EARLY PREDICTIVE POWER OF MAGNETIC RESONANCE IMAGING PARAMETERS DURING NEOADJUVANT CHEMOTHERAPY IN UTERINE CERVICAL CANCER

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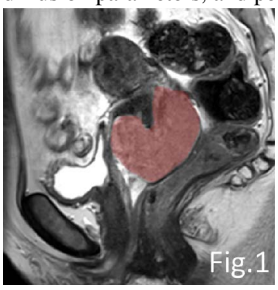
Target audience: gynecologists, radiologists

Purpose: In Japan, neoadjuvant chemotherapy (NAC) is the treatment of choice for locally advanced (International Federation of Gynecology and Obstetrics (FIGO) Stage Ib to IIb) uterine cervical cancer, in the purpose of introducing radical hysterectomy. When NAC fails, modification of treatment strategy is needed, including surgery before completion of two courses of NAC or radiation therapy. In order to determine the treatment strategy, early predictive biomarkers could be useful. The purpose of this study is to prospectively evaluate performance of quantitative measurements in the magnetic resonance imaging (MRI) for the early prediction of NAC effectiveness in cervical cancer: tumor volume parameters, diffusion parameters, and perfusion parameters.



Materials and methods: We prospectively assessed 13 patients with cervical squamous cell carcinoma clinical stages Ib to IIb (FIGO staging system) all of which received NAC followed by radical hysterectomy. MR exams were performed thee times for each patient: 1) pre-treatment, 2) after the 1st course of NAC, and 3) after the 2nd course of NAC just before the radical hysterectomy by using either 1.5T or 3T scanners. Perfusion MRI were obtained in 13/13 and 10/13 subjects before and after the 1st course NAC.

The DWI protocol was: b-value of 0, 100, 500, 1000s/mm^2, TR/TE 6400/76ms, matrix 128x120, slice thickness 4mm, gap 1mm, SPAIR for fat suppression.

The perfusion protocol was: 3D-gradient echo (3D-GRE), TR/TE 2.61/0.97, FA: 10, matrix 192x162, slice thickness 5mm, gap 1mm. It consisted of 90 measurements for 12 slices for 210 seconds after a gadolinium-based contrast agent was injected as a bolus. For T1 measurement, 3D-GRE sequence with dual FA (2/11) method was used. All parameters were obtained from volume of interest (VOI) of the tumor of each study (figure 1).

The correlation coefficient (R) was measured between eventual tumor volume regression rates (the golden standard of the effectiveness of NAC in this study, defined as formula below) and following 15 parameters listed on Table 1. The analysis significances (p value) were also shown on Table 1.

Tumor volume parameters

Vol_{pre}= pre-treatment tumor volume

Vol_{NAC1} = tumor volume after the 1st course

early tumor volume regression rate = $[Vol_{pre} - Vol_{NAC1}] / Vol_{pre}$

Diffusion parameters

mean apparent diffusion coefficient ($_{mean}$ADC) values and minimum ADC($_{min}$ADC) values for each study ($_{mean}ADC_{pre}$, $_{mean}ADC_{NAC1}$, $_{min}ADC_{pre}$, $_{min}ADC_{NAC1}$), the difference of each parameters during the 1st course ($_{mean}ADC_{\_diff[NAC1\text{-}pre]}$, $_{min}ADC_{\_diff[NAC1\text{-}pre]}$)

Perfusion parameters

K^{trans} (the transfer constant of contrast from the plasma to the tissue extra-cellular extra-vascular space) and Ve (the fractional volume of the tissue extracellular extra-vascular space) of tumors of each study (K^{trans}_{pre}, K^{trans}_{NAC1}, Ve_{pre}, Ve_{NAC1})[1,2], and the difference of each parameters during the 1st course($K^{trans}_{\_diff[NAC1\text{-}pre]}$, $Ve_{\_diff[NAC1\text{-}pre]}$)

The golden standard of the effectiveness

eventual tumor volume regression rate = $[Vol_{pre} - Vol_{NAC2}] / Vol_{pre}$

*Vol_{NAC2} = tumor volume after the 2nd course

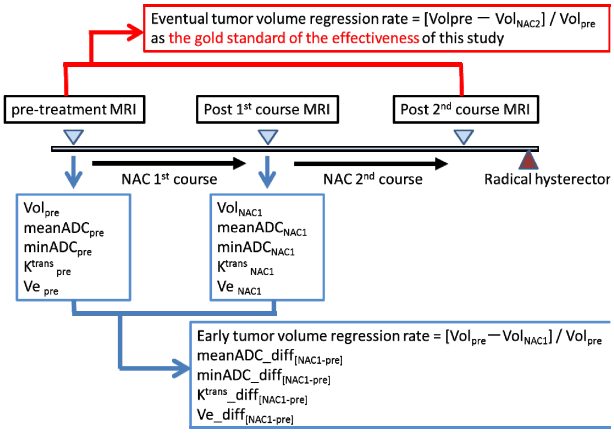
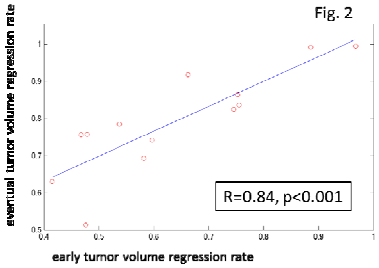


Table.1	R	p value
l_pre	0.42	0.15
l_NAC1	-0.50	0.07
rly tumor volume regressic	0.84	<0.001
ean ADC_pre	-0.14	0.64
ean ADC_NAC1	-0.22	0.46
ean ADC_diff [NAC1-pre]	-0.17	0.56
nimum ADC_pre	0.04	0.88
nimum ADC_NAC1	-0.33	0.26
nimum ADC_diff [NAC1-pr	-0.36	0.22
ans_pre	0.35	0.23
ans_NAC1	0.19	0.58
ans_diff [NAC1-pre]	-0.17	0.62
_pre	-0.64	<0.05
_NAC1	0.29	0.41
_diff [NAC1-pre]	0.63	<0.05

Results: Correlation coefficient (R) of each parameter with eventual tumor volume regression rate is summarized in Table 1. Early tumor volume regression rate showed strong correlation (R=0.84, p<0.001, figure.2). Ve_{pre} and $Ve_{\_diff[NAC1-pre]}$ also showed moderate correlation (R=0.64, p<0.05, R=-0.63, p<0.05, respectively). Correlations of other parameters with eventual tumor volume regression rate were not significant.



Discussion: Early tumor volume regression rate, Ve_{pre}, and $Ve_{\_diff[NAC1-pre]}$ might represent the eventual effectiveness of NAC for cervical cancer. Early tumor volume regression rate has a significant advantage, because it can be obtained using conventional MRI without contrast agent. The reason for the correlation of Ve_{pre} and its early change ($Ve\_diff_{[NAC1-pre]}$) with eventual tumor volume regression rate is not clarified, but low pretreatment Ve and the increase of Ve during early chemotherapy might reflect microstructural changes relating to chemotherapy sensitivity.

Conclusion: In NAC for cervical cancer, early tumor volume regression rate, pretreatment Ve, and early Ve change might help to determine and individualize the treatment strategy.

References:

1. Mark A. Zahra, et al. Int. J. Radiation Oncology Biol. Phys. 2009;74(3):766-773.

2. M. O. Leach, et al. Eur Radiol. 2012;22(7):1451-1464.