

## **Whole-body DWI: does it have a role in oncology?**

### **Introduction**

#### *Whole-body oncological imaging: PET/CT and whole-body MRI*

Imaging plays a crucial role in oncology, and is being used for screening, diagnosis and staging, prognosis assessment, image-guided treatment, assessment of treatment response, and detection of tumor recurrence. Whole-body imaging provides the opportunity to evaluate cancerous lesions throughout the entire body. Positron emission tomography (PET)/computed tomography, most frequently performed with the radiotracer 2-deoxy-2-[18F]fluoro-D-glucose (FDG), is often regarded as one of the most accurate non-invasive diagnostic tools that is currently available for whole-body oncological imaging [1]. However, whole-body magnetic resonance imaging (MRI) may be an attractive alternative to FDG-PET/CT because of several reasons, among which the absence of potentially harmful ionizing radiation [2] and its lower costs [3]. A disadvantage of frequently employed conventional whole-body MRI sequences such as (contrast-enhanced) T1-weighted, (fat-suppressed) T2-weighted, and short inversion time inversion recovery (STIR) imaging, however, is that subtle lesions may be overlooked because of poor lesion-to-background contrast. Furthermore, these sequences are mainly used to detect structural abnormalities, whereas it is increasingly being recognized that complementary functional imaging methods are required to improve lesion characterization and follow-up [4]. Thus, it is of importance to integrate functional MRI sequences in oncological whole-body MRI protocols.

#### *Potential roles of whole-body DWI in oncology*

One of the most promising functional whole-body MRI techniques that has the potential to be readily implemented in clinical practice is whole-body diffusion-weighted MRI (DWI) [5, 6]. DWI is a completely noninvasive technique that provides information on the random (Brownian) motion of water molecules. Most tumors exhibit an impeded diffusivity due to increased cellularity, while most normal tissues have a relatively higher diffusivity. As such, a high lesion-to-background contrast can often be achieved with DWI. On the other hand, (therapy-induced) necrosis and apoptotic processes may lead to an increase in diffusivity due to loss of cell membrane integrity and decrease in cellularity [7]. Whole-body DWI may be used for several purposes in oncology, among which cancer screening, cancer staging, and (early) assessment of the effectiveness of anticancer therapies.

### **Practical considerations for whole-body DWI**

#### *Respiratory motion-compensated vs. free breathing acquisitions*

Previously, respiratory motion compensation techniques were considered mandatory for DWI in the chest and abdomen. However, a disadvantage of breath-hold acquisitions is the limited scan time per breath-hold, as a result of which only relatively thick slices can be obtained that are not suitable to create multiplanar reformats. Respiratory-gating does allow for the acquisition of thin slices, but considerably prolongs scan time. Consequently, neither breath-hold nor respiratory-gated acquisitions seem to be realistic approaches for whole-body DWI. A major breakthrough was the introduction of the concept of Diffusion-weighted Whole-body Imaging with Background body signal Suppression (DWIBS), which involves a free-breathing acquisition [5]. Importantly, diffusion-weighted image contrast is maintained during free breathing, because bulk tissue motion (such as respiratory motion) is rigid body motion that does not lead to phase dispersion and subsequent signal loss [5, 6, 8, 9]. A free-breathing acquisition does not suffer from unutilized scan time and provides the opportunity to acquire thin slices (typically 4 mm) with a high number of signal averages that can be used to create multiplanar reformats. Although a free-breathing acquisition introduces slight imaging

blurring, image quality is mostly diagnostic and scan time is clinically acceptable (with state-of-the-art systems, a whole-body DWI examination can be performed in less than 30 minutes).

#### *Coils/coil setups*

A whole-body DWI examination can be performed with different coils/coil setups. Although it has been reported that it is possible to use a built-in-body coil for signal reception, such an approach is suboptimal, because no parallel acquisition techniques can be used (with subsequent risk of severe image distortions) and signal-to-noise-ratio (SNR) is lower than when surface coils are used. [10]. Therefore, it is highly recommended to use surface coils for (whole-body) DWI. Two approaches can be used for whole-body imaging with surface coils. The first is by using a so-called sliding table and repositioning surface coil approach [11]. With this approach, spacers are placed on the original patient table. Subsequently, an additional table platform is mounted on top of these spacers. In this way, sufficient space can be created to freely move the lower part of a surface coil along the z-axis, without the need to reposition the patient who is lying on top of the additional table platform. After scanning the different stations, adjacent stations can be merged to create the whole-body image. Disadvantages of this approach, however, are narrowing of the bore diameters (as a result of which it may be difficult to accommodate large-sized patients within the MRI scanner) and the need for careful coil repositionings (although this requires only a few additional minutes for whole-body scanning). The second approach is by using whole-body surface coil technology, which is currently provided by several major vendors. Eventually, it is expected that the availability of whole-body surface coil designs will increase and that they will become the method of choice to perform a whole-body MRI/DWI examination. Other recent advances in this field (among which the development of wide-bore systems, light-weight coils, and digital broadband technology) have further improved workflow, patient comfort, and image quality of whole-body MRI/DWI examinations.

#### *1.5 T vs. 3.0 T*

So far, most whole-body DWI examinations have been performed at 1.5 T. However, SNR in DWI is relatively low, even though a high number of signal averages can be acquired when a free-breathing acquisition is employed. Therefore, there is a great deal of interest to move to higher field strengths that provide higher SNR. It has indeed been shown that whole-body DWI at 3.0 T offers higher SNR compared to that at 1.5 T, but the former still suffers from a higher risk of B<sub>0</sub> and B<sub>1</sub> inhomogeneities and susceptibility artefacts [12]. Nevertheless, thanks to some important recent technological developments, among which improved B<sub>1</sub> shimming and the advent of multi-source radiofrequency (RF) transmission technology (which allows for faster scanning and provides improved image uniformity and consistency compared to single-source RF transmission [13]), whole-body DWI at 3.0 T has become clinically feasible. Another advantage of performing (whole-body) DWI at higher field strengths is that it becomes possible to effectively use the so-called slice-selection gradient reversal [SSGR] fat suppression technique (which exploits the high sensitivity of echo-planar imaging to chemical shift artefacts (water-fat shift) in the phase-encoding direction) in addition to conventional fat-suppression techniques such as frequency selective and STIR-based fat suppression [14].

#### **Results from recent clinical studies**

Several studies in various malignancies have shown that whole-body MRI with DWI may improve lesion detectability and staging accuracy compared to whole-body MRI without DWI [15-19]. Comparative studies between whole-body MRI/DWI and FDG-PET/CT are rapidly emerging [16, 17, 19-23], but their number is still too scarce to draw any conclusions on

which of these imaging modalities is most accurate in which setting. Another approach is to consider whole-body DWI and FDG-PET as complementary imaging methods [24]. Clearly more research is needed to establish the clinical roles of whole-body DWI. One of the challenges is to optimize whole-body MRI/DWI protocols in order to obtain all necessary diagnostic and/or prognostic information within a clinically acceptable scan time (< 30 minutes).

### **Limitations and challenges**

#### *ADC measurements*

Assessment of tissue diffusivity by means of apparent diffusion coefficient (ADC) measurements may aid in tissue characterization. Nevertheless, although ADCs of malignant lesions have generally been reported to be significantly lower than those of benign lesions, there is considerable overlap between both groups. Consequently, the clinical utility of ADC measurements remains questionable. An exception may be the differentiation between lymphoma and other lesions, since the former has been reported to have a very low ADC [25, 26]. Another issue is that ADC measurements may be unreliable in case of misregistration between datasets that were acquired with different b-values (e.g. due to motion and echo-planar imaging-related distortions). This issue may be solved by measuring the signal intensity of a lesion on native, high-b-value images only, and normalize the measured lesion signal intensity using the signal intensity of a reference organ (e.g. the spinal cord) on the same high-b-value image. Such an approach has shown to be superior to the ADC in discriminating benign from malignant pulmonary nodules [27]. Although such a semi-quantitative approach may potentially improve lesion characterization, quantitative (ADC) measurements are still necessary when using DWI for therapy response assessment.

#### *Lymph nodes and contrast agents*

Similar to the differentiation between benign and malignant lesions, the discrimination between non-malignant and malignant lymph nodes with DWI may be difficult, because of substantial overlap in ADCs between both groups [28]. Furthermore, normal-sized lymph nodes may be less reliably assessed due the combination of image distortions, insufficient spatial resolution, and partial volume effects [28]. A promising new concept to improve the diagnosis of lymph node metastasis is by performing DWI after the administration of ultrasmall superparamagnetic iron oxide (USPIO) particles. With this approach, malignant lymph nodes may show high signal intensity while non-malignant lymph nodes are expected to exhibit low signal intensity because of uptake of USPIO particles and subsequent T2(\*) shortening and signal loss [29]. The advantage of USPIO-enhanced DWI is that acquired images can be both quantitatively and qualitatively (visually) assessed for lymph node metastasis. Unfortunately, the availability of USPIO contrast agents is limited at present. Therefore, the utility of combining DWI with other contrast agents, among which gadofosveset trisodium (Vasovist), is currently being explored [30-32].

#### *Cardiac motion*

Cardiac motion can lead to deformation and acceleration of neighbouring voxels, including those in the mediastinum and liver [33]. Subsequent signal loss and artificially increased ADCs may impair the evaluation of lesions. Partial solutions are the use of lower b-values (which may increase the detectability of lesions around the heart compared to DWI with higher b-values, although at the expense of decreased specificity for malignant lesions), cardiac gated acquisitions (although such an approach may be not clinically feasible due to severe scan time prolongation), and the acquisition of complementary conventional sequences

(e.g. STIR imaging has been reported to be more sensitive than DWI for detection and subtype classification of pulmonary adenocarcinomas [34]).

### Summary

Whole-body MRI, particularly whole-body DWI, may be used for several purposes in oncology, including screening, staging, and therapy monitoring. It has become possible to perform a state-of-the-art whole-body DWI examination under free breathing (DWIBS) using a whole-body surface coil design, at either 1.5 T or 3.0 T. Results from recent clinical studies on whole-body MRI/DWI are promising, suggesting that DWI improves lesion detection and staging accuracy. However, its value relative to other imaging modalities (particularly [FDG-]PET/CT), and the most efficient whole-body MRI/DWI protocols (in terms of diagnostic and prognostic information and examination time) still have to be established. Other challenges that have to be addressed are the improvement of tissue and lymph node characterization at DWI, and the development of solutions that minimize the effect of physiological motion (particularly cardiac motion) on the qualitative and quantitative evaluation of (whole-body) diffusion-weighted images.

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