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THE ROLE OF DIFFUSION-WEIGHTED MR IMAGING AND ADC VALUES IN THE DIAGNOSIS OF GASTRIC TUMORS*

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Background: **The aim of this study was to investigate the role of diffusion-weighted MR imaging (DWI) in the diagnosis of gastric tumors by means of measuring the apparent diffusion coefficient (ADC) values of these lesions, and making a comparison with the endoscopic biopsy results.**
Subjects and Methods: **Seventy patients having gastric tumor constituted the case group. For the control group 30 healthy individuals were included. Abdominal MRI examinations were performed with a 1,5 Tesla unit. DWI examinations were obtained by single shot spin echoplanar imaging. The ADC was measured based on the tissue of the gastric tumoral entities and normal gastric mucosa in the control group.**
Results: **Mean ADC values were $0,84 \pm 0,17 \times 10^{-3}$ mm^2/s and $1,79 \pm 0,08 \times 10^{-3}$ mm^2/s in gastric tumor group and in control group, respectively, being statistically significant ($p < 0.05$). There was no significance among ADC values of adenocarcinoma subgroups. The comparison of the ADC values in the adenocarcinoma and lymphoma cases were also found to be statistically significant.**
Conclusions: **DWI is beneficial in the diagnosis of malignant gastric lesions by the aid of ADC measurements. Although ADC quantification seems to be invaluable in the evaluation of histopathologic subgroups of adenocarcinoma, it can help in the diagnosis of gastric lymphoma.**

Key-words: Stomach, neoplasms – Stomach, MR.

Diffusion-weighted magnetic resonance imaging (DWI) is an imaging modality being increasingly used in the evaluation of intraabdominal pathologies, particularly after the development of fast sequences such as echoplanar imaging (EPI) (1, 2). Müler et al. first studied DWI in hepatic and splenic pathologies in 1994, and they had some reasonable results (3). This was followed by other studies involving the use of DWI in liver, kidney, and other abdominal pathologies (4, 5). In these studies, apparent diffusion coefficient (ADC) values were calculated, and the difference in these ADC values were stated to be useful in the differential diagnosis of lesions, being significantly decreased in case of malignancy (6, 7).

The aim of this study is to investigate the role of diffusion-weighted MR imaging (DWI) in the diagnosis of gastric tumors by means of measuring the ADC values of these lesions, and making a comparison with the endoscopic biopsy results. To date, as far as we are concerned, the use of ADC in the diagnosis of gastric tumors is not studied.

Materials and methods

A total of 70 patients having gastric tumor [32 females, 38 males; mean age: 59.86 (25-82) years] constituted the case group. For the control group 30 healthy individuals [13 female, 17 male; mean age: 49.03 (35-63) years] were included. Patients diagnosed to have gastric tumor with endoscopic biopsy were evaluated with conventional MRI and DWI. Gastric tumor patients with a poor general condition, and with metallic instruments incompatible with MRI were not included into the study.

Ethics committee approval for the study was obtained. Informed consent was taken from the patients before MRI examination. The patients were encouraged to drink water in order to provide gastric distension to better demonstrate gastric tumors.

MR Imaging

Routine abdominal MRI examinations were performed with 1.5 Tesla Siemens Magnetom Symphony (Siemens, Erlangen, Germany) MR unit by using phase-array body coil. Axial T2-weighted True-FISP sequence (TR: 4.4sn; TE: 2,2sn; Average: 2; FlipAngel: 80°; Matrix: 256 × 256; Number of Slices: 25; Slice Thickness: 5 mm; FOV: 300; gap between slices: 15%) with breath hold was followed by DWI with single-shot spin echoplanar sequence and selective chemical shift fat supression technique [TR/TE: 3700/76; Matrix: 128 × 128; Number of Slices: 30; FOV: 400; gap between slices: 15%; Slice Thickness: 5 mm; Examination Time: 156 seconds; PAT Factor: 2; PAT mode: modified sensitivity coding parallel acquisition (GRAPPA)] (Table I). The protocol used for echo-planar DWI was trace-b: 50-b: 400-b: 800-ADC, shortly 'trace diffusion'. MR imaging parameters are summarized in Table I.

Image analysis

The images obtained by DWI were transferred to a workstation (Leonardo syngo 2002B Siemens Ag Medical Solutions, Berlin, Germany) in order to configure and analyse the ADC maps. The ADC measurements were done from the most hypointense region of the gastric

Table I. — Imaging parameters.

TR	3700
TE	76
Slice Thickness	5 mm
Slice Gap	1 mm
Average	4
Bandwith	1346
Matrix	128 × 128
FOV	400
Time	156 sec
Number of Slices	30
Gap between Slices	15%
PAT Factor	2

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tumor by placing circular region of interest (ROI) on the lesion in patient group and from the normal gastric wall in control group. The areas of ROI 45-70 mm^2 in the patient group and 3.2-7 mm^2 in the control group.

The signal intensity changes of the lesions were determined due to their appearance on b = 800 'trace' images and due to their signal on ADC map. The gastric tumors were seen hyperintense on b = 800 images and hypointense on ADC map. The consistency of the diagnoses of gastric cancer based on DWI and ADC measurements were evaluated by comparison with endoscopic biopsy results.

Statistical analysis

With SPSS programme, one-way ANOVA test was used to compare the ADC values of the gastric tumor cases and the control group. Kruskal-Wallis test was used in the comparison of the ADC values in adenocarcinoma subgroups, while using Mann-Whitney U test for the comparison of gastric lymphoma cases and adenocarcinoma subgroups. The level of significance was accepted as 5%.

Results

All the gastric tumors in this study had an increased signal on DWI and decreased signal on ADC maps. Mean ADC values were $0,84 \pm 0,17 \times 10^{-3}$ mm^2/s and $1,79 \pm 0,08 \times 10^{-3}$ mm^2/s in gastric tumor group and in control group, respectively, which was statistically significant ($p < 0.05$). In other words, mean ADC values of gastric tumors were significantly lower than that of normal gastric mucosa (Table II). On the other hand, there was no significance among the ADC values of adenocarcinoma subgroups ($p > 0.05$) (Fig. 1, 2).

The comparison of the ADC values in the adenocarcinoma and lymphoma cases were found to be statistically significant, being $0,85 \pm 0,16 \times 10^{-3}$ mm^2/s and $1,09 \pm 0,08 \times 10^{-3}$ mm^2/s, respectively. The mean ADC values of adenocarcinoma cases was significantly lower than that of lymphoma cases ($p < 0.05$) (Table III) (Fig. 3).

The cut-off value in ROC (Receiver Operator Characteristics) curve for differentiating gastric malignancy and normal gastric wall according to ADC values was found to be $1,12 \times 10^{-3}$ mm^2/sec. Based on this value, the sensitivity was 100% and specificity was 98,6%.

Table II. — Descriptive statistics for ADC values in gastric tumor group and control group.

		N	Mean	St. Deviation	St. Error
ADC	Gastric tumor	70	0.8410	0.16632	0.01988
	Normal	30	1.7887	0.07829	0.01429

*($p < 0.05$).

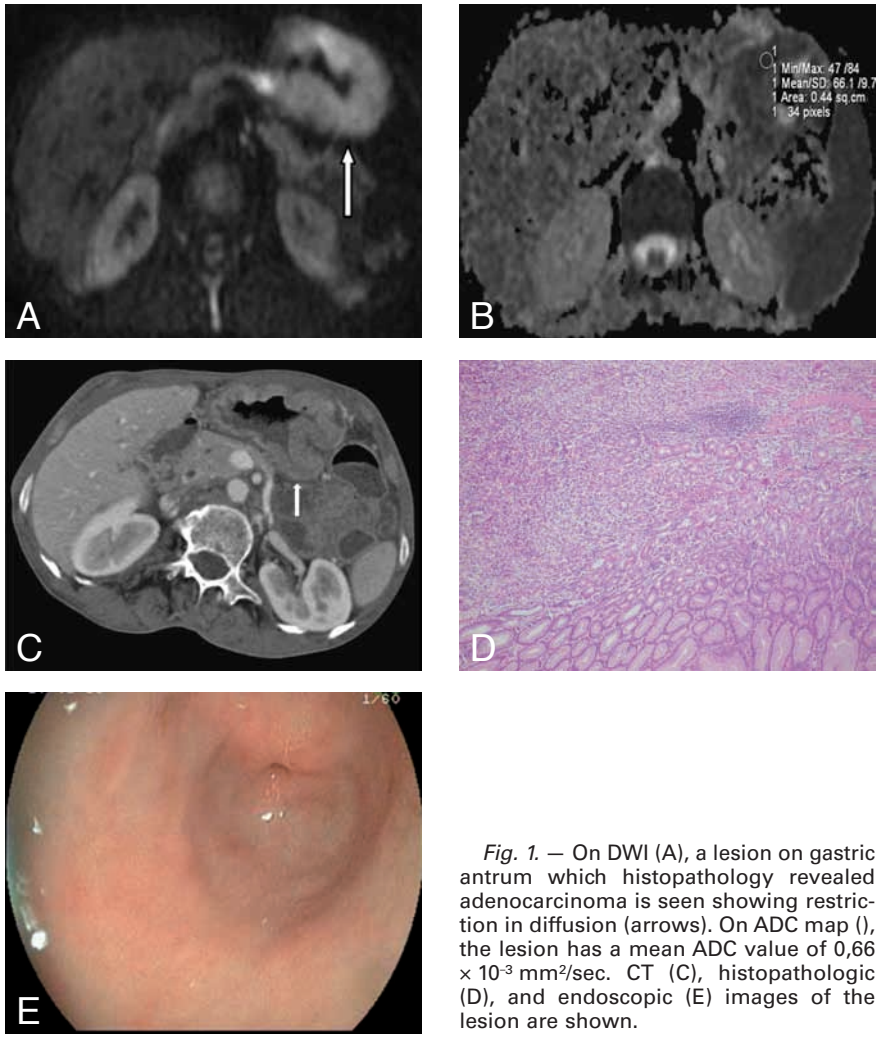

Fig. 1. — On DWI (A), a lesion on gastric antrum which histopathology revealed adenocarcinoma is seen showing restriction in diffusion (arrows). On ADC map (), the lesion has a mean ADC value of $0,66 \times 10^{-3}$ mm^2/sec. CT (C), histopathologic (D), and endoscopic (E) images of the lesion are shown.

Discussion

Gastric cancer is the second most common malignancy worldwide, and is influenced by geographic, ethnic, and socioeconomic factors. It is seen rather less common in western countries (8-11). It usually has metastatic spread at the time of diagnosis (12). Despite advanced diagnostic modalities, there is still some difficulty in the diagnosis and staging of gastric tumors (13).

Diffusion is the randomized microscopic movements of water molecules, and is a sensitive parameter in tissue characterization. In vivo evaluation of diffusion is possible by DWI and ADC measurement. DWI has been widely used in the evaluation of stroke (14).

Due to movement artefacts and heterogenous structure of the intraabdominal organs, the use of DWI has been difficult in the abdomen. Following advanced fast imaging sequences in MRI such as echo-planar imaging (EPI), these artefacts were rather eliminated and DWI has been able to be used in the evaluation of abdominal organs (3, 15-17). DWI has for a number of years been a diagnostic tool in the field of neuroradiology, yet only

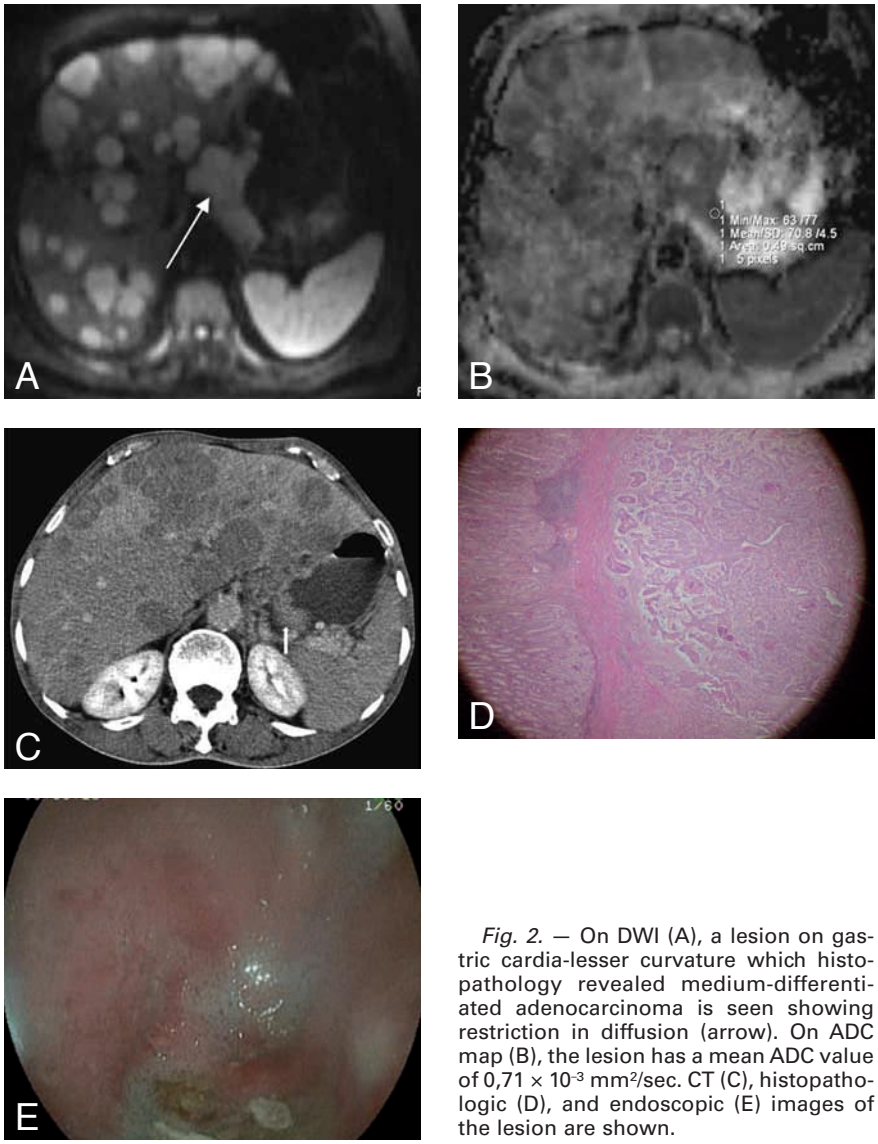

Fig. 2. — On DWI (A), a lesion on gastric cardia-lesser curvature which histopathology revealed medium-differentiated adenocarcinoma is seen showing restriction in diffusion (arrow). On ADC map (B), the lesion has a mean ADC value of 0,71 × 10^{-3} mm^2/sec. CT (C), histopathologic (D), and endoscopic (E) images of the lesion are shown.

since the end of the 1990s, with the introduction of echoplanar imaging (EPI) and the use of sequences capable of performing diffusion studies during a single breath hold, has it found diagnostic applications at the level of the abdomen. The inherent sensitivity to motion and the magnetic susceptibility of Dw sequences nonetheless still create problems in the study of the abdomen due to artefacts caused by the heartbeat and intestinal peristalsis, as well as the presence of various parenchymal-gas interfaces (18). Most studies of abdominal DWI have been performed with ssEPI. The single-shot technique allows one to acquire images within a fraction of a second, effectively freezing physiologic motion (19).

A pilot study was performed in two volunteers; DWI without and with pulse triggering (in the same individual) did not show substantial differences in calculated ADC values or image quality (data not shown). Thus, our investigation was performed with free breathing and without pulse triggering. Repetition times in a pulse-triggered sequence change in patients who are nervous, have an irregular pulse, or both. This can change the signal intensities of the DW MR images with a possible negative effect on the accuracy and image quality of the ADC maps. Obtaining images during normal respiration is a major advantage in the clinical routine (20).

Generally in biologic tissues, microscopic motion includes both the molecular diffusion of water and the blood microcirculation in the capillary network, and both diffusion and perfusion affect the ADC values. Selecting "b" values above 400 mm2/sec is shown to better differentiate malignancies from benign lesions. In high-grade tumors, the increased cellular density leads to decreased extracellular volume of the tumor and thus lower ADC values (21, 22). In our study, we measured ADC values using 'b' values as: b = 50 mm^2/sec, b = 400 mm^2/sec, and b = 800 mm^2/sec.

DWI is reported to be useful in the characterization and diagnosis of the tumors of liver, pancreas, ovary, colon, cervix, urinary bladder, prostate, and breast, with more restriction in diffusion and lower ADC values in malignant tumors than in benign ones (23-25). The results of our study are concordant with these studies.

The principle underlying DWI is that the thermal motion of water molecules in extracellular fluid enables the acquisition of images that reflect both histological structure and cellularity and therefore it can detect the changes of tissue structure at molecular level. It also enables the quantitative evaluation of apparent diffusion coefficient (ADC). Compared with benign lesions, diffusion of malignant tumors with high cellular tissue decreased and the ADC value in malignant tumors is lower than that of benign lesions. Several latest studies have shown that ADC has a potential for clinical appreciation in

Table III. — Descriptive statistics for ADC values in adenocarcinoma and lymphoma cases.

	n	Median	Mean ADC	St. Deviation	Minimum	Maximum
Adenocarcinoma	67	0.85	0.83	0.16	0.40	1.10
Lymphoma	3	1.09	1.09	0.08	1.03	1.14

* ($p < 0.05$).

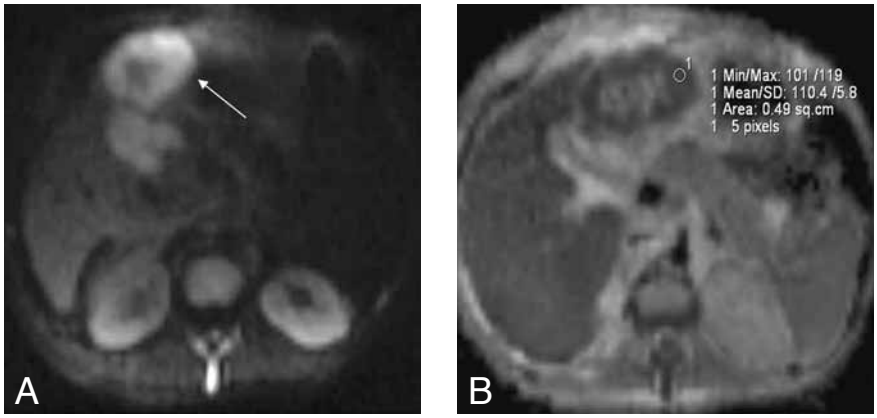

Fig. 3. — On DWI (A), a lesion (arrow) on gastric antrum which histopathology revealed diffuse large cell lymphoma is seen showing restriction in diffusion. On ADC map (), the lesion has a mean ADC value of 1,10x10^{-3} mm^2/sec. CT (C) image of the lesion is shown.

differentiating benign and malignant lesions with good specificity. On the other side, DWI, based on its imaging mechanism, could detect the changes of ADC in different tissues. Measurement of the ADC provides a quantitative estimate of the restrictive nature of the motion of water molecules within tissue for each voxel in a diffusion-weighted image. This study was thus designed to compare the ADC values between malignant lesions and normal gastric mucosa through EPI-DWI. Briefly, the higher the cellular density is, the lower the ADC value will be in DWI, and vice versa. For malignant tumors, they have a relatively high cellular density and therefore will produce a low ADC value on DWI, while for benign lesion, its density is generally low and thus will produce a high ADC value on DWI (20, 23).

In our study, mean ADC values were $0,84 \pm 0,17 \times 10^{-3}$ mm^2/s and $1,79 \pm 0,08 \times 10^{-3}$ mm^2/s in gastric tumor group and in control group, respectively, mean ADC values of gastric tumors being significantly lower than that of normal gastric mucosa ($p < 0.05$). On the other hand, there was no significance among the ADC values of adenocarcinoma subgroups ($p > 0.05$). Also, the mean ADC values in the adenocarcinoma group and lymphoma cases were $0,85 \pm 0,16 \times 10^{-3}$ mm^2/s and $1,09 \pm 0,08 \times 10^{-3}$ mm^2/s, respectively, the mean ADC values of the former being significantly lower than the latter ($p < 0.05$). As far as we are concerned, our study is the first in the literature studying gastric tumors by quantitative measurement of ADC values.

Satashi et al. (13) studied 15 patients with gastric cancer, and found that DWI could describe high-grade gastric cancer by means of increased signal on DWI and decreased signal on ADC map.

One of the most important advantages of DWI is the capability of obtaining numerical data by means of ADC measurement, which can provide an estimation of malignancy potential of the lesions prior to histopathologic examination (24-26). In our study, we found a cut-off value in ROC curve for differentiating gastric malignancy and normal gastric wall according to ADC values, being 1,12x10^{-3} mm^2/sec, with a sensitivity of 100% and specificity of 98,6%.

To mention in a few words about the comparative role of PET/CT in the evaluation of gastric cancer, the sensitivity and accuracy of PET/CT were found to be inferior to those of contrast enhanced CT in the diagnosis of regional lymph node metastases, while its sensitivity, accuracy, positive predictive value, and negative predictive value were superior in the diagnosis of distant metastases (27).

In conclusion, DWI and ADC values can successfully differentiate gastric tumors from normal gastric mucosa, and we think DWI will have an increasing use in the future in the diagnosis and clinical analysis of gastric tumors. As for the question about the capability of DWI to estimate the nature of the gastric tumors, we think that further studies with a wide range of cases having different histopathologic subgroups should be carried out.

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