High Fields: State of the Art Sodium and Phosphorus Imaging in Humans

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Hydrogen (^{1}H) is by far the most imaged nucleus in the domain of magnetic resonance imaging due its favorable physical properties and its high concentration (about 100 M) in the human body in the form of water and fat. However, there are many other nuclei aside from protons, usually referred to as X-nuclei, that can be used for MR spectroscopy and imaging. The main prerequisites are a non-zero nuclear spin and a sufficient concentration to be detectable by means of NMR. The only naturally occurring isotope of sodium (^{23}Na) fulfills all of these requirements, but lacks the sensitivity of protons. Reasons for this are primarily the 1000-fold lower in vivo concentration and the small gyromagnetic ratio. The acquisition of sodium images is further complicated by the rapidly decaying signal, which is a direct consequence of the spin-3/2 nature of the nucleus and the corresponding electric quadrupolar interaction between the nucleus and its environment.

The interesting physical properties of the ^{23}Na nucleus and the additional information which can be gained from it have always provided an incentive to further develop the existing imaging techniques. The availability of ultra-high field (UHF) scanners and the concomitant increase in signal-to-noise ratio (SNR) allowed reducing the scanning times and thus increased the applicability of sodium magnetic resonance imaging. Nevertheless, ^{23}Na-MRI remains challenging due to the low in vivo concentrations (human brain tissue: 30-35 mM)(1) and the short transverse relaxation times (human brain tissue: fast component: T_{2f} = 2-5 ms, slow component T_{2s} = 15-25 ms)(2). Unlike protons, the sodium nucleus possesses an electric quadrupole moment which makes it sensitive to electric field gradients in its molecular environment. Thus, free and motion restricted sodium ions exhibit a different physical behavior in the human body (3). Differentiation between extra- and intracellular sodium can provide useful information in case of many pathologies such as tumors, ischemia or articular cartilage degeneration (4–6).

Shift reagents also allow to efficiently discriminate signals from intra- and extracellular sodium (7–9). However, their use is limited to animal studies either due to their toxicity or the lack of a clinical approval for their application in humans. Nevertheless, they can be used to assess the performance of other non-invasive methods such as multiple-quantum filtering. One of the most commonly used technique among those is triple-quantum-filtered (TQF) imaging (5,10–13) for which animal studies using shift reagents have shown that at least 60% of the observed TQ signal originates from intracellular sodium (14,15). The remainder of the TQ signal is probably due to interactions of sodium ions in the extracellular compartment with macromolecules.

The phosphorus (^{31}P) metabolites, such as phosphocreatine (PCr), adenosine triphosphate (ATP), and inorganic phosphate (Pi), play a key role in the metabolic energy production. ^{31}P magnetic resonance spectroscopy (MRS) allows to measure and quantify the concentrations of the latter non-invasively and permits in this way the assessment of cellular viability and integrity as well as the extraction of

physiologically relevant parameters such as the intracellular pH (16–20). Up to now, only a few studies have investigated the suitability of ^{31}P MRS for the differentiation of tumor types or the assessment of malignancy (21). The clinical application of ^{31}P MRS is primarily hindered by the coarse spatial resolution and the long acquisition times, which are a direct consequence of the small in vivo concentration of the metabolites. In addition to the low SNR, the long longitudinal relaxation times (T_1) on the order of seconds and the short transverse relaxation times (T_2) on the order of tens of milliseconds further impede an efficient signal acquisition with a high spectral resolution (22).

It has been shown previously that the SNR can be increased substantially if data acquisition is performed at ultra-high field (UHF) (23) and even more so if a multi-channel coil is used for signal reception instead of a standard surface coil (24). However, new challenges arise when MRS is performed at UHF. High specific absorption rates preclude in most cases the use of proton decoupling (25,26) and limit the application of adiabatic pulses. Moreover, it becomes more difficult to design pulses having a sufficient bandwidth to excite all the relevant phosphorus metabolites (27). The reduced homogeneity of the main static magnetic field (B_0) and the resulting intra-voxel dephasing due to the low spatial resolution are other issues which need to be considered.

In this contribution we will present examples and applications to acquire conventional TQF images with a state-of-the-art multi-channel phased array coil was investigated at 9.4 T. Spiral and double-spiral sampling patterns were used to time-efficiently acquire spin-density weighted (SDW) and TQF images. In order to reduce SAR while keeping an acceptable TR for an efficient data acquisition, the FA for the TQ preparation was modulated along the partition-encoding direction. The impact of this approach on SNR and spatial resolution was evaluated by means of simulations and phantom measurements. Optimal sequence parameters were determined for in vivo imaging and used on six healthy volunteers. Furthermore, we will present ^{31}P 3D chemical shift imaging (CSI) (13,14) at 9.4 Tesla with a home-built multi-nuclear coil setup. Healthy volunteers and tumor patients were scanned to investigate the feasibility and performance of ^{31}P spectroscopy in normal tissue and brain tumors.

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