Age-dependent sodium content in human calf skin measured with sub-millimeter spatial resolution ^{23}Na-MRI at 7.0 T

Peter Linz[1], Davide Santoro[2], Wolfgang Renz[3], Jan Ruff[3], Michael Deimling[3], Dominik N. Müller[4,5], Jens Titze[1,4], Friedrich C Luft[5], and Thoralf Niendorf[2]

[1]Department of Nephrology and Hypertension, University Clinic Erlangen, Erlangen, Germany, [2]Berlin Ultrahigh Field Facility, Max-Delbrueck Center for Molecular Medicine, Berlin, Germany, [3]Siemens Healthcare, Erlangen, Germany, [4]Nikolaus-Fiebiger-Center for Molecular Medicine, University Erlangen-Nuernberg, Erlangen, Germany, [5]Experimental and Clinical Research Center (ECRC), Max-Delbrueck Center for Molecular Medicine, Berlin, Germany

Introduction: Excessive salt (NaCl) intake contributes to hypertension and target-organ damage; however, surprisingly little is known about sodium (Na) disposition in the body. An increase in tissue Na content influences the development of hypertension in animal models [1]. These studies demonstrated that sodium is stored in the extracellular compartments of the skin bound to proteoglycans. Realizing the opportunities of MRI this study is aiming a non-invasive measurement of skin-Na with sub-millimeter in-plane spatial resolution using ^{23}Na-MRI at 7.0 T with the ultimate goal to examine the intra-subject reproducibility and to explore the age dependence of skin Na-concentrations ([Na]) in healthy human volunteers.

Methods: After obtaining informed consent lower legs from nine healthy male volunteers (25 - 68 years) were examined on a 7.0 T whole body system (Magnetom, Siemens Healthcare, Erlangen, Germany) using a home built ^{23}Na-surface-coil with two loop elements of (5 x 6) cm^2 [2]. The coil was positioned in a ^{1}H-birdcage-coil (Siemens Healthcare, Erlangen, Germany) used for anatomical imaging. The posterior section of the lower left leg was positioned onto external agarose standards containing 0, 20, 40 and 60 mmol/L NaCl. Agarose concentration was adjusted to 5% to minimize T_2^* differences between the reference standards and tissue. For the assessment of the intra-subject reproducibility each volunteer was examined five times including independent preparation, positioning and data acquisition. A standard proton localizer was used for anatomical reference. ^{23}Na-MRI was performed using a gradient echo sequence (FA / TE / TR = 90° / 2.3 ms / 135 ms, receiver bandwidth = 280 Hz/pixel, FOV = 128 mm, spatial resolution = (0.9 x 0.9 x 30) mm^3, 32 averages, total acquisition time = 10 min). For normalization of B1$^+$-inhomogeneities of the ^{23}Na-coil a uniform agarose gel containing 40 mmol/L NaCl was B1$^+$-mapped [2]. Skin-[Na] was determined in a linear trend analysis comparing signal intensities derived from skin with signal intensities deduced from agarose standards in the normalized ^{23}Na-images.

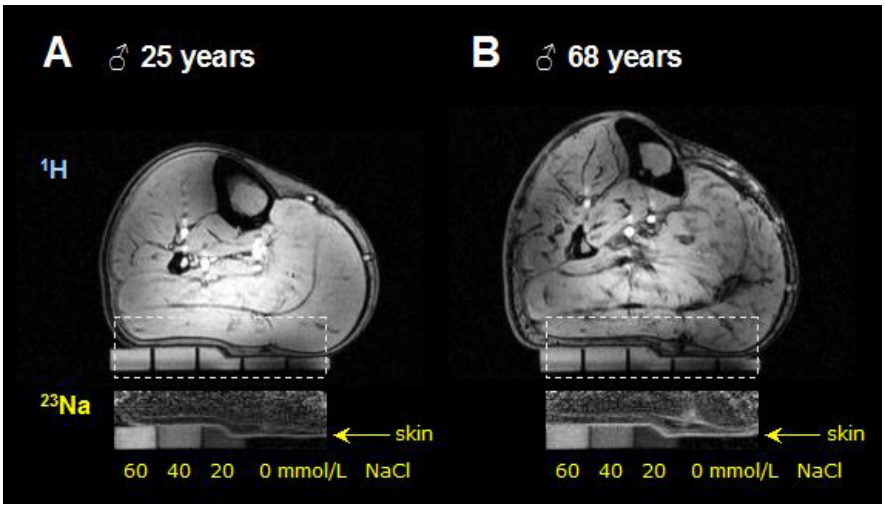

Fig. 1: *Anatomical reference images and ^{23}Na-MRI images of the calf showing the youngest vs. oldest volunteer involved in this 7.0 T MRI study:* ***A)*** *25-year old man with skin-[Na] = 41 ± 2 mmol/L.* ***B)*** *68-year old man with skin-[Na] = 57 ± 3 mmol/L.*

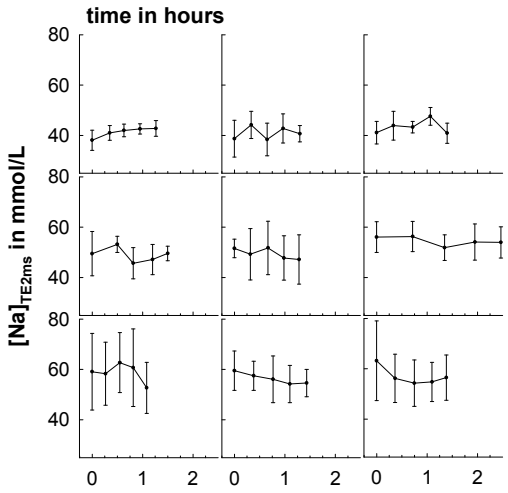

Fig. 2: *Intra-subject reproducibility of skin-[Na] acquisitions in nine individuals of increasing ages (to the right and downwards).*

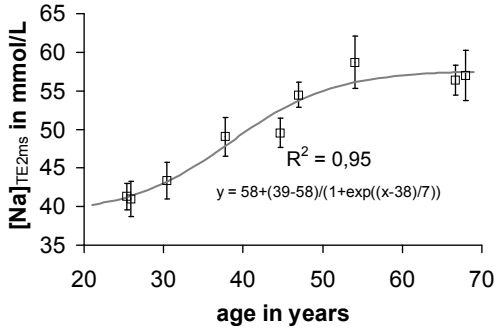

Fig. 3: *Synopsis of [Na]-measurements in nine healthy men of different ages. Each data point represents the mean ± SD of five independent acquisitions in one individual. Skin-[Na] increases with age in a sigmoidal shape. Best correlations were achieved with a Boltzmann-fit.*

Results: Inter-volunteer differences in the Na content of skin were found as demonstrated in Fig. 1. The Na content of a 68-year old man was found to be approximately 1.4-fold higher than the Na content of a 25-year old subject. Fig. 2 surveys the intra-subject variability for all subjects which was found to be below 6 %. The Na skin content is plotted versus age in Fig. 3. This graph shows an increase of skin-[Na] over age which can be well represented by a sigmoidal fit with a maximum slope at 38 ± 5 years.

Conclusion and Discussion: The important findings in our study are that sub-millimeter spatial resolution ^{23}Na-MRI at 7.0 T has utility in measuring compartmentalized Na stores that exceed hitherto forwarded methodologies. Our ^{23}Na-MRI data show the tremendous amount of sodium that can be stored in the thin skin and indicate that [Na] of the human skin is larger than in muscle-tissue or subcutaneous fat. The age-related increase in skin-Na content might be induced by an up-regulation of negatively charged glycosaminoglycans (non-osmotical storage), an increase in tissue vascularisation or lymph vessels (osmotically active Na). We suggest that ^{23}Na-MRI at 7.0 T has utility that could be applied in epidemiological studies to investigate the effects of salt on blood pressure.

References: [1] Titze J and Machnik A. Curr Opin Nephrol Hypertens. 2010 Jul;19(4):385-92. [2] Linz P et al., Proc ISMRM 2011, 2970.