CEST-MRI
Chemical-Exchange-Saturation-Transfer-MRI

Dorothea Wölk

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Short outlook over the talk:

- Introduction
- Idea and principles of CEST-MRI
- How it works
- Different Applications of CEST-MRI
- Summary and Sources
Why CEST-MRI

- the normal MRI gives $T_1$, $T_2^*$ and proton-density weighted pictures
- contrast-agents often only correspond to the magnetization
- most contrast-agents refer to the $T_2$-relaxation time
- contrast-agents often toxic
- only one contrast per measurement
The Idea of CEST-MRI

CEST-MRI = chemical-exchange-saturation-transfer-MRI

In 2000, Balaban and his colleagues considered a new way to create MRI-contrast:

The Idea: use the chemical shift and the diffusion to water for a measurement through saturating a small pool of protons, and watch the exchange of protons indirectly through the change of the water-signal.

→ new contrast with the normal $T_1$-relaxation time
→ indirect measurement of (metabolic) exchange-processes
To take a CEST-MRI following is needed:

- a pool with protons that will exchange to water
- special RF-Pulse to saturate the protons
- normal $T_1$-water measurement
- mathematical processing of the data
Exchangeable Protons

Not necessary only protons that exchange:
**Exchangeable Protons**

Small pool of exchangeable protons:

- must posses exchangeable protons or molecules
- exchange means to the water-molecule
- the exchangerate $k_{ex}$ must be sufficiently fast
- the chemical shift $\Delta \omega$ have to be big enough $\Delta \omega > k_{ex}$
- no need for dia-/paramagnetic specifications
- can be a externally induced contrast agent
- can create non-toxic contrast agents
The Saturation-Pulse

At the water-fat-shift saturation is used:

Saturate exchangeable protons means dephasing their spin in that way, that the resulting signal vanishes.
The Saturation-Pulse

Saturate exchangeable protons with RF-pulse
→ the protons exchange with water-protons and the water signal gets lower.
→ if $t_{sat}$ longer than the exchange the water-signal gets lowered visibly because the saturation builds up
a) the exchange of the saturated protons

b) decreased water-signal (set to the frequencies)

c) normalized water Spectrum

\[
\frac{S_{sat}}{S_0} \quad \text{(black)}
\]

\[
MTR_{asym} = \frac{S_{sat}(−\Delta \omega)−S_{sat}(+\Delta \omega)}{S_0} \quad \text{(red)}
\]
Many approaches to describe CEST-mathematically;

For the $MTR_{asym}$ one makes following assumption:

- two pools
- chemical-shift $\Delta \omega > k_{ex}$
- exchangerates:
  \[ k_{ex} = k_{sw} + k_{ws} \propto k_{sw} \]
CEST-contrast = proton-transfer-ratio (PTR)

analytical solution:

\[ PTR = \frac{k_{sw} \alpha x_{CA}}{T_{1w} + k_{sw} x_{CA}} \left[ 1 - e^{-\left( T_{1w} + k_{sw} x_{CA} \right) t_{sat}} \right] \]

- \( k_{sw} \) = exchangerate saturation-pool → water
- \( \alpha \) = saturation efficiency
- \( x_{CA} \) = concentration ratio solute-protons/water
- \( T_{1w} \) = \( T_1 \) of water
- \( t_{sat} \) = saturation time
The magnetic fields

From experiments:

\[ B_0 \uparrow \rightarrow T_1 \uparrow \& T_2 \downarrow \]

- \( \Delta \omega \) proportional to strength of the main-field
- higher \( \Delta \omega \) allows agents with faster exchangerate
- long \( T_1 \) means slower recovery from saturation \( \rightarrow \) larger CEST-contrast

Increase \( B_0 \) increases the sensitivity \( \rightarrow \) CEST is suitable for high-field measurements
The Pulse-Sequences

One saturation-pulse before the $T_1$-image sequence

- one long saturation pulse
- repetition of many short pulses

to minimize the recovery of from the saturation $\rightarrow$ shorter pulse and redephasing after every taken slice
Problems while taking CEST-MRI:

**Time**: $t_{\text{sat}} > 2 \text{ sec} \rightarrow$ time for measurement $> 9 \text{ min}$ per saturation (need more for imaging).
For faster measurement

- limited offset sampling
- reduce sampling points in k-space

**Desaturation**: Spins flip back from saturation and signal gets lower.
Solutions may be:

- shorter pulse and rephasing after every taken slice
- reduce taken time for measurement
Different Z-Spectra of molecules

(a) diaCEST
Ammonia

(b) paraCEST

(c) lipoCEST

(d) hyperCEST

- Ammonia (black) and water (white)
- Glycerin ethyl ester
- Liposome filled with agent
- Free Xe (blue), coated Xe (green)
Lysine rich proteins in CEST-MRI

a) MRI-picture

b) CEST-MRI-picture, the signal intensity is color-labeled
CEST-contrast occurs only upon application of saturation-pulses at particular frequencies (characteristic frequencies) so detection of multiple agents simultaneously by their CEST-offset are possible.
Example: Two-frequency-CEST-MRI of Liposomes in Mice

1) CEST-Spec in of the Liposom-agents in vitro
2) CEST-MRI-picture, 24h after infuse in Lymph-node (expected: symmetric dispersion)
3) CEST-Spec after infusion, left-side and right-side
Summary

- CEST-MRI measures indirect exchange of protons/molecules → (indirect) measurement of processes in the tissue
- 'long' measurements possible because of $T_1 \propto x \cdot 100 \text{ ms}$
- 'multicolor'-measurement
- suitable for high-field measurements
- further development with more exchange-mechanism and further contrasts arise
Thank you for your attention!

Sources:

- Chemical Exchange Saturation Transfer: What is in a Name and What Isn’t? - Peter C. M. van Zijl and Nirbhay N. Yadav - Magnetic Resonance in Medicine 65:927-948 (2011)

- Nuts and Bolts of CEST MR imaging - Guanshu Liu, Xiaolei Song, Kannie W.Y.Chan, Michael T. McMahon - NMR Biomed. 2013 July


- CEST: from basic principles to applications, challenges and opportunities - E. Vinogradov, A. Sherry, R. Lenkinski - J Magn Reson. 2013 April 229: 155