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# Anatomically weighted second-order total variation reconstruction of <sup>23</sup>Na MRI using prior information from <sup>1</sup>H MRI

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#### ARTICLE INFO

#### ABSTRACT

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Sodium (<sup>23</sup>Na) MRI is a noninvasive tool to assess cell viability, which is linked to the total tissue sodium concentration (TSC). However, due to low in vivo concentrations, <sup>23</sup>Na MRI suffers from low signal-to-noise ratio (SNR) and limited spatial resolution. As a result, image quality is compromised by Gibbs ringing artifacts and partial volume effects. An iterative reconstruction algorithm that incorporates prior information from <sup>1</sup>H MRI is developed to reduce partial volume effects and to increase the SNR in non-proton MRI. Anatomically weighted second-order total variation (AnaWeTV) is proposed as a constraint for compressed sensing reconstruction of 3D projection reconstruction (3DPR) data. The method is evaluated in simulations and a MR measurement of a multiple sclerosis (MS) patient by comparing it to gridding and other reconstruction techniques. AnaWeTV increases resolution of known structures and reduces partial volume effects. In simulated MR brain data (nominal resolution  $\Delta x^3 = 3 \times 3 \times 3$  mm<sup>3</sup>), the intensity error of four small MS lesions was reduced from (6.9  $\pm$  3.8)% (gridding) to  $(2.8 \pm 1.4)\%$  (AnaWeTV with T<sub>2</sub>-weighted reference images). Compared to gridding, a substantial SNR increase of 130% was found in the white matter of the MS patient. The algorithm is robust against misalignment of the prior information on the order of the <sup>23</sup>Na image resolution. Features without prior information are still reconstructed with high contrast. AnaWeTV allows a more precise quantification of TSC in structures with prior knowledge. Thus, the AnaWeTV algorithm is in particular beneficial for the assessment of tissue structures that are visible in both <sup>23</sup>Na and <sup>1</sup>H MRI.

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#### Introduction

Sodium (<sup>23</sup>Na) MRI provides a noninvasive measure of tissue viability. Elevated levels of total sodium concentration (TSC) can be associated with pathological changes in tissue for a number of diseases such as cancer (Nagel et al., 2011b: Ouwerkerk et al., 2003: Thulborn et al., 1999). stroke (Hilal et al., 1983; Hussain et al., 2009; Jones et al., 2006; Thulborn et al., 2005), muscular disease (Constantinides et al., 2000a; Nagel et al., 2011a; Weber et al., 2011) or cartilage degeneration (Schmitt et al., 2011; Wheaton et al., 2004). In multiple sclerosis (MS), recent studies indicate elevated <sup>23</sup>Na concentrations even in normalappearing white and gray matter of the brain (Inglese et al., 2010; Maarouf et al., 2014; Paling et al., 2013; Zaaraoui et al., 2012). However, the quantification of TSC is challenging. The low nuclear magnetic resonance (NMR) sensitivity and low in vivo concentration of <sup>23</sup>Na lead to low signal-to-noise ratios (SNR), thus limiting the achievable spatial resolution of the images. As a consequence, image quality is corrupted by partial volume effects and Gibbs ringing artifacts. Furthermore, the biexponential relaxation behavior of the slowly tumbling <sup>23</sup>Na ions has to be taken into account (Hubbard, 1970). Short T<sub>2</sub><sup>\*</sup> relaxation times result in a further broadening of the point spread function (PSF) and require dedicated imaging sequences (Konstandin and Nagel, 2013a).

Since 2007, Compressed Sensing (CS) (Candès et al., 2006; Donoho, 2006) and related iterative reconstruction algorithms have experienced an ever growing popularity for MRI reconstructions (Lustig et al., 2007). Even though these techniques are widely applied in proton imaging, they are still rarely used in non-proton MRI (Ajraoui et al., 2010; Behl et al., 2014; Hu et al., 2008; Kampf et al., 2010; Madelin et al., 2011). While these approaches exploit the sparsity of images in some transform domain, the incorporation of prior anatomical knowledge in the reconstruction provides further opportunities to improve image quality. Even the use of a support region that matches the object shape as the most basic anatomical information can improve image quality (Ajraoui et al., 2012; Gnahm et al., 2014). Images of different nuclei are generally highly correlated: in the case of <sup>23</sup>Na MRI, anatomical structures such as the cerebrospinal fluid (CSF) are well visible, matching well with <sup>1</sup>H MRI.

Proton images are available with excellent SNR and high resolution within short measurement times. Algorithms that incorporate prior anatomical information from proton MRI for resolution enhancement have been used well before the onset of CS, mostly in





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MR spectroscopic imaging (Eslami and Jacob, 2010; Haldar et al., 2006; Hu et al., 1988; Liang and Lauterbur, 1991; Plevritis and Macovski, 1995). Constantinides et al. (2000b) proposed the first algorithm incorporating anatomical information for <sup>23</sup>Na MRI. Common to all these methods is the need for segmentation of the proton reference image before reconstruction. It would be desirable to develop algorithms that do not rely on segmentation, which is an additional source of error. Haldar et al. (2008) proposed to use anatomical weighting factors with quadratic regularization to reconstruct low-SNR proton images. However, quadratic regularization does not harness image sparsity in the context of CS. Here, we propose an anatomically weighted second-order total variation (AnaWeTV) constraint that advances the idea of anatomical weighting factors to fulfill the requirements of CS. Prior information is obtained from registered proton images with higher resolution. The performance of the algorithm is demonstrated in data simulations and for in vivo <sup>23</sup>Na MRI of a MS patient.

#### Methods

#### Image reconstruction

The idea of anatomical weighting as suggested for quadratic regularization (Haldar et al., 2008) is refined to meet the requirement of CS in terms of l<sub>1</sub>-norm minimization. An anatomically weighted secondorder total variation (AnaWeTV) is proposed:

$$R_{\text{AnaWeTV}}(x) = \sum_{\alpha = x, y, z} \left( \lambda \left\| W_{\alpha} D_{\alpha}^{(1)} x \right\|_{1} + (1 - \lambda) \left\| W_{\alpha} D_{\alpha}^{(2)} x \right\|_{1} \right), \tag{1}$$

where *x* is the image vector,  $D_{\alpha}^{(1)}$  denotes the first-order derivative computing the finite differences in dimension  $\alpha$ , and  $D_{\alpha}^{(2)} = D_{\alpha}^{(1)T}D_{\alpha}^{(1)}$  is the second-order derivative. The relative weighting of the first- and second-order derivatives is chosen by  $\lambda = 0.77$  (Block et al., 2007; Geman and Yang, 1995).  $W_{\alpha}$  is a diagonal matrix containing anatomical weighting factors taking values between 0 and 1. For a weighting factor of 1, Eq. (1) becomes the normal second-order total variation (TV2) (Block et al., 2007; Geman and Yang, 1995). For a small weighting factor  $(W_{\alpha})_{ii}$ , intensity changes between voxel *i* and its neighboring voxels in direction  $\alpha$  are less penalized. Thus, intensity changes in the reconstructed image are promoted at positions of known tissue boundaries.

The anatomical weighting factors are calculated directly from a registered high-SNR, high-resolution <sup>1</sup>H MR reference image. The confidence  $c_{\alpha}$  of a tissue boundary is defined as the first derivative of the reference image *r* that has been normalized to its maximum value:

$$c_{\alpha,i} = \left(D_{\alpha}^{(1)}r\right)_{i}.$$
(2)

 $W_{\alpha}$  is then calculated from the inverse  $w_{\alpha}$  of the confidence  $c_{\alpha}$ ,

$$(W_{\alpha})_{ii} = \begin{cases} 0.1 \frac{w_{\alpha,i} - \min(w_{\alpha})}{w_{\max} - \min(w_{\alpha})} & \text{for } w_{\alpha,i} < w_{\max} \\ 1 & \text{for } w_{\alpha,i} = w_{\max} \end{cases}$$
(3)

with

$$w_{\alpha,i} = \min\left\{ \left( c_{\alpha,i} \right)^{-1}, w_{\max} \right\}$$
(4)

The parameter  $w_{\text{max}}$  is used to control the amount of included prior information. For small values of  $w_{\text{max}}$ , only the strongest signal variations in the reference contribute.

The image is reconstructed by minimizing the objective function

$$f(x) = \frac{1}{2} \|Ax - y\|_2^2 + \sum_i \tau_i R_i,$$
(5)

where *A* is the system matrix, which is composed of a Fourier transformation followed by Kaiser-Bessel gridding (Jackson et al., 1991) to the kspace trajectory. *x* is the image vector and *y* is the vector containing measured data.  $R_i$  are regularization terms with a constant weighting  $\tau_i$ . AnaWeTV is always used in combination with a regularization of the support region, which is derived as a binary mask (BM) from the reference proton image (Gnahm et al., 2014). For simplicity, reconstructions with combined BM- and AnaWeTV-regularization will be denoted with AnaWeTV instead of AnaWeTV&BM throughout this paper. The objective function is minimized using a conjugate gradient algorithm (Zhang et al., 2006). The code was implemented in C++ using the FFTW3 library (Frigo and Johnson, 2005). The algorithm is stopped if the criterion

$$\frac{\|x_{k+1} - x_k\|_2}{\|x_{k+1}\|_2} < 10^{-6} \tag{6}$$

is fulfilled ten times in a row.

AnaWeTV was compared to BM&TV2 as well as gridding. In <sup>23</sup>Na MRI, it is common to apply a Hamming filter (Hamming, 1989; Konstandin and Nagel, 2013b; Stobbe and Beaulieu, 2008) to increase SNR and to reduce Gibbs ringing artifacts. Therefore, a Hamming filtered gridding reconstruction was performed as well. Additionally, AnaWeTV was compared to the originally proposed method of anatomically weighted quadratic regularization (AnaWeQR) (Haldar et al., 2008). Weighting factors in the iterative reconstruction were optimized as detailed in (Gnahm et al., 2014).

#### Simulations

Radial k-space data were generated based on simulated T<sub>2</sub>weighted Spin Echo (T2w SE) <sup>1</sup>H MR brain images from the BrainWeb database (Cocosco et al., 1997; Kwan et al., 1996) as described in Gnahm et al. (2014), since this contrast is similar to a <sup>23</sup>Na MR image. Datasets for a healthy brain as well as for the same brain with artificially inserted MS lesions were simulated with a nominal resolution  $\Delta x^3 = 3 \times 3 \times 3$  mm<sup>3</sup> and 5000 projections, corresponding to 25% of the required Nyquist samples. The MS lesions were simulated to have 89% higher signal intensity than the surrounding white matter (WM). Another dataset was simulated for the healthy brain with reduced nominal resolution  $\Delta x^3 = 6 \times 6 \times 6 \text{ mm}^3$  and 5000 projections to fulfill the Nyquist criterion. Synthetic complex Gaussian noise was added to all datasets. The gridding reconstruction of the fully sampled dataset with  $\Delta x^3 = 1.5 \times 1.5 \times 1.5$  mm<sup>3</sup> served as ground truth. AnaWeTV reconstructions were performed with weighting factors from three reference images with different contrasts: T<sub>1</sub>-weighted Magnetization Prepared Rapid Gradient Echo (T1w MPRAGE), T<sub>2</sub>weighted Fluid Attenuated Inversion Recovery (T2w FLAIR) and the T2w SE. The T2w FLAIR and T1w MPRAGE contrast were obtained as BrainWeb custom simulations (Kwan et al., 1996). The T2w SE was identical to the ground truth image and therefore contained the same contrast as the simulated radial datasets. For the AnaWeQR reconstruction, the T2w SE image was used as reference.

Iterative reconstructions of the high-resolution ( $\Delta x^3 = 3 \times 3 \times 3 \text{ mm}^3$ ) dataset were performed with the following weighting factors:  $\tau_{BM} = 10$ ,  $\tau_{TV2} = 2.5 \times 10^{-4}$  (BM&TV2),  $\tau_{AnaWeQR} = 1$  (AnaWeQR),  $\tau_{BM} = 10$ ,  $\tau_{AnaWeTV} = 2.5 \times 10^{-4}$  (AnaWeTV, T1w MPRAGE reference),  $\tau_{BM} = 0$ ,  $\tau_{AnaWeTV} = 5 \times 10^{-4}$  (AnaWeTV, T2w FLAIR reference) and  $\tau_{BM} = 7$ ,  $\tau_{AnaWeTV} = 7.5 \times 10^{-4}$  (AnaWeTV, T2w SE reference). For the low-resolution ( $\Delta x^3 = 6 \times 6 \times 6 \text{ mm}^3$ ) dataset,  $\tau_{BM} = 4$ ,  $\tau_{TV2} = 1 \times 10^{-3}$  (BM&TV2) and  $\tau_{BM} = 0.7$ ,  $\tau_{AnaWeTV} = 2.5 \times 10^{-3}$  (AnaWeTV, T2w SE reference) were used.

The influence of registration errors of the prior information was tested on the  $3 \times 3 \times 3$  mm<sup>3</sup> dataset by misaligning the T2w SE reference in the anterior-posterior direction by 1.5, 3, and 4.5 mm. Furthermore, the reconstruction of features without prior information as well as the

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