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REVIEW

Diffusion-weighted magnetic resonance imaging in colorectal cancer

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Summary Magnetic resonance imaging (MRI) plays now a major role in patients with colorectal cancer regarding tumor staging, surgical planning, therapeutic decision, assessment of tumor response to chemoradiotherapy and surveillance of rectal cancer, and detection and characterization of liver or peritoneal metastasis of colorectal cancers. Diffusion-weighted MRI (DW-MRI) is a functional imaging tool that is now part of the standard MRI protocol for the investigation of patients with colorectal cancer. DW-MRI reflects micro-displacements of water molecules in tissues and conveys high degrees of accuracy to discriminate between benign and malignant colorectal conditions. Thus, in addition to morphological imaging, DW-MRI has an important role to accurately detect colorectal neoplasms and peritoneal implants, to differentiate benign focal liver lesions from metastases and to detect tumor relapse within fibrotic changes. This review provides a comprehensive overview of basic principles, clinical applications and future trends of DW-MRI in colorectal cancers.

Abbreviations: ADC, apparent diffusion coefficient; CRT, chemoradiotherapy; DW-MRI, diffusion-weighted magnetic resonance imaging; DCE, dynamic contrast enhanced; MRI, magnetic resonance imaging; MDCT, multidetector computed tomography; FDG-PET/CT, fluoro-deoxy-glucose positron emission tomography computed tomography.

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Introduction

Colorectal cancer is the fourth most common cancer in men and the third most common cancer in women worldwide [1]. In addition, the incidence of colorectal cancer significantly increased from 1983—1987 to 1998—2002 in all parts of the world [2]. In the same time, thanks to screening, improvement of surgical techniques and the use of neoadjuvant chemoradiotherapy (CRT), the overall survival rate of patients with colorectal cancer has increased to reach 98% for stage 0, 93% for stage I, 86% for stage II, 67% for stage III, and 19% for stage IV [3].

During recent years, magnetic resonance imaging (MRI) has gained wide acceptance for the management of patients with colorectal cancer. Currently, MRI is definitively considered as a pivotal imaging modality in rectal cancer [4]. Indeed, MRI has demonstrated high performances in the assessment of local extent of rectal cancer [4] and is considered as the first choice imaging modality for the primary staging and restaging after CRT [4].

Major refinements in hardware and software, the use of hypergradients and improvements in surface coils have resulted in improved spatial resolution and reduced acquisition time so that functional MRI such as diffusion-weighted (DW) MRI has become possible. DW-MRI plays a role in the assessment of response to CRT and in the detection of local recurrence after treatment of rectal cancer [5—16]. Finally, DW-MRI has demonstrated high degrees of accuracy for the diagnosis of hepatic metastasis and peritoneal carcinomatosis of colorectal cancer [17—24].

The aim of this review was to briefly describe the basic physical principles of DW-MRI and present a comprehensive description of current applications for the diagnosis, staging and assessment of therapeutic response in colorectal cancer as well as discuss future trends and challenges.

Basic principles

DW-MRI investigates and highlights the differences in mobility of water molecules in the extracellular space of biological tissues [25]. Basically, water molecules randomly diffuse in the intracellular, the intravascular and the interstitial compartments. Diffusivity of water molecules in biological tissues depends on many factors including temperature, tissue cellularity, tortuosity of extracellular spaces, integrity of cell membranes and viscosity of fluids [26]. In DW-MRI, the signal intensity reflects the impeded diffusion of water molecules.

Free displacement of water molecules is observed in fluids such as cerebrospinal fluid or cysts. On the opposite, this mobility is restricted by obstacles in the molecular environment such as in high-cellularity tumors and high protein content abscesses [25]. In order to obtain water molecule micro-displacement contrast, a preliminary diffusion-gradient induces a phase shift within the slice selection plane that results in nulling the signal of moving water molecules. Consequently, only immobile molecules receive the MR radiofrequency pulse and may generate a signal. The use of high diffusion-gradient (*b*-factor, expressed in s/mm^2) results in images that are more sensitive to immobility [25]. On the other hand, DW-MRI has a T2-weighted component that allows high T2-weighted tissues (such as cerebrospinal fluid or cysts) to generate a signal. This latter signal can be removed thanks to the application of at least 2 values of diffusion gradients of increasing strength (basically $b = 0$ and 1000 s/mm^2) in two separate imaging sequences enabling to compute an apparent diffusion coefficient (ADC) map [25]. ADC reflects therefore the degree of restriction of water molecule diffusion. Thus, a low ADC value indicates high restriction. Consequently, regarding tumor tissues low ADC values correlate with high-cellularity (Table 1) [27].

In conclusion, the analysis of high *b*-value DW-MR images is a powerful tool to detect impeded diffusion in tissues such as high-cellularity malignant tumors resulting as a high intensity bright spot, and a low ADC value.

Detection and characterization of colorectal cancer

Rectal cancer detection

Digital examination along with endoscopy remains the mainstay for the diagnosis of rectal cancer, while MRI is now the first line examination modality for the preoperative staging and assessment of circumferential margin involvement [28—30]. However, for small rectal cancers whose location is not mentioned by the referring physician, or in case of specific pathologic conditions such as desmoplastic reaction, fibrotic or inflammatory changes due to inflammatory bowel disease, pelvic extra-intestinal malignancy or radiotherapy, the identification of rectal involvement may be difficult with conventional MRI sequences or computed tomography (CT) [31]. In such cases, DW-MRI can be a useful tool to detect malignant transformation within nonspecific mural wall thickening [32,33]. In this regard, Barral et al. have demonstrated that DW-MRI helps detect malignant foci in patients with rectal involvement by inflammatory bowel disease [33].

Rectal cancers show signal intensity lower than that of the normal rectal wall [34]. The adjunct of DW-MRI to the more conventional T2-weighted sequence improves lesion conspicuity of rectal cancers by comparison to T2-weighted images alone with a sensitivity of up to 96% and a positive predictive value of up to 100% [34—36].

Rectal cancer characterization

Using quantitative analysis, the ADC value of rectal cancers is significantly lower than that of normal rectal wall [34]. According to Soyer et al., the ADC value of rectal cancer ranges between 1.036 and 1.069×10^{-3} mm^2/s whereas the ADC value of normal rectal wall is 1.387×10^{-3} mm^2/s, with a low degree of overlap [34]. Depending on the expected effect, a threshold ADC value can be selected to maximize sensitivity or specificity. In this regard, a threshold ADC value of 1.240×10^{-3} mm^2/s has a sensitivity of 100% and a specificity of 94% whereas a threshold ADC value of 1.176×10^{-3} mm^2/s has a specificity of 100% and a sensitivity of 84% for the diagnosis of rectal cancer [34].

ADC value has been suggested as a potential biomarker for rectal cancer [27,37]. Researchers have highlighted an inverse correlation between ADC value and tumor aggressiveness. Indeed, in rectal cancer, ADC value correlates with mesorectal fascia invasion, lymph node involvement, histological differentiation, CA19-9 and Ki-67 levels, and AgNOR counts [37,38]. Conversely, there are conflicting results regarding the correlation with T-stage, and no correlations with carcinoembryonic antigen levels or lymphangiovascular invasion have been identified [37,38]. Of note, it has been demonstrated that DW-MRI helps differentiate between