# Automatic sodium maps reconstruction using PatchMatch algorithm for phantom detection

Ferran Prados[1,2], Bhavana S Solanky[2], Patricia Alves Da Mota[2], Manuel Jorge Cardoso[1], Wallace J Brownlee[2], Niamh Cawley[2], David H Miller[2], Xavier Golay[3], Sebastien Ourselin[1], and Claudia Angela Michela Gandini Wheeler-Kingshott[2,4]

*[1]Translational Imaging Group, Medical Physics and Biomedical Engineering, University College London, London, United Kingdom, [2]NMR Research Unit, Queen Square MS Centre, Department of Neuroinflammation, UCL Institute of Neurology, University College London, London, United Kingdom, [3]Brain Repair & Rehabilitation, UCL Institute of Neurology, University College London, London, United Kingdom, [4]Brain Connectivity Center, C. Mondino National Neurological Institute, Pavia, Italy*

## Synopsis

**Quantitative sodium magnetic resonance imaging ($^{23}$Na-MRI) enables the non-invasive measurement of in vivo total $^{23}$Na concentration (TSC) in the human brain. This involves a complex process of reconstructing datasets acquired to calculate a TSC map. Quantitative TSC map calibration relies on external reference phantoms with known concentration for linear calibration. This commonly involves manually segmenting the phantoms by trained raters, hindering automatic image analysis, and presenting a bottleneck in the TSC computation. We propose to substitute the manual segmentation by OPAL, a novel, fast, robust and reliable technique for segmenting sodium phantoms that allows fully-automatic reconstruction of TSC maps.**

## Introduction

Quantitative sodium magnetic resonance imaging ($^{23}$Na-MRI) enables the non-invasive measurement of in vivo total $^{23}$Na concentration (TSC) in the human brain[1]. This involves a complex process of reconstructing datasets acquired to calculate a TSC map[2]. Quantitative TSC map calibration relies on external reference phantoms with known concentration for linear calibration[3]. This commonly involves manually segmenting the phantoms by a trained rater, hindering automatic analysis of the images, and presenting a bottleneck in the TSC map computation. Moreover, the manual segmentation of the sodium phantoms reduces reproducibility due to intra-rater and inter-rater variability.

Here we propose to substitute the manual segmentation with an automated method. Recently, it has been demonstrated that the Optimitzed PatchMatch Label fusion algorithm[3] (OPAL) has an excellent performance in terms of segmentation accuracy and computation time when compared with recently published methods[4]. By introducing OPAL into our pipeline for phantom segmentation, we aim to make the processing of TSC maps more time efficient and reproducible.

## Methods

*Protocol:* 10 healthy controls and 14 Multiple Sclerosis (MS) patients were scanned on a 3T Philips Achieva. They underwent two protocols in the same session using: 1) A proton scan using a 32-channel head coil, which included a PD/T2 (1x1x3 mm$^3$) and a 3DT1-weighted (1x1x1 mm$^3$) scans; 2) $^{23}$Na scan using a fixed-tuned $^{23}$Na transmit/receive coil (Rapid Biomedical), which included a 3D-Cones UTE sequence[4] (3x3x3 mm$^3$) and a 1H PD/T2w sequence. Two 4% agar phantoms with 40 and 80 mM NaCl were placed on either head side for calibration[5].

*Manual phantom segmentation:* Three observers manually outlined both phantoms in all participants using JIM (Xinapse systems); the time needed to manually segment the phantoms was about 30 minutes per subject. Additionally, white matter (WM) lesions were marked by an experienced observer from the PD images.

*Automatic phantom segmentation:* OPAL[3] was used to automatically detect the phantoms. The template library was composed of 24 sodium images and the associated manual phantom segmentations from the manual step. In order to increase the size of the library, all the scans were left-right flipped, increasing the template library to 48 samples. For each subject a leave-one-out technique was used, where the manual segmentation for that particular subject was omitted from the library. OPAL was used with the parameters suggested by Ta et al. The time needed for detecting both phantoms was <0.5 seconds.

*Processing:* Probabilistic brain tissue segmentation was performed over the 3DT1 images using GIF[6]. The segmentation masks were registered to the $^{23}$Na TSC maps. A set of symmetric affine registrations[7] were computed and concatenated. Masks were resampled to sodium space with linear interpolation using a point-spread function[8] to preserve mask continuity. The registration steps were: the 3DT1 and pseudo-T1 images (PDw-T2w images[9]) were registered, the transformation between T2w and 1H PD/T2w was calculated, and finally 1H PD-T2w was registered to TSC map.

*Partial volume correction:* With the aim of removing the cerebrospinal fluid (CSF) sodium contribution in the tissues, we used a voxel-wise modified partition-based correction method[10].

*Statistics:* The mean and standard deviation of grey matter (GM), cortical grey matter (CGM), deep grey matter (DGM) and WM $^{23}$Na values were calculated using both manually segmented phantoms and their automatic segmentations. Two-tailed t-tests were used to look for differences between pipelines for each tissue class in controls and patients. In addition, for each method TSC differences between patients and controls were assessed.

## Results and Discussion

The new fully-automatic pipeline obtains non-significantly different means in healthy controls, while significantly higher means in patients as well as a lower standard deviation (both groups), demonstrating it obtains more informative TSC maps (Table 1 and 2). The difference between patients and controls becomes more significant with the new fully automatic pipeline for each tissues class (Table 3). Finally, the new pipeline saves 30 minutes per subject comparing with manual computation time.

## Conclusion

We have introduced a novel fast, robust and reliable technique for segmenting sodium phantoms that allows fully-automatic reconstruction of TSC maps. The new automatic pipeline has shown less variability and hence higher sensitivity to changes in $^{23}$Na concentration. This will enable less user-dependent variation on the results and faster processing of large batches of data.

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## Figures

| Controls N=20 | GM Mean | GM Std | CGM Mean | CGM Std | DGM Mean | DGM Std | WM Mean | WM Std |
|---|---|---|---|---|---|---|---|---|
| Manual | 40.11 | 1.86 | 41.92 | 3.21 | 34.29 | 2.80 | 31.21 | 3.97 |
| Automatic | 40.06 | 1.97 | 41.97 | 3.12 | 34.39 | 2.73 | 31.31 | 3.92 |
| | 0.99, p>0.05 | | 0.99, p>0.05 | | 0.95, p>0.05 | | 0.99, p>0.05 | |

Table 1: Mean and standard deviation sodium concentration in mM per tissue for controls using the different pipelines, last row shows correlation and two-tailed t-test between pipelines

| Patients N=14 | GM Mean | GM Std | CGM Mean | CGM Std | DGM Mean | DGM Std | WM Mean | WM Std |
|---|---|---|---|---|---|---|---|---|
| Manual | 42.64 | 2.60 | 43.33 | 3.68 | 37.16 | 2.31 | 34.81 | 3.32 |
| Automatic | 44.37 | 2.98 | 45.11 | 3.07 | 38.27 | 2.57 | 35.76 | 3.20 |
| | 0.97, p<0.05 | | 0.97, p<0.05 | | 0.92, p<0.05 | | 0.96, p<0.05 | |

Table 2: Mean and standard deviation sodium

concentration in mM per tissue for subjects using the different pipelines, last row shows correlation and two-tailed t-test between pipelines

| | GM | CGM | DGM | WM |
|---|---|---|---|---|
| **Manual** | 0.033 | 0.058 | 0.012 | 0.025 |
| **Automatic** | 0.002 | 0.004 | 0.002 | 0.006 |

Table 3: Two tailed t-test controls vs patients