MR Imaging of nX-nuclei (23Na and Friends) from Controversies to Potential Applications: Quantification of Tissue Sodium Concentration

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Highlights

- Physiology of sodium
- Tissue viability
- Tissue Sodium Concentration (TSC)
- Selection of appropriate sequences
- The importance of the right hardware
- Corrections and signal calibrations
- New developments

Sodium (^{23}Na) is one of the most abundant elements in the human body. Due to its physiological importance, sodium magnetic resonance imaging (MRI) has drawn substantial attention to monitor the viability and the status of biological tissues since its introduction in 1985 [1].

Sodium ions are found in intra- and extracellular compartments at concentrations of about 10-20 and 140-150 mmol/l, respectively. This concentration gradient, which is maintained by the energy dependent Na+/K+-ATPase (the sodium-potassium pump), has a major importance in the physiology of cells [2-4].

One of the goals of sodium MRI is the quantification of regional tissue sodium concentration (TSC)[5]. This parameter, which is the weighted average of intracellular and extracellular sodium concentrations, is used to assess disease status, monitor disease progression and the outcome of therapeutic interventions.

Several studies have shown that sodium MRI delivers relevant information about cellular viability in pathologies of the central nervous system such as stroke [6-8], Alzheimer's disease [9], Multiple Sclerosis [10-14], Huntington's disease [15], and tumors [16]. Sodium MRI has been also successfully implemented to image the heart, kidneys, and the musculoskeletal apparatus [17-22].

Sodium MRI is, however, challenging because the sodium nucleus has a low NMR sensitivity, its concentration in tissues is low (30 - 50 mmol/l in the brain), and its spin quantum number is 3/2. This means that sodium ions have a nuclear quadrupolar moment that interacts with electric field gradients surrounding the sodium ions. In biological tissues this can give rise to fast bi-exponential relaxations of both, the transverse and longitudinal MR magnetizations [23].

In the human brain, for example, the transverse sodium signal decay exhibits a fast-relaxing component in the range of 0.8-5 ms (T_{2f}) and a slow-relaxing component in the range of 15-30 ms (T_{2s}). Longitudinal relaxation (T_1), in theory bi-exponential too [23], has been only reported using mono-exponential models with relaxation times in the range of 15-40 ms. In liquid environments, such as the cerebrospinal fluid (CSF), the quadrupolar interaction averages to zero due to motional narrowing, and a mono-exponential signal relaxation in the range of 50-60 ms is found for both transverse and longitudinal relaxation times.

To minimize signal losses and to access TSC measures free of bias effects caused by the fast-relaxing bi-exponential signal, ultra-short echo times sequences (UTE), in which the echo time should ideally be shorter than 0.5 ms, are now the standard choice [24].

Efficient MR sequences, with carefully chosen k-space trajectories such as twisted projection imaging (TPI) [25,26], density adapted 3D-radial [27], stacks of spirals (SoS) [28], 3D cones [29], and FLORET [30] are essential to maximize image signal-to-noise ratio (SNR) and to reach high image resolution, thereby keeping total acquisitions times (TA) relatively short. Furthermore, in the last decade sodium MRI greatly benefitted from the use of high- and ultra-high magnetic fields (≥ 3T) [31-35].

Another very important aspect is the selection of the optimal radiofrequency (RF) coils, as they can have a strong effect on final images. Besides the classical single-tuned or double-tuned sodium coils, single-tuned phased-array coils can be used to improve SNR by making use of the increased sensitivity of smaller elements [36].

The most common approach for mapping TSC consists in a spin-density (SD) weighted acquisition. This is possible because of the short T_1 of sodium. In its simplest form, the SD approach consists in the application of a short, non-selective 90° RF pulse immediately followed by a signal read-out that is performed in presence of active gradients describing a k-space trajectory originating at the center of k-space. After a relatively short repetition time (TR ≥ 150 ms), which allows the spin system to relax, the same pulse-acquire scheme is repeated in combination with another k-space trajectory until the k-space is uniformly sampled.

Data acquired with non-Cartesian sequences is then reconstructed into images by either a non-uniform Fourier transform, a gridding algorithm followed by a standard Fourier transform, or by iterative reconstruction algorithms. Reconstructed images are then corrected for coil transmission field (B_1^+), coil reception sensitivity (B_1^-), and if required, for global saturation effects [31-33].

SD images are then transformed into TSC maps by means of a signal calibration curve. This is obtained from one, two, or more reference phantoms of known sodium concentrations and known relaxation times, placed in the same field-of-view (FOV). Alternatively, calibration phantoms can be scanned separately with the same sequence parameters and same coil loading in a so-called phantom replacement method.

The SD approach, however, suffers from sub-optimal SNR efficiency. Therefore, shorter TRs (100-120 ms) are generally adopted. Nevertheless, shorter TRs introduce saturation effects which could ideally be corrected using a T1 map at the same resolution. However, sodium images are usually corrected using a global T_1 relaxation time, leading to quantification error of about 10% in liquid environments [33].

New approaches for the measurement of TSC are emerging. These are based on steady-state types of sequences [37] such as the variable flip angle approach, in which two acquisitions at two different flip angles are used to compute simultaneously T_1 and spin density maps in short acquisition times and with a high degree of accuracy [38].

In summary, TSC is a valuable biomarker that could be used in clinical practice to monitor tissue viability and to support therapeutic decisions. Sodium MRI measurements require the use of dedicated RF coils, dedicated MR sequences and dedicated reconstruction techniques. The use of a high- or ultra-high magnetic field strength (≥ 3T) is not obligatory, but it is clearly beneficial in terms of SNR and image resolution.

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