ORIGINAL ARTICLE

Field Strength and Diffusion Encoding Technique Affect the Apparent Diffusion Coefficient Measurements in Diffusion-Weighted Imaging of the Abdomen

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Objectives: The purpose of this study is to determine what effects a variety of diffusion encoding techniques at 1.5 T and 3 T have on measured abdominal apparent diffusion coefficient (ADC) values obtained in a healthy population.

Materials and Methods: Sixteen healthy male volunteers were enrolled in this prospective Institutional Review Board-approved study following written informed consent. Imaging was performed on a 1.5 T and a 3 T magnetic resonance system (Siemens, Erlangen) with several abdominal axial diffusion weighted imaging (DWI) acquisitions: an orthogonal diffusion encoding with b-values of 0/400 seconds/mm^2, and a series of four 3-scan trace weighted acquisitions with b-values of 0/50, 0/400, 0/800, 0/50/400/800 seconds/mm^2, respectively. The mean ADC values were calculated for 3 regions of interest (ROI) in 5 locations (right hepatic lobe, spleen, pancreatic head, body, and tail). The ADC data were analyzed using a repeated-measures analysis of variance.

Results: There was a significant difference between measured ADC values at 1.5 T and 3 T for liver ($P < 0.001$), but not for pancreas ($P = 0.427$) or spleen ($P = 0.167$). There was no significant difference ($P > 0.999$) in the measured ADC values between the orthogonal encodings and the 3-scan trace weighted encoding with the same b-value. There were significant differences ($P < 0.001$) between all 4 weighting schemes for the 3-scan trace with the measured ADC decreasing with increasing b-value.

Conclusion: Measured abdominal ADC values depend on the exact selection of b-value used for encoding for liver, pancreas, and spleen. In addition, the measured ADC values depend on the field strength of the scanner for liver.

Key Words: abdominal imaging, diffusion weighted imaging, apparent diffusion coefficient, field strength

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Magnetic resonance imaging is a safe, noninvasive means for evaluating the abdomen. As faster techniques and sequences have been developed, use of diffusion-weighted imaging (DWI) has expanded beyond intracranial applications, into abdominal applications.[1] This technique is especially promising, as it yields both qualitative and quantitative information, can be added to existing imaging protocols without a substantial increase in the overall examination time (1–5 minutes), and does not require the administration of exogenous contrast medium.

DWI measures the random motion of water molecules in the body. This free motion of water is inhibited in both the intracellular and extracellular spaces by increased cellularity and intact cell membranes. Oncologic applications have been of particular interest because lipophilic cell membranes in hypercellular tumor tissue may serve as barriers to free diffusion in the intracellular and extracellular spaces.[2,3]

DWI can be used in several ways in patients with cancer. First, it serves as a qualitative screening sequence, aiding in tumor detection by showing subtle signal alterations which can then be further characterized by dynamic contrast-enhanced T1-weighted imaging. Recent papers have described the benefits of DWI in the detection of lymphadenopathy, peritoneal carcinomatosis, and hepatic, pancreatic, and other masses.[4–8] In addition to this solely qualitative approach, Apparent Diffusion Coefficient (ADC) measurements have been recently used as a quantitative tool for predicting and monitoring tumor response to treatment[9–13] as the free diffusion of water increases with tumor cell breakdown. However, there are many potential confounding factors in ADC measurements including number of b-values, strength of diffusion encoding, spin-echo versus stimulated echo, diffusion encoding direction, diffusion encoding waveform, breath-hold versus nonbreath-hold, field strength, tissue relaxation properties, noise, fitting procedure, etc. These factors may potentially alter the measured ADC value even in the absence of a change in diffusion.

If quantitative abdominal DWI values are to be clinically useful, particularly for predicting or monitoring therapeutic effects, there must be a clear understanding of the various factors which can artificially impact the measured ADC value. Though many studies have demonstrated the feasibility of DWI in the abdomen,[14–18] less has been published about the effects of field strength and encoding technique on abdominal ADC measurements. It is of great importance to determine the magnitude of the various potential confounding factors in obtaining quantitative ADC measurements to better understand and avoid the potential pitfalls, both in the clinical management of individual patients and in scientific studies across multiple individuals.

Therefore, the purpose of this study was to test the hypothesis that there are no significant differences in abdominal ADC values obtained in a healthy population using a variety of diffusion weightings for trace-weighted and orthogonal diffusion encoding at both 1.5 T and 3 T. Healthy volunteers were used to investigate the influence of these factors on the ADC measurement technique itself, without introducing additional pathologic variation as a potentially confounding factor.

MATERIALS AND METHODS

An employee of Siemens Healthcare (Malvern, PA) assisted in the design of the imaging protocol. The other authors had full control of the data and information submitted for publication.

Clinical Study

This Health Insurance Portability and Accountability Act (HIPAA)—compliant, prospective study was approved by the local Institutional Review Board (IRB). During a 2-month period, 16 healthy male volunteers (mean age: 36.5 years, range: 30–52 years)

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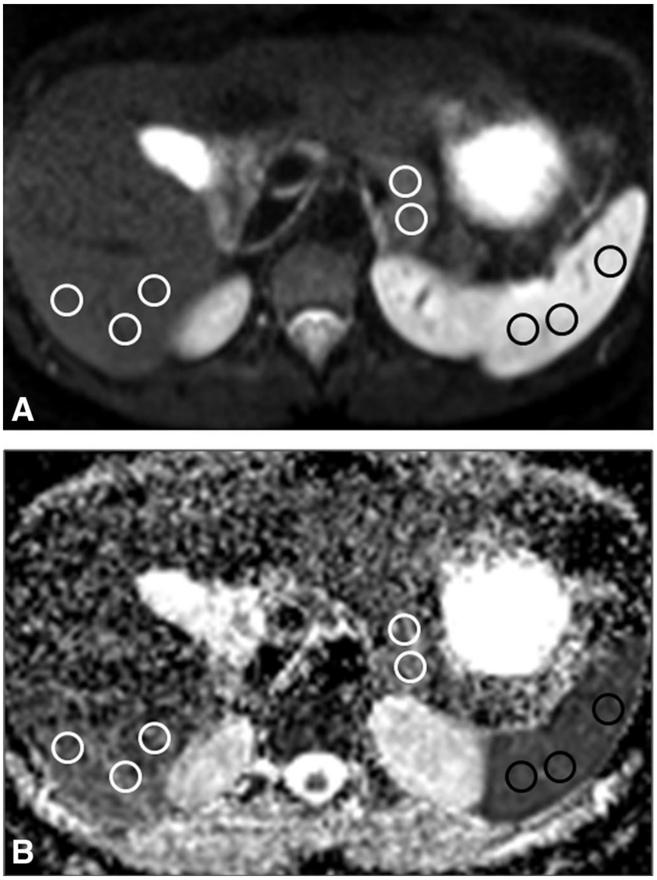

FIGURE 1. A, Axial 2D diffusion weighted image (DWI) of liver, spleen, and pancreatic tail, acquired with b value of 0 seconds/mm². Three ROIs each are placed in these anatomic areas (in the pancreatic tail, only 2 ROIs are illustrated. B, The same ROIs have been copied from the DWI onto the corresponding apparent diffusion coefficient map.

were imaged on a 1.5 T and a 3 T MR system (MAGNETOM Avanto and MAGNETOM Trio a TIM System, Siemens Medical Solutions, Germany) running the latest software version available at the time of the study (Syngo MR B13, Siemens Medical Solutions, Germany). These 16 subjects also participated in a previously reported study on abdominal DWI reproducibility.[19] A single dedicated body matrix array coil positioned over the abdomen combined with the spine array coils were used for signal reception. The imaging protocol included an orthogonal diffusion encoding with b-values of 0/400 seconds/mm^2, and a series of 4 3-scan trace weighted acquisitions with b-values of 0/50, 0/400, 0/800, 0/50/400/800 seconds/mm^2, respectively. The difference between orthogonal and trace-weighted is that in trace-weighted encoding any anisotropy information contained in the 3 orthogonal directions is averaged out and in orthogonal encoding it is maintained. All series were acquired during free breathing without respiratory triggering. The parameters were 3200 milliseconds repetition time, 74 milliseconds (1.5 T) or 76 milliseconds (3 T) echo time, axial slice thickness 6 mm, number of slices 30, bandwidth 2604 Hz/pixel, number of averages 4, acquisition time 56 seconds (133 seconds for the 0/50/400/800 acquisition only), matrix 108 × 128, parallel acceleration factor 2, 90° flip angle, dual spin-echo diffusion encoding with echo-planar imaging readout, and spectrally selective fat saturation during free breathing. ADC values were calculated automatically for each DWI series, using the inline ADC calculation function of the MR system and displayed as corresponding ADC maps. Each volunteer was scanned using this standardized sequence protocol on both MR systems within one hour with the magnet order (1.5 T MR system first vs. 3 T MR system first) being randomized.

In addition to the human subjects a single ex vivo bovine liver phantom was also imaged using the same pulse sequences and same MR systems as described above. Each pulse sequence was repeated 5 times, and the 3 T data was acquired first with the 1.5 T data being acquired within an hour after the 3 T data.

Quantitative MR Image Analysis

Quantitative analysis was performed by a fourth year radiology resident, on a freestanding MR imaging workstation (Leonardo, Siemens Medical Solutions, Germany). Region-of-interest (ROI) measurements were obtained in the posterior right hepatic lobe, the spleen, and the pancreas. The latter was further divided into head, body, and tail as follows: head, area of pancreas to right of left border of superior mesenteric vein; body, area of pancreas between left border of superior mesenteric vein and left border of aorta; and tail, area of pancreas between left border of aorta and splenic hilum. ROI placements at 1.5 T were performed in areas as similar as possible to those at 3 T. This was achieved by visually assessing the ROI positioning at 1.5 T first before placing the ROI at 3 T by using visual landmarks, eg, the main portal vein and its right branches within the liver, the splenic hilum, and the main renal vessels. The ROI placement was confirmed by a senior radiologist with 10 years of experience post fellowship training. Because of the relatively small slice thickness of 6 mm, a fair match up of the slice locations within the same individual at the 2 different field strengths could be achieved. The right hepatic lobe was used to take advantage of the higher SNR from the relatively close proximity to the coils.

For each organ location studied, 3 nonoverlapping circular ROIs with a standardized size of 21 pixels were placed on the images acquired without a diffusion weighted gradient (b-value = 0) at homogeneous artifact-free areas. Care was taken to avoid any large blood vessels (Fig. 1). By applying the copy and paste function of the workstation, identical ROI positions could be achieved on corresponding ADC maps. The resulting mean ADC values in each of the 3 ROIs for each of the 5 organ locations were recorded for every ADC map. Therefore, a total of 150 data points per volunteer were collected: 3 ROIs per organ location, 5 organ locations, 5 diffusion encoding techniques, and 2 field strengths. The same standardized ROI size and placement strategy was used for the ex vivo phantom data, resulting in an additional 150 data points (3 ROIs, 5 techniques, 2 field strengths, and 5 repetitions).

Statistical Data Analysis

The ADC values were organized by subject (each volunteer), using within-subject factors of field strength (1.5 T or 3 T), organ location (liver, spleen, pancreatic head, pancreatic body, or pancreatic tail), and diffusion encoding technique (orthogonal, 0/50, 0/400, 0/800, 0/50/400/800). The ADC data were analyzed with a repeated-measure ANOVA (analysis of variance) to test the null hypothesis that the organ location, field strength, and encoding technique had no influence on the ADC values. A full-factorial model was used, and *P*-values less than 0.05 were considered statistically significant. Additionally, a second ANOVA was used to test whether there was any significant effect because of the ROI placement itself. The Greenhouse-Geisser method was used to correct for departures from sphericity, and the Bonferroni method was used to adjust for multiple comparisons. The ex vivo liver phantom data was analyzed separately using a similar approach except that there was only a single organ location (liver) and there were 5 repetitions in place of 16 subjects.

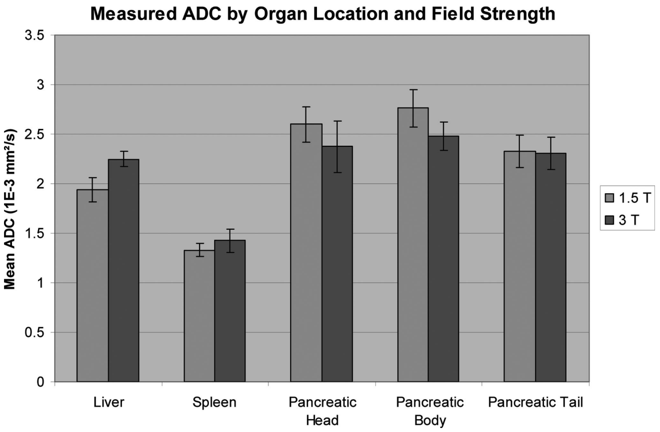

FIGURE 2. Mean apparent diffusion coefficient (ADC) values in the various anatomic locations for each field strength (the error bars mark the 95% confidence intervals (CI) for the mean, and the means are taken over all subjects and encoding techniques). Note that significant differences can be identified whenever the CI does not overlap as indicated by the error bars. Specifically, the ADC values were not significantly different ($P = 0.330$) between the 2 field strengths, except for liver which was 15.9% higher at 3 T than at 1.5 T ($P < 0.001$). The ADC values in the various anatomic locations were significantly different ($P < 0.001$) from each other, with the spleen having the lowest overall ADC and the pancreatic body having the highest.

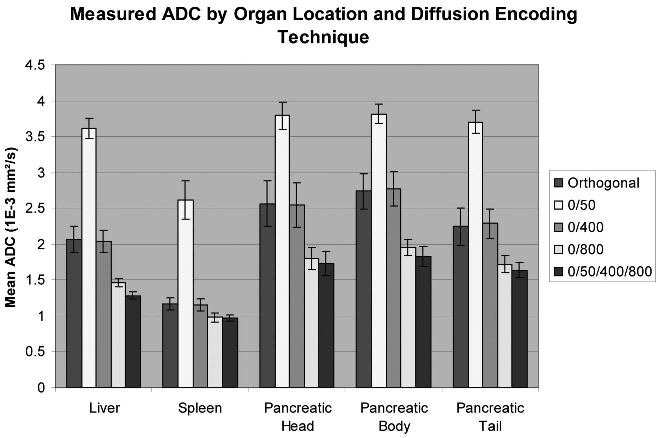

FIGURE 3. Mean apparent diffusion coefficient (ADC) values in the various anatomic locations for each diffusion-encoding technique (the error bars mark the 95% confidence intervals for the mean, and the means are taken over all subjects and field strengths). Note that significant differences can be identified whenever the CI does not overlap as indicated by the error bars. The measured ADC values in all organs showed a consistent and significant ($P < 0.001$) decrease with increasing diffusion weighting. The orthogonal diffusion encoding technique used a b-value of 0/400 and was not significantly different ($P > 0.999$) than the trace-weighted scheme with the same diffusion weighting.

RESULTS

There were highly significant differences in mean measured ADC values ($P < 0.001$) among the various organ locations as shown in Figure 2. Note that the error bars represent the 95% confidence intervals (CI). The spleen had the most restricted diffusion, with mean ADC values of 1.38×10^{-3} mm²/s, (CI: [1.29, 1.46]), whereas the pancreatic body had the least restricted diffusion with ADC values of 2.62×10^{-3} mm²/s (CI: [2.48, 2.76]) evaluated over both field strengths and all diffusion encoding techniques. Also, although there was a moderately significant difference ($P = 0.022$) between the pancreatic body and tail there was no significant difference between the pancreatic head and body ($P > 0.999$) nor between the pancreatic head and tail ($P = 0.974$).

There was no significant ($P = 0.330$) main effect of field strength on the measured ADC values when considering all organ locations together, however there was a significant ($P < 0.001$) interaction with field strength when the organ locations were considered individually (Fig. 2). Specifically, the measured ADC values were 15.9% (CI: [8.6%, 23.1%]) higher at 3 T than at 1.5 T in the liver, which was significant ($P < 0.001$). For the ex vivo bovine liver phantom the ADC values were found to be 11.1% (CI: [7.5%, 14.7%]) higher at 3 T than at 1.5 T, and this difference was also significant ($P < 0.001$). None of the other organ locations showed significantly different measured ADC values at 1.5 T and 3 T.

Figure 3 shows the highly significant ($P < 0.001$) effect of the diffusion encoding technique on measured ADC value with each organ showing the same general trend of decreasing measured ADC value with increasing diffusion weighting. Note, however, that the measured ADC values obtained with orthogonal diffusion encoding (with b-values 0/400) were not significantly different ($P > 0.999$) from those obtained with the 0/400 trace-weighted encoding. Also, note that for the spleen and all 3 pancreas locations there was no significant difference ($P > 0.05$) between the measured ADC values obtained with the 0/800 and the 0/50/400/800 techniques.

Table 1 shows the effect of the field strength and encoding technique on the measured ADC values for each organ. In Table 1 the means and standard deviations are taken over all subjects and ROI. Note again the general trend seen in Figure 1 that, for all studied diffusion encoding techniques, the difference between 1.5 T and 3 T tends to be significant only for liver. The only 2 exceptions to this trend are liver using the b-value 0/50/400/800 technique which was not significant, and the pancreatic body using the b-value 0/800 technique which was significant. Despite these 2 exceptions, the three-way interaction between organ location, field strength, and encoding technique was not significant ($P = 0.133$) overall. So the 2 exceptions are likely to be a simple statistical artifact of multiple comparisons which was accounted for in the ANOVA.

There was no significant effect ($P = 0.708$) on the ADC values because of the placement of the ROI in the second ANOVA.

DISCUSSION

In our study the measured ADC values in abdominal DWI were found to be a function not only of the tissue imaged, but also of the diffusion encoding technique selected. Additionally, for liver only, the measured ADC value appears to depend on the field strength. This indicates that follow-up studies seeking to use the ADC value to monitor therapy or disease progression will need to take care to use the same diffusion encoding technique as the original study; otherwise the results of the follow-up study may not be directly comparable to the results of the original study. Also, if liver is of interest, it would be important to make sure that the follow-up study is performed at the same field strength as the original study.

We noted a general trend of lower measured ADC values obtained with stronger diffusion encoding strength. This is consistent with a bi-exponential mixture of perfusion and diffusion effects, and may help explain why the measured ADC values were not independent of the diffusion encoding scheme. In other words,

TABLE 1. The Effect of Field Strength and Encoding Technique on Measured Apparent Diffusion Coefficient (ADC) Values in Liver, Spleen, and Pancreas

		Measured ADC Value: Mean (95% CI)				
Organ Location	**Field Strength**	**0/400**	**Orthogonal**	**0/50**	**0/800**	**0/50/400/800**
Liver	1.5 T	1.82 (1.66, 1.98)*	1.87 (1.66, 2.08)*	3.37 (3.11, 3.62)*	1.36 (1.28, 1.45)*	1.27 (1.21, 1.33)
	3 T	2.26 (2.07, 2.44)*	2.27 (2.09, 2.44)*	3.86 (3.78, 3.94)*	1.56 (1.50, 1.62)*	1.29 (1.23, 1.36)
Spleen	1.5 T	1.09 (1.02, 1.16)	1.15 (1.08, 1.23)	2.49 (2.29, 2.69)	0.98 (0.90, 1.06)	0.94 (0.89, 0.99)
	3 T	1.22 (1.09, 1.34)	1.19 (1.09, 1.30)	2.74 (2.33, 3.14)	0.98 (0.92, 1.03)	1.00 (0.94,1.06)
Pancreatic head	1.5 T	2.65 (2.35, 2.95)	2.72 (2.41, 3.03)	3.92 (3.80, 4.04)	1.90 (1.71, 2.08)	1.81 (1.64, 1.99)
	3 T	2.43 (2.05, 2.81)	2.42 (2.06, 2.77)	3.66 (3.35, 3.98)	1.71 (1.50, 1.92)	1.65 (1.45, 1.86)
Pancreatic body	1.5 T	2.89 (2.58, 3.19)	2.94 (2.64, 3.25)	3.85 (3.73, 3.97)	2.12 (1.96, 2.29)*	2.00 (1.82, 2.18)
	3 T	2.66 (2.41, 2.90)	2.53 (2.27, 2.78)	3.78 (3.59, 3.96)	1.79 (1.63, 1.95)*	1.66 (1.48, 1.83)
Pancreatic tail	1.5 T	2.33 (2.13, 2.53)	2.26 (2.01, 2.51)	3.68 (3.40, 3.95)	1.75 (1.61, 1.88)	1.64 (1.51, 1.77)
	3 T	2.24 (1.99, 2.50)	2.23 (1.93, 2.52)	3.73 (3.52, 3.94)	1.70 (1.56, 1.83)	1.63 (1.52, 1.74)

The Values in the Square Brackets are the 95% Confidence Intervals (CI).
*Difference between 1.5 T and 3 T is significant at the $P = 0.05$ level.

perfusion effects which occur at low b-values appear as an artificially elevated measured ADC, so a technique which focuses more on low b-value information will have correspondingly more perfusion information and thus higher measured ADC values. Thus the general trend of lower measured ADC with higher b-value encoding.

Because of this trend it may be advisable to use an encoding scheme such as 50/400 or 100/800 instead of the encoding schemes presented here because the impact of any perfusion effects could potentially be reduced or avoided simply by eliminating the nondiffusion-weighted image. Further investigation would be required to determine whether such measurements would be less sensitive to changes in the encoding scheme. However, it appears that tissue anisotropy is not a significant concern for abdominal DWI (except kidney) as evidenced by the fact that the ADC values measured using the orthogonal technique were the same as those measured using the trace-weighted technique with the same amount of diffusion weighting. This result is consistent with other studies which have specifically investigated the anisotropy of liver and kidney ADC measurements.[20,21]

Perhaps the most puzzling result of this study is the finding that, for the liver only, the measured ADC is a function of the field strength with the ADC being measured as significantly higher at 3 T than at 1.5 T. This effect was seen both for in vivo human liver and for ex vivo bovine liver. Although it is premature to make any final conclusions about the cause of this effect, it is consistent with the fact that the liver has the lowest signal of the 3 tissues studied here and would therefore be the most likely to be affected by noise floor issues at 1.5 T which would artificially reduce the measured ADC. Noise floor issues occur when the SNR is so low that the magnitude reconstruction biases the signal upwards. If the high b-value image is close to the noise floor then it will be artificially elevated and therefore the ADC will be artificially reduced. Though significant, the difference between 1.5 T and 3 T in this study is small ($<16\%$), so this effect may not require a large amount of bias in the high b-value image signal at 1.5 T. However, other studies with fewer volunteers failed to find a significant difference,[22] so more research is needed to determine whether this effect is reproducible and to verify its cause. If the cause is, indeed, the noise floor issue, then it may be advisable to limit the high b-value to ensure that there is sufficient signal in the liver to avoid bias. However, in the meantime caution is warranted in comparing ADC data measured at different field strengths, at least in the liver.

Quantitative diffusion-weighted MR imaging of the abdomen is of particular interest in oncologic patients, as effective chemotherapy and radiation treatment should result in tumor necrosis and disruption of cellular membranes which will increase the extracellular space and, therefore, increase water diffusion. Recent work by Cui et al used ADC measurements to predict and monitor the effect of chemotherapy on hepatic metastases from gastric and colorectal carcinomas.[23] They concluded that low pretherapy ADC values predict a favorable treatment response whereas an early increase of the ADC values post initiation of chemotherapy within 3 to 7 days indicates a favorable treatment response.[23] This is of utmost importance as an early post treatment rise in ADC values precedes any reduction in tumor size usually used to assess treatment response.[23] These results are in line with earlier studies from Koh et al and Theilmann et al who also demonstrated that changes in ADC values of hepatic metastases precede reduction in tumor size.[11,24]

Quantitative diffusion-weighted MR imaging has also been used to assess organ fibrosis.[25–27] Akisik et al recently showed that pancreatic ADC values in patients without pancreatic disease were significantly higher than in patients with mild or severe chronic pancreatitis.[25] The authors conclude that an ADC value of less than 1.79 ($\times 10^{-3}$ mm^2/s) was optimal for delineating normal pancreas from chronic pancreatitis. The same holds true for patients with liver fibrosis. Taouli et al performed DWI ($b = 50$, 300, 500, 700, and 1000 seconds/mm^2) on 23 patients with chronic hepatitis and on 7 healthy volunteers.[27] They found significantly lower hepatic ADCs in patients with severe hepatic fibrosis when compared with patients with mild or no hepatic fibrosis. The authors conclude that quantitative DWI can be used for prediction of the presence of moderate and advanced liver fibrosis. As soon as therapy options for patients with chronic pancreatitis or hepatic fibrosis become widely available, longitudinal MR imaging using quantitative DWI may be useful in these populations to monitor treatment effects and disease progression.

Although abdominal DWI has been found in other studies to be robust and repeatable, this study indicates it is important to be careful in interpreting follow-up images. Naive examination of the measured ADC values without knowledge of the exact encoding technique and field strength may lead to erroneous conclusions as differences that are merely because of changes in the measurement technique could be interpreted as differences because of progression of disease or therapy. Overall, quantitative DWI in the abdomen appears to be influenced by multiple factors such as field strength, b-values, and sequence type. Bruegel et al reported a mean hepatic ADC value of 1.21×10^{-3} mm^2/s (measured in the right lobe of 90 patients without liver cirrhosis), which is approximately 30%

smaller than our results at 1.5 T and 50% smaller than our results at 3 T.[5] This discrepancy is consistent with the trend that we have observed here regarding the selection of the b-values (0/400 versus 50/300/600) and the resulting impact of the perfusion component. Similar discrepancies are seen in the spleen, where Bruegel et al report a mean ADC value of 0.82×10^{-3} mm^2/s in 96 patients, which again is approximately 50% smaller than our results.[5] Finally, the mean ADC value in the pancreas as reported by Erturk et al is 1.2×10^{-3} mm^2/s, which also is approximately 50% smaller than our results.[26] Erturk et al acquired their results in 38 patients by using a breath hold technique at 1.5 T with b values of 0 and 400, and Kwee et al found a significant effect because of respiratory triggering so the choice of breath-hold or free-breathing or respiratory triggered can also introduce some significant effects.[26,28] Although not explicitly examined in this study, we chose to use a free-breathing technique based on results by Kwee et al and on clinical workflow considerations, but we note that the field is still rapidly evolving and so similar studies using breath holding or respiratory-triggering may also be valuable in the future.

Our study had some limitations. First, all of the diffusion encoding schemes tested used a nondiffusion-encoded image (b-value = 0), so the detected variability may be, in-part, because of erroneously interpreting perfusion effects as diffusion as described above. This cannot be rigorously investigated without either a phantom with both known perfusion and diffusion or through further clinical studies using modified protocols. Also, to keep our imaging variables as constant and homogeneous as possible, all of our imaging was performed on 2 scanners from a single vendor where the protocols could be matched almost exactly. This ideal scenario may not be achievable in daily clinical practice. Finally, our study population was relatively small and consisted entirely of middle-aged healthy male subjects, so age- and gender-related effects could not be tested.

In conclusion, we reject the hypothesis that there are no significant differences in abdominal ADC values obtained in a healthy population using a variety of diffusion weightings for trace-weighted and orthogonal diffusion encoding at both 1.5 T and 3 T. They depend strongly on the diffusion encoding technique with higher diffusion weightings, resulting in lower measured ADC values. Also, measured ADC values are higher at 3 T than at 1.5 T for liver, but not for other tissues.

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AUTHOR QUERIES

AUTHOR PLEASE ANSWER ALL QUERIES **1**
