Diagnostic and Interventional Imaging (2013) **94**, 571—573

EDITORIAL

ADC normalization: A promising research track for diffusion-weighted MR imaging of the abdomen

Diffusion-weighted magnetic resonance imaging (DW-MRI) is a technique that helps quantify the movement of water molecules at a cellular level. DW-MRI is sensitive to the thermally driven random motion of water protons, which is dependent of their interactions with cell membranes and macromolecules. Consequently, the diffusion of water in tissues reflects at various degrees a combination of tissue cellularity, tortuosity of extracellular spaces, integrity of cell membranes and viscosity of fluids. When present, high cellularity, necrosis, inflammation and fibrosis substantially alter the diffusion properties of water and, thus, affect the returned signal.

To date, two models have been applied to abdominal imaging using DW-MRI [1]. One is the mono-exponential model, which is the most commonly used in daily practice. The other one is a bi-exponential model, which accounts for separating tissue diffusivity and tissue microcapillary perfusion. The bi-exponential model is based on the intravoxel incoherent motion (IVIM) theory that was introduced by Le Bihan et al. as a joint method to measure perfusion and diffusion [1]. Multiple b value IVIM models (i.e., more than 10 b values) based on the bi-exponential fitting theory are complex and time consuming because of a long post-processing time and show high degrees of variability and reproducibility, especially for the perfusion related parameter D* [2,3]. Consequently, bi-exponential post-processing using multiple b values is not routinely performed although it is being widely evaluated in research [3—7].

Dramatic advances in image quality during recent years, mainly due to substantial refinements in hardware and coil systems, have made DW-MRI a promising technique for the detection and characterization of a wide range of pathologic condition in the abdomen and pelvis [8—17]. The implementation of ultrafast MRI techniques, such as echo-planar imaging (EPI) combined with parallel imaging using multicoil state-of-the-art MRI scanners, has made DW-MRI of the abdomen a feasible option in clinical practice. Scan acquisitions can be performed relatively quickly, does not require administration of gadolinium-chelate and enables qualitative and quantitative assessment of tissue diffusivity (diffusion coefficients). Beyond detection and characterization, DW-MRI shows also promise for monitoring abdominal cancer response to therapy [9]. Although DW-MRI has received considerable attention and has been subjected to marked developments in the area of liver disease, by contrast less has been made regarding the pancreas. One reason may be that the pancreas is a deep, central and relatively small organ in the abdomen, far from coil elements so that DW-MRI of this organ may be rendered difficult because of signal loss by comparison with the liver. However, a careful selection of technical parameters for DW-MRI image acquisition may contribute to increase the pancreatic signal. Signal-to-noise ratio may be improved by using a minimum TE, by increasing the number of averages, and decreasing bandwidth. Another reason may be that encouraging results achieved with DW-MRI in the liver are not mirrored by those obtained in the pancreas.

2211-5684/$ — see front matter
http://dx.doi.org/10.1016/j.diii.2013.05.003

As illustrated recently, one major limitation of DW-MR imaging is the difficulty to differentiate between pancreatic adenocarcinoma and mass-forming pancreatitis because of overlap in ADC values [18,19]. Differentiation between mass-forming pancreatitis and pancreatic cancer with conventional ADC measurement is not so straightforward because of inconsistencies and conflicting results between published studies [20]. Some studies reported greater ADC values for mass-forming pancreatitis than for pancreatic cancers, others reported greater ADC values for pancreatic cancers than for mass-forming pancreatitis whereas others did not find any significant differences in ADC values between these two conditions. One reason may be that mass-forming pancreatitis may contain variable proportions of fibrosis and inflammation, which may explain variations among studies and overlap in ADC values between mass-forming pancreatitis and pancreatic cancers [19].

The preliminary results by Barral et al. suggest that normalized ADC helps characterize focal pancreatic lesions and further discriminate between pancreatic cancers and mass-forming pancreatitis [20]. In their study, the use of the conventional ADC was less discriminating because of marked overlap in ADC values between these two entities, and this was consistent with the results of other researchers [5]. The results of their study show that ADC measurements using a normalized ADC is more discriminating than the more common ADC to differentiate between focal pancreatic lesions, and more specifically between malignant pancreatic tumors and mass-forming pancreatitis [20].

The concept of normalized ADC using a reference organ is relatively new and has been found to improve reproducibility and reduce variability in ADC measurement of the hepatic parenchyma and focal liver lesions at 1.5-T [21,22]. ADC normalization has been defined already in the abdomen using the spleen as a reference organ but there is no definite consensus about the most appropriate organ to date [21,22]. One advantage of using the adjacent organ (hepatic parenchyma or pancreatic parenchyma) instead of the spleen as a reference organ is that measurements are made easier with ROIs used for calculation placed on the same level of slice and because it is assumed that the adjacent parenchyma is subjected to the same field heterogeneity and susceptibility effects than the lesion. As a limitation, however, the apparently healthy adjacent parenchyma used for normalization may be involved at some degrees by an underlying disease. This limitation may apply more particularly in the liver that may be involved by steatosis or fibrosis that affect the ADC value [23].

In the pancreas, normalized ADC has been defined using the adjacent pancreas as a reference organ [20]. Thus, normalized ADC is defined as the ratio of focal pancreatic lesion ADC to apparently normal adjacent pancreas ADC. For the above-mentioned reasons, normalization should thus decrease the potential influence of artifacts on ADC calculation. More specifically, regarding the pancreas, ADC is similar in the different pancreatic segments and a disease in the upstream pancreas (i.e., body and tail) does not cause significant alteration in the ADC value of the pancreatic parenchyma downstream (i.e., in pancreatic head) [24,25]. Finally, in theory, the ADC of the normal parenchyma should not change with time or treatment whereas tumor necrosis should increase the ADC of the lesion. However, in fibrous pancreatic parenchyma an overlap between tumor (such as pancreatic ductal adenocarcinomas) and adjacent tissue may baffle ADC normalization. In addition, as regards to liver behavior, fatty infiltration of the pancreas may occur during chemotherapy or in patients with underlying chronic disease and increases ADC value [26,27]. Thus, changes in pancreatic parenchyma during treatment while absence of tumor response or tumor necrosis may result in misinterpretation of normalized ADC. Of note, return to normal value of normalized ADC could obscure tumor response and a decrease of normalized ADC may erroneously be interpreted as tumor progression.

In conclusion, to limit the possible influence of endogenous and exogenous parameters on the resulting ADC value, Barral et al. have used a normalized ADC to improve characterization of pathologic conditions with DW-MRI [20]. This approach has been evaluated for the characterization of focal pancreatic lesions only in this study so far, so that there is no strong evidence for a definite recommendation. In addition, Barral et al. have restricted their investigation to a limited number of pathologic conditions of the pancreas [28]. However, in light of their preliminary results, it can be reasonably assumed that ADC normalization is a promising tool to improve accuracy of ADC measurement and diagnostic performances. As a limitation, potential pitfalls such as pancreatic fibrosis and fatty involution should be considered when using normalized ADC. Currently, one major limitation of DW-MRI is the inability to distinguish between MFP and ductal adenocarcinoma due to an overlap of ADC values that mirrors an overlap in histological findings. The lack of standardization in DW-MRI (including acquisition protocol and signal analysis) is an important limitation for a valid inter-study comparison. To overcome these limitations, normalized ADC along with IVIM models can be considered future research tracks because technological innovation continues to improve the quality of clinical DW-MRI and more refined data processing systems are now available.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References

[1] Guiu B, Cercueil JP. Liver diffusion-weighted MR imaging: the tower of Babel? Eur Radiol 2011;21:463—7.
[2] Koh DM, Collins DJ, Orton MR. Intravoxel incoherent motion in body diffusion-weighted MRI: reality and challenges. AJR Am J Roentgenol 2011;196:1351—61.
[3] Andreou A, Koh DM, Collins DJ, et al. Measurement reproducibility of perfusion fraction and pseudodiffusion coefficient derived by intravoxel incoherent motion diffusion-weighted MR imaging in normal liver and metastases. Eur Radiol 2013;23:428—34.
[4] Chandarana H, Lee VS, Hecht E, Taouli B, Sigmund EE. Comparison of biexponential and monoexponential model of diffusion weighted imaging in evaluation of renal lesions: preliminary experience. Invest Radiol 2011;46:285—91.
[5] Klauss M, Lemke A, Grünberg K, et al. Intravoxel incoherent motion MRI for the differentiation between mass forming

chronic pancreatitis and pancreatic carcinoma. Invest Radiol 2011;46:57—63.
[6] Guiu B, Petit JM, Capitan V, et al. Intravoxel incoherent motion diffusion-weighted imaging in nonalcoholic fatty liver disease: a 3.0-T MR study. Radiology 2012;265:96—103.
[7] Luciani A, Vignaud A, Cavet M, et al. Liver cirrhosis: intravoxel incoherent motion MR imaging-pilot study. Radiology 2008;249:891—9.
[8] Koh DM, Sohaib A. Diffusion-weighted imaging of the male pelvis. Radiol Clin North Am 2012;50:1127—44.
[9] Mannelli L, Kim S, Hajdu CH, Babb JS, Taouli B. Serial diffusion-weighted MRI in patients with hepatocellular carcinoma: prediction and assessment of response to transarterial chemoembolization. Preliminary experience. Eur J Radiol 2013;82:577—82.
[10] Taouli B. Diffusion-weighted MR imaging for liver lesion characterization: a critical look. Radiology 2012;262:378—80.
[11] Padhani AR, Koh DM, Collins DJ. Whole-body diffusion-weighted MR imaging in cancer: current status and research directions. Radiology 2011;261:700—18.
[12] d'Assignies G, Fina P, Bruno O, et al. High sensitivity of diffusion-weighted MR imaging for the detection of liver metastases from neuroendocrine tumors: comparison with T2-weighted and dynamic gadolinium-enhanced MR imaging. Radiology 2013, http://dx.doi.org/10.1148/radiol.13121628.
[13] Colosio A, Fornès P, Soyer P, Lewin M, Loock M, Hoeffel C. Local colorectal cancer recurrence: pelvic MRI evaluation. Abdom Imaging 2013;38:72—81.
[14] Baltzer PA, Schelhorn J, Benndorf M, Dietzel M, Kaiser WA. Diagnosis of focal liver lesions suspected of metastases by diffusion-weighted imaging (DWI): systematic comparison favors free-breathing technique. Clin Imaging 2013;37:97—103.
[15] Soyer P, Corno L, Boudiaf M, et al. Differentiation between cavernous hemangiomas and untreated malignant neoplasms of the liver with free-breathing diffusion-weighted MR imaging: comparison with T2-weighted fast spin-echo MR imaging. Eur J Radiol 2011;80:316—24.
[16] Soyer P, Boudiaf M, Placé V, et al. Preoperative detection of hepatic metastases: comparison of diffusion-weighted, T2-weighted fast spin echo and gadolinium-enhanced MR imaging using surgical and histopathologic findings as standard of reference. Eur J Radiol 2011;80:245—52.
[17] Vilgrain V, Daire JL, Sinkus R, Van Beers BE. Diffusion-weighted MR imaging of the liver. J Radiol 2010;91:381—90.
[18] Wang Y, Miller FH, Chen ZE, et al. Diffusion-weighted MR imaging of solid and cystic lesions of the pancreas. Radiographics 2011;31:E47—64.
[19] Momtahen AJ, Balci NC, Alkaade S, Akduman EI, Burton FR. Focal pancreatitis mimicking pancreatic mass: magnetic resonance imaging (MRI)/magnetic resonance cholangiopancreatography (MRCP) findings including diffusion-weighted MRI. Acta Radiol 2008;49:490—7.
[20] Barral M, Sebbag-Sfez D, Hoeffel C, et al. Characterization of focal pancreatic lesions using normalized apparent diffusion coefficient at 1.5-Tesla: preliminary experience. Diagn Interv Imaging 2013, http://dx.doi.org/10.1016/j.diii. 2013.02.011.
[21] Do RK, Chandarana H, Felker E, et al. Diagnosis of liver fibrosis and cirrhosis with diffusion-weighted imaging: value of normalized apparent diffusion coefficient using the spleen as reference organ. AJR Am J Roentgenol 2010;195:671—6.
[22] Papanikolaou N, Gourtsoyianni S, Yarmenitis S, Maris T, Gourtsoyiannis N. Comparison between two-point and four-point methods for quantification of apparent diffusion coefficient of normal liver parenchyma and focal lesions: value of normalization with spleen. Eur J Radiol 2010;73:305—9.
[23] Leitão HS, Doblas S, d'Assignies G, et al. Fat deposition decreases diffusion parameters at MRI: a study in phantoms and patients with liver steatosis. Eur Radiol 2012:2626—8, http://dx.doi.org/10.1007/s00330-012-2626-8.
[24] Barral M, Soyer P, Ben Hassen W, et al. Diffusion-weighted MR imaging of the normal pancreas: reproducibility and variations of apparent diffusion coefficient measurement at 1.5- and 3.0-Tesla. Diagn Interv Imaging 2013;94:418—27.
[25] Braithwaite AC, Dale BM, Boll DT, Merkle EM. Short- and midterm reproducibility of apparent diffusion coefficient measurements at 3.0-T diffusion-weighted imaging of the abdomen. Radiology 2009;250:459—65.
[26] Soyer P, Spelle L, Pelage JP, et al. Cystic fibrosis in adolescents and adults: fatty replacement of the pancreas — CT evaluation and functional correlation. Radiology 1999;210:611—5.
[27] Lugo-Olivieri CH, Soyer PA, Fishman EK. Cystic fibrosis: spectrum of thoracic and abdominal CT findings in the adult patient. Clin Imaging 1998;22:346—54.
[28] Van Beers B, Lalonde L, Soyer P, et al. Dynamic CT in pancreatic lymphoma. J Comput Assist Tomogr 1993;17:94—7.

P. Soyer[a,*,b,c], M. Kanematsu[d], B. Taouli[e], D.-M. Koh[f], R. Manfredi[g], V. Vilgrain[h], C. Hoeffel[i], B. Guiu[j]

[a] *Department of body and interventional imaging, hôpital Lariboisière, Assistance Publique—hôpitaux de Paris, 2, rue Ambroise-Paré, 75475 Paris cedex 10, France*
[b] *UMR Inserm 965, hôpital Lariboisière, 2, rue Amboise-Paré, 75010 Paris, France*
[c] *Université Paris-Diderot, Sorbonne Paris-Cité, 10, rue de Verdun, 75010 Paris, France*
[d] *Department of radiology, Gifu university hospital, 1-1 Yanagido, 501-1194 Gifu, Japan*
[e] *Department of radiology, body MR imaging and translational and molecular imaging institute, Mount Sinai medical center, 1, Gustave Levy place, 10029 New York, United States*
[f] *Department of radiology, Royal Marsden hospital, Royal Marsden NHS Foundation Trust, Downs Road, SM2 5PT Sutton, United Kingdom*
[g] *Department of radiology, university of Verona, P. le L.A. Scuro 10, 37134 Verona, Italy*
[h] *Department of radiology, hôpital Beaujon, 100, boulevard du Général-Leclerc, 92110 Clichy, France*
[i] *Department of radiology, hôpital Robert-Debré, 11, boulevard Pasteur, 51092 Reims cedex, France*
[j] *Department of diagnostic and interventional radiology, hôpital Le Bocage, 14, rue Paul-Gaffarel, 21079 Dijon, France*

* Corresponding author.
E-mail address: philippe.soyer@lrb.aphp.fr (P. Soyer)