Learning Goals

- introduction to advanced imaging techniques in MR, CT and CBCT
  - basic MRI principles -> Physics of Imaging Techniques

- Goals:
  1. How does the technique work?
  2. What kind of images do we receive?
  3. Where is this applied to?

- Literature is given in the respective lectures
- Slides of the lectures at
  https://www.umm.uni-heidelberg.de/inst/cbtml/lehre/index.html
Reading

- Wetterling et al., Sodium-23 magnetic resonance imaging during and after transient cerebral ischemia: multinuclear stroke protocols for double-tuned 23Na/1H resonator systems. Phys. Med. Biol. 2012(57) 6929
- Konstandin & Schad. 30 years of sodium/X-nuclei magnetic resonance imaging. Magn Reson Mater Phy (2014) 27: 1

Outline

- Motivation
- Challenges of X-Nuclei MRI
- Imaging Techniques of $^{23}$Na
- Applications
Motivation

- Ion fluxes in cells play an important role of cell activity
- Sodium–potassium pump (Na\(^+\)--K\(^+\)-ATPase), which pumps 3 Na\(^+\) ions out of and 2 K\(^+\) ions into the cell.
- Active transport mechanism is one factor to keep the resting membrane potential in cells at about −70 mV

[Diagram of sodium–potassium pump](https://www.slideshare.net/Amirmadhizadeh1/sodium-potassium-pump)

Motivation

- Different ion-specific channels are able to transmit information via electrical signals by gating the flow of ions across the cell membrane.
- Pathological change in concentration can be visualized by X-nuclei MRI.
- Can give additional functional information.

[Diagram of ion channels](https://users.rcn.com/jkimball.ma.ultranet/BiologyPages/W/Welcome.html)
### MR Properties of X-nuclei

<table>
<thead>
<tr>
<th>nucleus</th>
<th>spin $I$</th>
<th>gyromagnetic ratio $\gamma$ [10$^8$ rad s$^{-1}$ T$^{-1}$]</th>
<th>natural abundance of isotope in %</th>
<th>sensitivity $S$ for $B_0 = \text{const.}$ in % (rel. to $^1$H)</th>
<th>MRI:</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^1$H</td>
<td>$1/2$</td>
<td>2.675</td>
<td>99.98</td>
<td>100.00</td>
<td>111 mol</td>
</tr>
<tr>
<td>$^2$H</td>
<td>1</td>
<td>0.410</td>
<td>0.01</td>
<td>$9.60 \times 10^{-1}$</td>
<td></td>
</tr>
<tr>
<td>$^{11}$C</td>
<td>0</td>
<td>-</td>
<td>98.89</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$^{11}$C</td>
<td>$1/2$</td>
<td>0.673</td>
<td>1.11</td>
<td>$1.75 \times 10^{-2}$</td>
<td></td>
</tr>
<tr>
<td>$^{14}$N</td>
<td>1</td>
<td>0.193</td>
<td>99.63</td>
<td>$1.00 \times 10^{-1}$</td>
<td></td>
</tr>
<tr>
<td>$^{16}$O</td>
<td>0</td>
<td>-</td>
<td>99.76</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>$^{17}$O</td>
<td>$5/2$</td>
<td>-0.363</td>
<td>0.04</td>
<td>$1.11 \times 10^{-3}$</td>
<td></td>
</tr>
<tr>
<td>$^{19}$F</td>
<td>$1/2$</td>
<td>2.518</td>
<td>100.00</td>
<td>83.40</td>
<td></td>
</tr>
<tr>
<td>$^{23}$Na</td>
<td>$3/2$</td>
<td>0.708</td>
<td>100.00</td>
<td>9.27</td>
<td>45 mmol</td>
</tr>
<tr>
<td>$^{25}$Mg</td>
<td>$5/2$</td>
<td>-0.164</td>
<td>10.00</td>
<td>$2.68 \times 10^{-2}$</td>
<td></td>
</tr>
<tr>
<td>$^{31}$P</td>
<td>$1/2$</td>
<td>1.084</td>
<td>100.00</td>
<td>6.65</td>
<td></td>
</tr>
<tr>
<td>$^{31}$S</td>
<td>$3/2$</td>
<td>0.205</td>
<td>0.75</td>
<td>$1.70 \times 10^{-3}$</td>
<td></td>
</tr>
</tbody>
</table>

### MR Properties of X-Nuclei – Exp. Sodium

MR properties of X-nuclei

- low in vivo signal 10 000 – 50 000 times lower than \(^1\)H-signal
- short relaxation times
  - brain tissue: \(T_{2f}^* \approx 4\) ms, \(T_{2s}^* \approx 30\) ms, \(T_1 \approx 30\) ms

<table>
<thead>
<tr>
<th></th>
<th>(^{23})Na (11)</th>
<th>(^1)H (1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>relative sensitivity</td>
<td>(9.27 \cdot 10^{-2})</td>
<td>1</td>
</tr>
<tr>
<td>(S \propto c \cdot \gamma^2 \cdot I \cdot (I + 1))</td>
<td>45 (\cdot 10^{-3})</td>
<td>111</td>
</tr>
<tr>
<td>in-vivo concentration [M]</td>
<td>4.59 (\cdot 10^{-5})</td>
<td>1</td>
</tr>
</tbody>
</table>

high SNR-efficiency & short echo times !!

Imaging of \(^{23}\)Na

- broadband transmitter
- dedicated rf coils needed
- single tuned coils vs. double resonant coils
- dual-RF resonator allows for
  - homogeneous transmit \(B_{1}^+\) field
  - highly sensitive receive \(B_{1}^-\) field

Zöllner et al., NMR Biomed 2015
Imaging of $^{23}$Na

- aim to record a proton density weighted image
  - quantification of tissue sodium concentration
- relatively long TRs and UTEs are required to avoid $T_1$ and $T_2^*$ weighting in the images
- need for UTE sequences, radial readouts, rectangular RF pulse
- SNR increased by uniform k-space sampling
- measurement time: twisted projection, density adapted, etc.

<table>
<thead>
<tr>
<th></th>
<th>Cortex</th>
<th>Medulla</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_1$ (ms)</td>
<td>$T_{2mav}/T_{2mauc}$ (ms)</td>
<td>$T_1$ (ms)</td>
</tr>
<tr>
<td>36 ± 2</td>
<td>19 ± 1/19 ± 3</td>
<td>35.4 ± 2.4</td>
</tr>
<tr>
<td>34 (whole kidney)</td>
<td>204/22 (whole kidney)</td>
<td></td>
</tr>
</tbody>
</table>

Zöllner et al., NMR Biomed 2015

$^{23}$Na-Imaging: Radial Readout

- radial projection technique
- nonuniform k-space coverage
  - SNR loss of 25.5 %

$\alpha$

TE

$TE_{\min} \sim 0.4$ ms !!

Lauterbur Nature 1973
**Imaging of $^{23}$Na: Quantification**

- PD weighted images needed
- reference vials + CSF
- estimate $T_1$ and $T_2$ relaxation time
  - $T_{2\text{ref.f}} = 7.15$ msec, $T_{2\text{ref.l}} = 33.7$ msec
  - tissue $T_1$ and $T_2$ relaxation time
  - $T_1 = 34$ ms
  - $T_{2\text{tiss.f}} = 2.2$ msec, $T_{2\text{tiss.l}} = 20.4$ msec

\[
[Na]_{\text{m}} = \frac{S_{\text{m,Na}}}{S_{\text{m,3Na}}} [Na]_{\text{i}}
\]

Correction for $T_1$ effects: 0.6-exp($-\frac{TR}{T_{1\text{m}}}$) + 0.4-exp($-\frac{TE}{T_{2\text{m}}}$)
Correction for $T_2$ effects: 0.6-exp($-\frac{TE}{T_{2\text{m}}}$)

Haneder et al, Radiology 2011
Maril et al, Kidney Int., 2004
Imaging of $^{23}$Na: Quantification

- accurate TSC quantification requires a reliable correction of the RF excitation field and coil sensitivity
- 3% deviation in B1 map $\rightarrow$ 5% error in concentration
- different techniques in $^1$H MRI proposed
  - phase sensitive (PS)
  - double angle method (DAM)

Lommen et al, NMR Biomed 2015
Paschke et al, ESMRMB 2015

Renal Sodium Imaging – Initial Studies in Human

- coronal projection of a 3D $^{23}$Na image of the human abdomen @3T
  - (a) 25-min
  - (b) 12-min
- in-house build quadrature surface coil
- 3D gradient-echo sequence
  - TR/TE 30/1.8 ms, FOV 38 x 38 x 24 cm, and matrix 128x128 x16
Renal Sodium Imaging – Cortico-Medullary Sodium Gradient

Sodium MRI of the Human Kidney at 3 Tesla

Nicoletti Matelli, Yael Rose, Glenn H. Reynolds, Alex Fournier, Long Ng, and Robert E. Loebelkow

normal condition 12h water deprivation

Renal Sodium Imaging – Quantitative Approaches

3D DA-RAD sequence
- TR/TE 120/0.55ms, FA 85°, FOV 320x320 mm
- readout length per spoke was 20 msec, and 8000 projections

Total acquisition time of 16 minutes
- quantification of $^{23}$Na

normal condition water load
Renal Sodium Imaging – Quantitative Approaches

Quantitative and Qualitative
$^{23}$Na MR Imaging of the Human Kidneys at 3 T: Before and after a Water Load

Parameters:
- $^{23}$Na concentration in the renal cortex and medulla before and after water load
- Cortico-medullary sodium concentration gradient

Cortico-medullary sodium concentration gradient:
- Wide inter-individual ranges
- No significant correlations with age, gender, $[^{23}$Na]serum, BMI, GFR, ADC, or $R^2*$ values

Conclusion
- Cortico-medullary sodium concentration gradient
- Wide inter-individual ranges
- No significant correlations with age, gender, $[^{23}$Na]serum, BMI, GFR, ADC, or $R^2*$ values
Renal Sodium Imaging – Studies of Pathophysiologic Processes

- assess post-radiotherapeutic renal changes
  - 56-year-old patient after adrenal stereotactic body radiotherapy
  - cortico-medullary sodium gradient and sodium concentration are decreased in the left kidney


Renal Sodium Imaging – Studies of Pathophysiologic Processes

- central diabetes insipidus
  - intranasal administration of 20 µg desmopressin

Renal Sodium Imaging – Studies of Pathophysiologic Processes

- sodium removal from tissue stores in hemodialysis patients
  - $^{23}$Na-MRI quantitatively detects sodium stored in skin and muscle
  - allows studying sodium storage reduction in ESRD patients

Dahlmann et al, Kidney Int. 2014

Renal Sodium Imaging – Studies of Pathophysiologic Processes

- transplanted kidneys/renal allograft loss
  - Sodium concentration was lower in transplanted kidneys than in native kidneys
    \(153.5 \pm 11.9 \text{ vs. } 192.9 \pm 9.6 \text{ mM}\)
  - Sodium gradient of transplanted kidneys was lower than for native kidneys
    \(8.9 \pm 1.5 \text{ vs. } 10.5 \pm 0.9 \text{ mM/mm}\)

Bain Sodium Imaging – Multiple Sclerosis

- MRI is the most practical and widely applied biomarker to detect signs of pathological change and inflammatory activity.
- Sodium MRI is a sensitive marker of very subtle tissue normalities.
- Recent studies that identified elevated TSC values in chronic lesions.


Bain Sodium Imaging – Stroke

- Final infarction in acute stroke dependent on several factors:
  - Individual vascular collateral flow,
  - Admission glucose levels, hematocrit level and blood pressure,
- The most determining factor though is the time until recanalization and reperfusion is achieved.
- Concept of DWI/PWI mismatch strongly underestimates the amount of still viable tissue.

Neumaier-Probst et al. (2015). International Journal of Stroke, 10(SA100), 56–61
Sodium Cancer Imaging

Breast Cancer

Muscle Skeleton Imaging

Muscle

Healthy

Diabetics

Madelin and Regatte J Magn Reson Imaging. 2013