after completion of CRT and imaging scans. Radiographic changes were classified according to the Response Evaluation Criteria in Solid Tumors group (RECIST). Response was defined if complete or partial response was observed. Non-response was defined if progress or stable disease was observed. The differences of the imaging parameters between responders and non-responders were tested using the nonparametric Mann-Whitney test. The significance of changes of imaging parameters during therapy within a patient group was tested using a paired Wilcoxon test.

Results: Patients and post-treatment changes are shown in table 1. Imaging parameters between response group and non-response group at different time points are shown in table 2. In figure 1, ADCmean changes of patients with data from all three time points in response group (solid lines) and non-response group (dotted lines) are shown in similar pattern except patient # 3, which was post-surgically confirmed to be mucous tumor. Mucinous tumors were known to behave differently and do not respond well to CRT, as suggested by the static ADCmean from baseline to the intermediate time point. K^{trans} changes of patients with data from all three time points in response group (solid lines) are opposite to that of patients in non-response group (dotted lines) in figure 2. The change of mean K^{trans} is consistent with the sharp increase of ADC from baseline to the intermediate time point for non-response group, suggesting the contributing value of increased vascular permeability to ADC measurement. In figure 3, SUVmax changes of patients in response group (solid lines) and non-response group (dotted lines) decreased from baseline to the final time point. However, there was no significant difference of SUVmax between responders and non-responders at the final time point. However, due to small sample size, we did not get any statistical significant results at present.

Conclusion: From the limited data available from this study, we hypothesize that (1) in the early phase of CRT, the increase of ADC in responders represent treatment-induced apoptotic cell death and necrosis, whereas the increase of ADC in non-responders are result of vessel permeability after radiation. (2) The inflammation-induced SUV increase was not observed in both responders and non-responders during the course of CRT, supporting previous study that inflammation-induced SUV may have minimal impact in rectal cancer[(2)], or due to the partial volume effect to small lesions. (3) Future study with large cohort is needed to make statistical conclusion for our findings.

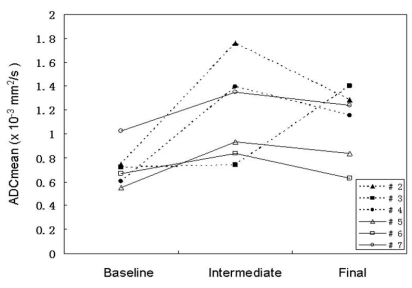
Table 1 Patients and treatment characteristics

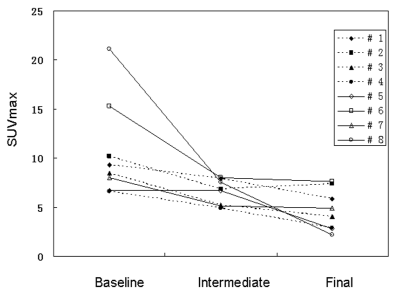
Patient No.	Gender /Age	Preoperative staging	Postoperative staging	Size change
#1	M/73	cT3	$ypT_3N_0M_0$	<30%
#2	M/63	cT3	$ypT_3N_0M_0$	<30%
#3	F/57	cT3	$ypT_3N_1M_0$	<30%
#4	M/71	cT3	$ypT_3N_0M_0$	<30%
#5	M/54	cT3	$ypT_3N_0M_0$	>30%
#6	M/56	cT3	$ypT_2N_0M_0$	>30%
#7	M/56	cT4	$ypT_3N_1M_0$	>30%
#8	M/60	cT3	$ypT2\ N_0M_0$	>30%

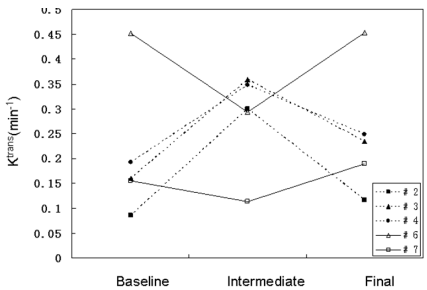
#1-4: non-responders; #5-8: responders according to RECIST

Table 2 Imaging parameters between response group and non-response group at measured time points

Parameters	Response Group			Non-response Group		
	Baseline	Intermediate	Final	Baseline	Intermediate	Final
ADCmean ($\times 10^{-3}$ mm^2/s)	0.868 ± 0.312	1.040 ± 0.274	0.999 ± 0.319	0.672 ± 0.071	1.150 ± 0.517	1.282 ± 0.127
K^{trans}(min^{-1})	0.26 ± 0.17	0.24 ± 0.11	0.24 ± 0.15	0.17 ± 0.07	0.35 ± 0.04	0.20 ± 0.07
SUVmax	12.8 ± 6.7	6.8 ± 1.3	4.3 ± 2.4	8.7 ± 1.5	6.2 ± 1.4	5.0 ± 2.0







Reference: (1). Neoplasia. Feb 2009;11(2):102-125 (2). J Nucl Med. Aug 2006;47(8):1241-1248.