Master‘s Program in Medical Physics

Biomedical Engineering I

Blood Flow II

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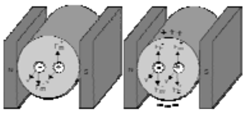
Blood Flow Measurement

- Electromagnetic

$$Q = \frac{\pi r U_{Hall}}{2B}$$



- Ultrasound
  - Time
  - Doppler

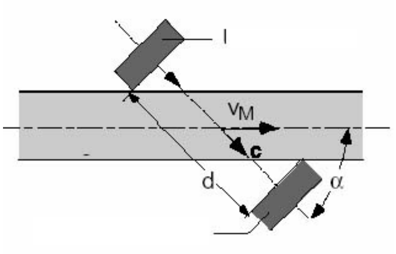
Physical Background

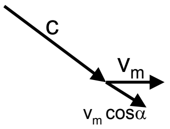
speed of sound: $c = \lambda f$

acoustic impedance: $Z = \rho c$

reflection coefficient: $r = \frac{Z_2 - Z_1}{Z_2 + Z_1}$ $t = 1 - r$

Time Measurement





$$\Delta t = \frac{d}{c - v_m \cos\alpha} - \frac{d}{c + v_m \cos\alpha} = \frac{2 d v_m \cos\alpha}{c^2 - v_m^2 \cos^2\alpha}$$

$$c^2 >> v_m^2 \cos^2\alpha$$

$$\Delta t = \frac{2 d v_m \cos\alpha}{c^2}$$

$$v_m = \frac{c^2 \Delta t}{2 d \cos\alpha}$$

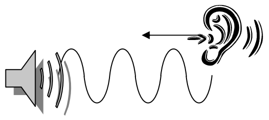
Example

- diameter 1.5 cm
- v_m = 0.1 m/s
- angle of incidence: α=60°
- c= 1.5 km/s
- $\Delta T = (v_m / c^2)(2d \cos \alpha)$
- $\Delta T = 0.1/(2.25\ 10^6)\ 1.5\ 10^{-2}\ s \approx 0.66\ 10^{-9}\ s$ = **0.66 ns**

Time-Voltage-Converter:
Load capacitor within that time and then measure voltage (current-free).
Capacity Q = I * T (T: time)

The Doppler Effect

- physics: sender-receiver move relative to each other
- ultrasound: motion relative to medium
    - sender and receiver at rest: $c = \lambda_s f_s$
    - receiver moves with v_r: $c' = c + v_r = \lambda f_r$



„more peaks per second"
„higher" speed of sound

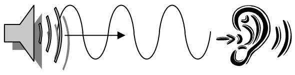
$$f_r = \frac{c'}{\lambda} = \frac{c+v_r}{\lambda} = \frac{c}{\lambda}\left(1+\frac{v_r}{c}\right) = f_s\left(1+\frac{v_r}{c}\right)$$

- sender moves with v_S: wavelength shorted

$$\Delta x = v_s T_s = \frac{v_s}{f_s}$$

(distance the sender moved during one period)

$$\lambda_r = \lambda_s - \Delta x = \lambda_s - \frac{v_s}{f_s}$$



„shorter distance between peaks"

$$f_r = \frac{c}{\lambda_r} = \frac{c}{\lambda_s - \frac{v_s}{f_s}} = \frac{f_s}{1 - \frac{v_s}{c}}$$

Remark

$$\frac{1}{1-x} = 1 + x + \frac{x^2}{2} + \ldots$$

$$f_r = \frac{f_s}{1 - {}^{v_s}\!/_{c}} = \left(1 + \frac{v_s}{c}\right) f_s$$

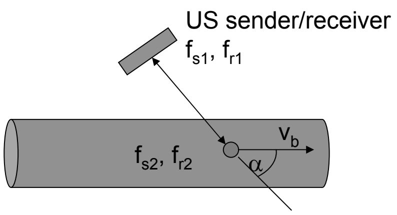
Same result for moving sender and moving receiver

It is the relative velocity that matters!

Blood Velocity Measurement Using US

$$f_{r2} = f_{s1}\left(1 - \frac{v_r}{c}\right) = f_{s1}\left(1 - \frac{v_b}{c}\cos\alpha\right) = f_{s2}$$

$$f_{r1} = f_{s2}\left(1 - \frac{v_s}{c}\right) = f_{s2}\left(1 - \frac{v_b}{c}\cos\alpha\right)$$



$$\Delta f = f_{s1} - f_{r1} = f_{s1} - f_{s2}\left(1 - \frac{v_b}{c}\cos\alpha\right) = f_{s1} - f_{s1}\left(1 - \frac{v_b}{c}\cos\alpha\right)^2$$

$$= f_{s1} - f_{s1}\left(1 - 2\frac{v_b}{c}\cos\alpha + \left(\frac{v_b}{c}\right)^2 \cos^2\alpha\right) = 2\frac{v_b}{c}\cos\alpha \cdot f_{s1}$$

Typical Values

speed of sound: $c = 1500\,m/s;$

velocity of blood: $v = 1\,m/s;$

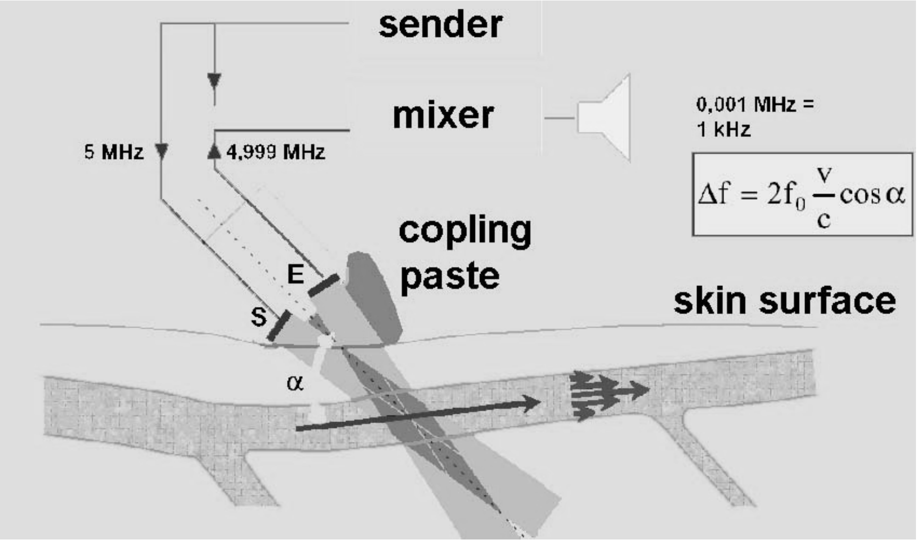
transmitted US-frequency: $f = 5\,MHz;$

$\alpha = 30°;$

Doppler-frequency $\Delta f = \dfrac{2v \cdot \cos\alpha}{c} f = 5.8\,kHz.$

➔ Audio Range

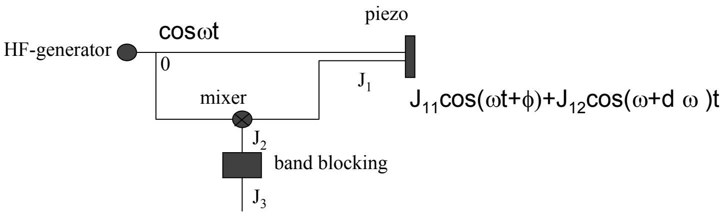
Blood velocity measurement using US



Method

- continuous: CW
  - sender emits all the time
  - 2. crystal as detector; measures spectrum
    - no spatial resolution
    - real-time measurement
- impulse measurement
  - periodically emit pulses
  - time = location
    - choice of repetition frequency relevant

Continuous Wave (CW) - US



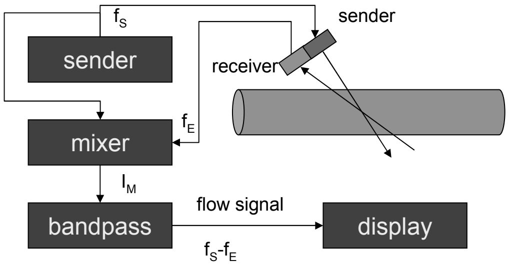
$$J_2 = J_1 \cos \omega t = J_{11} \cos \omega t \cdot \cos(\omega t + \phi) + J_{12} \cos \omega t \cos\left(\omega t + \Delta \omega t\right)$$

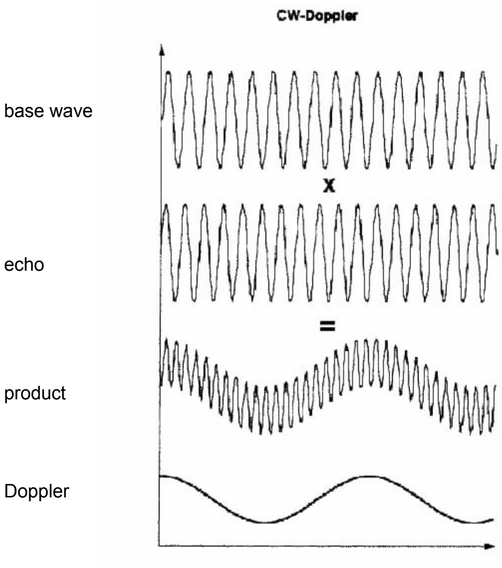
$$= J_{11} \frac{1}{2}\left[\cos(\phi) + \cos(2\omega t + \phi)\right] + J_{12} \frac{1}{2}\left[\cos(\Delta \omega t) + \cos(2\omega t + \Delta \omega t)\right]$$

$$J_3 = J_{12} \frac{1}{2} \cos(\Delta \omega t)$$ after band blocking about 2ω

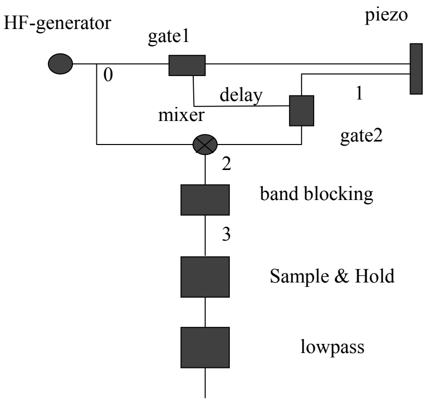
Used Transformation: $\cos(x)\cos(y) = \frac{1}{2}\left[\cos(x-y) + \cos(x+y)\right]$

Continuous Wave (CW) - US





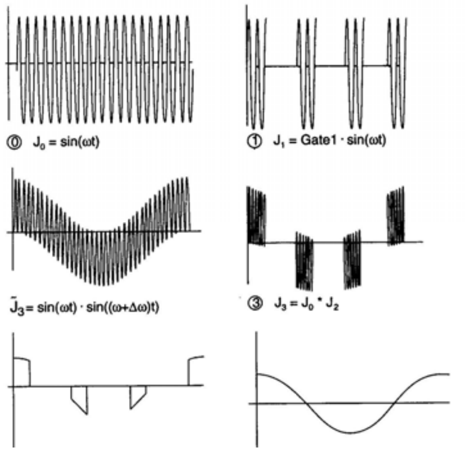
Pulse Wave (PW) - US



gate 1 = ~ gate 2

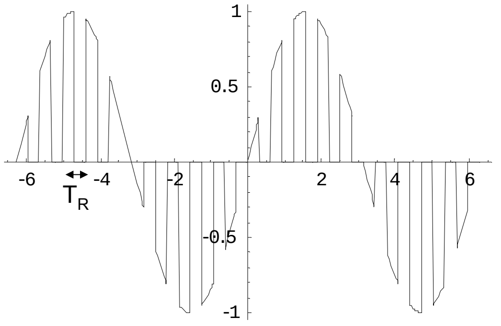
$$J_3{}^* = \cos\omega t\cos(\omega+\Delta\omega)t = \frac{1}{2}\cos(\Delta\omega t)+\frac{1}{2}\cos(2\omega t+\Delta\omega t)$$

Pulse Wave (PW) - US



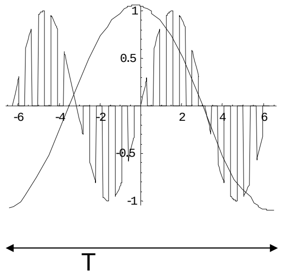
Resolution

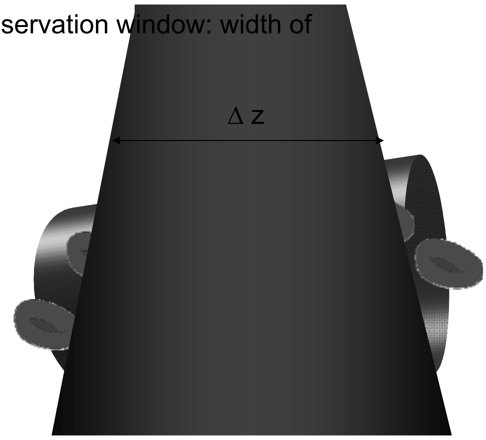
- **<u>Resolution:</u>**
- $T_R = 1/f_R$ impulse repetition time: maximal frequency detectable
- from Doppler: $f_D=(2v/c)\ f_s$
- $f_s = c/\lambda$, $f_D = 2\ v/\lambda$
- **1: $f_D = 2\ v_z/\lambda$**
- **2: sampling theorem: $f_D < f_R/2$**
- from 1 and 2: $v_z < f_R\ \lambda\ /4$: maximally detectable velocity
- $f_R = c/2z$ (depth of tissue, both directions: from source to reflector and back)
- $v_z < \lambda\ c/8z$: as function of tissue depth



Frequency Resolution

- **frequency resolution: Δf_D:**
- system measurement time $T = N\ T_R$
- $\Delta f_D = 1/T$: minimal detectable frequency of system
- T< time the scatterer remains in the observation window: width of the sound ray Δz
- $T < \Delta z/v \rightarrow 1/\Delta f_D < \Delta z/v \rightarrow \Delta f_D > v/\Delta z$
- from (1): $\Delta f_D = 2\ \Delta v/\lambda \rightarrow \Delta v\ \Delta z > \lambda v/2$



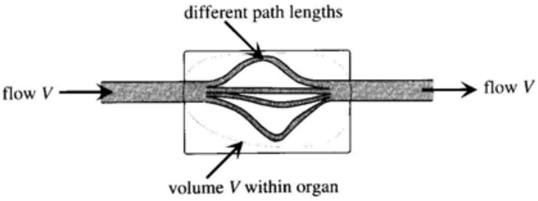


Cardiac Output

- cardiac output = ejected blood volume /time
  - one of the most relevant parameters in intensive medicine/pacemakers
    - evaluation of cardiovascular system

Indicator Dilution Technique

- insert indicator (dye) in vein
- detect indicator concentration in artery
- model:



Dilution Techniques

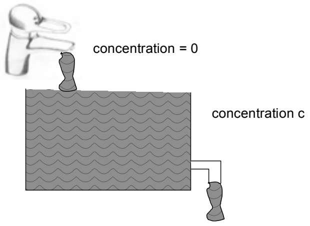
flow in with concentration 0

flow out with concentration c

➡

$$dm = -cdV = -cAvdt = -cQdt$$

$$c = \frac{m - dm}{V}$$



$$c = \frac{m}{V}$$

$$\Rightarrow \quad \frac{dc}{dt} = -\frac{dm}{Vdt} = -c\frac{Q}{V}$$

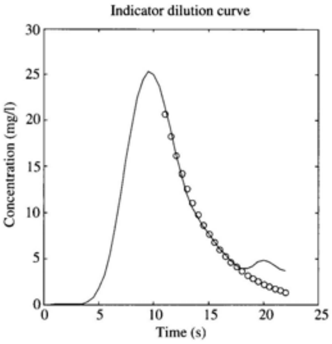
$$\Leftrightarrow \quad \frac{dc}{c} = -\frac{Q}{V}dt$$

$$\Rightarrow \quad \ln c = -\frac{Q}{V}t + const$$

$$c(t) = c_{\max} e^{-\frac{Q}{V}t}$$

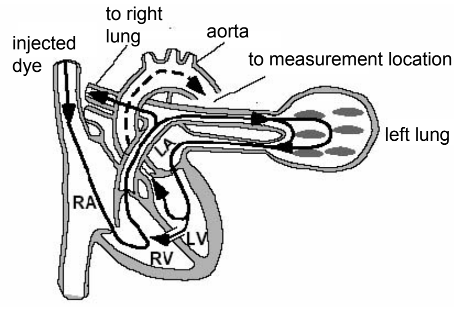
Bolus Injection

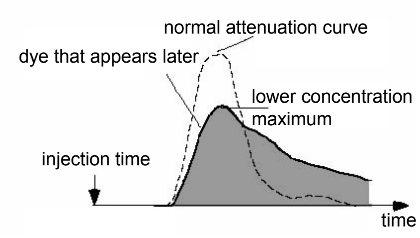
Contained blood: $V = Q \cdot \bar{t}$ …mean transit time



$$\bar{t} = \frac{\int_0^\infty t \cdot c(t)dt}{\int_0^\infty c(t)dt}$$

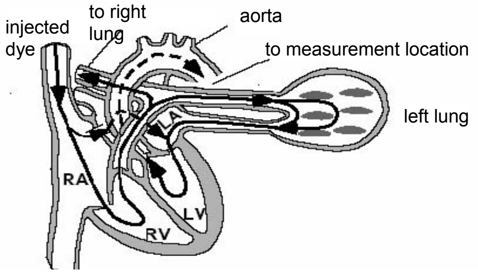
Left-Right-Shunt (*Ventricular Septal Defect*)

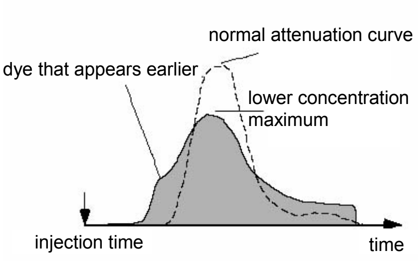




backflow: less output per time
= elongated curve

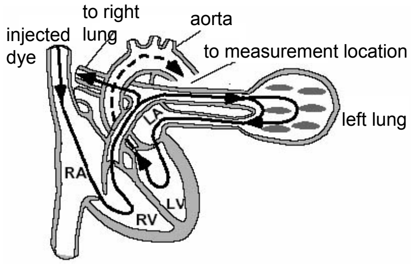
Right-Left-Shunt (*Atrial Septal Defect*)

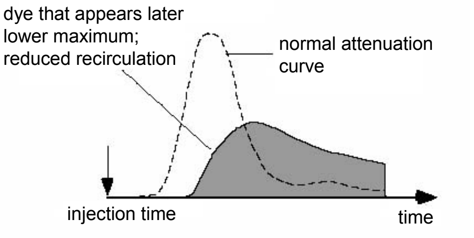




early inflow: earlier parts of curve

Cardiac Insufficiency



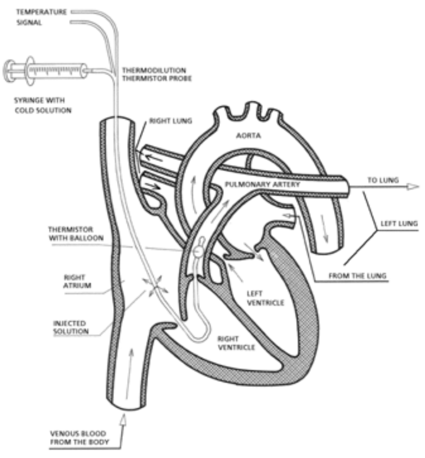


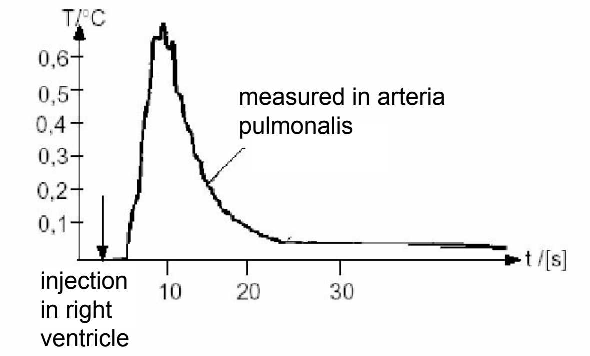
less output:
smaller slope of curve

Indicator Attenuation Measurement

- Inject dye into the venous bloodstream close to the heart through a catheter.
- Arterial blood is drawn off through another catheter and the dye concentration is measured.
- Indocyanine green (ICG) is most commonly used
    - low toxicity
    - does not persist for long in bloodstream
    - maximum optical absorption at 805 nm
    - at this wavelength, the absorption of haemoglobin is independent of oxygenation, so that absorption is only a function of concentration.

Thermal Dilution Method





measured in arteria pulmonalis

injection in right ventricle

Thermal Dilution Method

Heat gained by the indicator:

$$\Delta W_i = c_i \cdot m \cdot \Delta T$$
$$= c_i \cdot V_i \cdot \rho_i \cdot (T_{final} - T_i)$$

Heat loss from the blood:

$$\Delta W_B = c_B \cdot V_B \cdot \rho_B \cdot (T_B - T_{final})$$

$$V_B = Q \cdot t - V_i$$

no loss off heat:

$$\Delta W_i = c_i \cdot V_i \rho_i \cdot \left(T_{final} - T_i\right) = c_B \cdot \left(Qt - V_i\right) \cdot \rho_B \cdot \left(T_B - T_{final}\right) = \Delta W_B$$

$$Q = \frac{V_i}{t}\left[1 + \frac{c_i \cdot \rho_i \cdot (T_{final} - T_i)}{c_B \cdot \rho_B \cdot \left(T_B - T_{final}\right)}\right] \approx \frac{V_i}{t}\left[1 + \frac{(T_{final} - T_i)}{\left(T_B - T_{final}\right)}\right]$$

Repetition

- Definition and properties of Fourier Transform and its application to easy examples.
- Fourier Transform of Differential and Integral Equations.
- electrical measurement values
    - Voltage, current, power, different impedance: Ohm, Capacitor, Inductivity. Kirchhoff rules.
- Fluid dynamics: Pressure, Flow, Reynolds Number, Bernoulli-Equation, Flow in tubes (vessels).
- Blood Pressure Measurements: invasive and non invasive.
    - Influence of catheter, compliance and air bubbles
- Blood Flow Measurements: invasive and non invasive.

Bruker Biospec® 94/20 USR: 9.4 Tesla

**Cooperation Faculty of Medicine Mannheim &
Central Institute of Mental Health (ZI)**

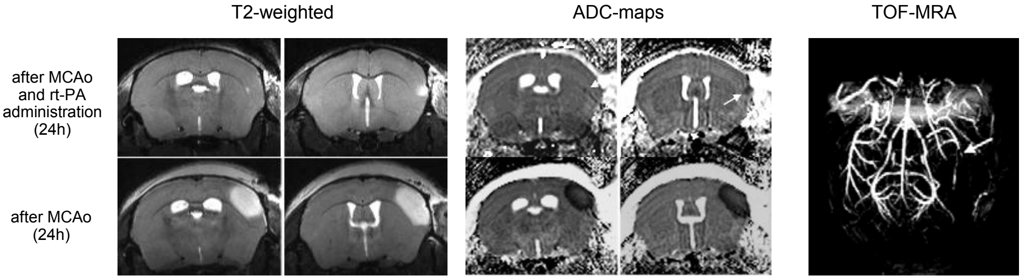
field strength: 9.4 Tesla

bore: 21cm (with gradient insert: 11cm)

Mouse Stroke: ^{1}H CryoCoil MRI

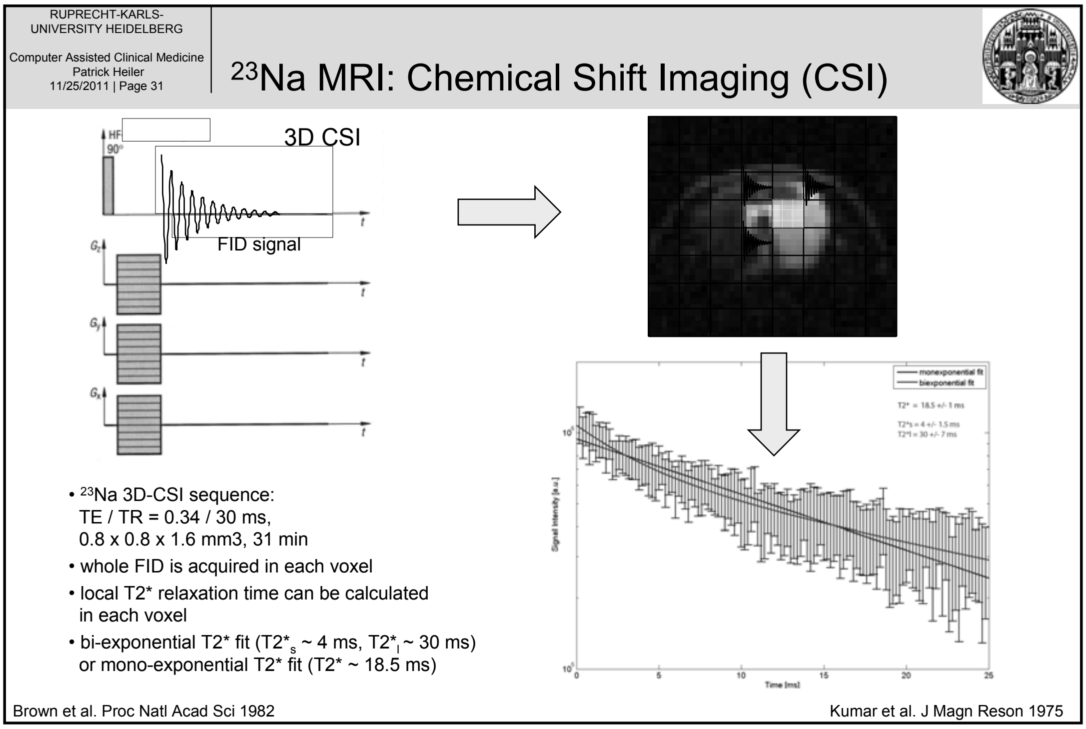
stroke model mouse:

- ten male *C57 black/6J* mice (Charles River, Germany), weight 20 to 25 g, were used throughout the study.
- MCA was exposed by a small craniotomy (n = 5). A micropipette was introduced into the lumen of the MCA and 2 ml of purified murine alpha-thrombin were injected to induce the formation of a clot.
- in a second group (n = 5), additionally rt-PA (10 mg/ml; Actilyse) was intravenously injected into the tail vein 40 min after MCAo to induce thrombolysis. 10% of tr-PA were administered as a bolus and 90% by perfusion during 40 min.



Orset et al. Stroke 2007

Heiler et al. ISMRM 2010



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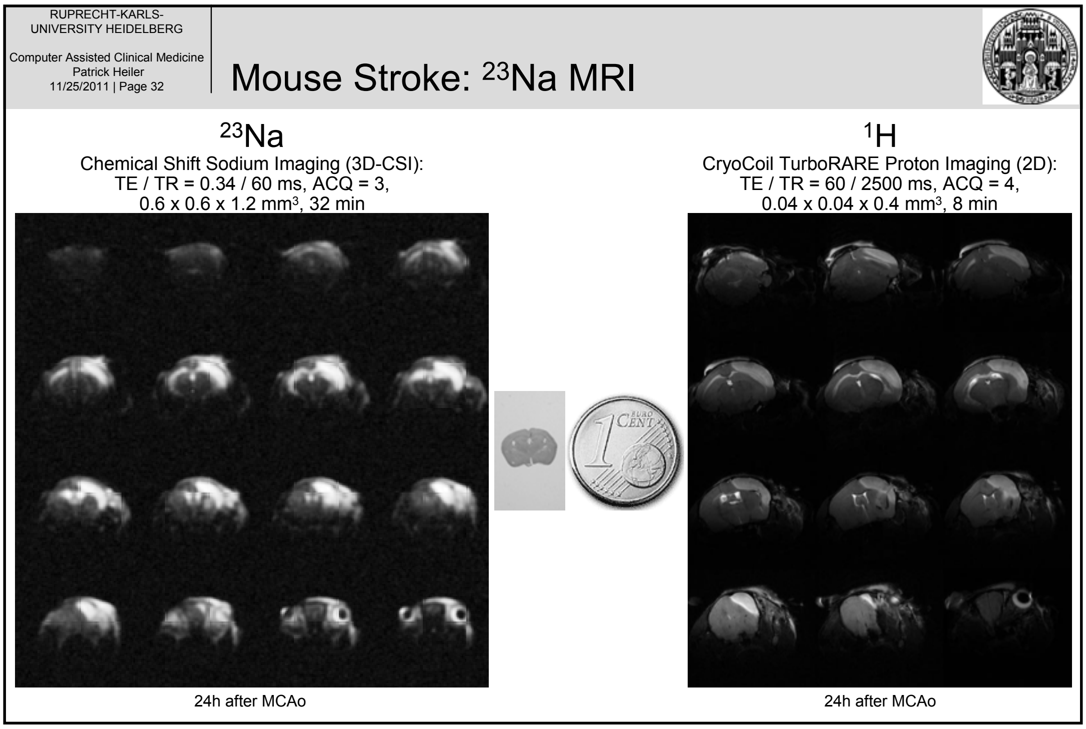
^{23}Na MRI: Chemical Shift Imaging (CSI)

- ^{23}Na 3D-CSI sequence:
  TE / TR = 0.34 / 30 ms,
  0.8 x 0.8 x 1.6 mm3, 31 min
- whole FID is acquired in each voxel
- local T2* relaxation time can be calculated in each voxel
- bi-exponential T2* fit ($T2^*_s$ ~ 4 ms, $T2^*_l$ ~ 30 ms) or mono-exponential T2* fit (T2* ~ 18.5 ms)

Brown et al. Proc Natl Acad Sci 1982

Kumar et al. J Magn Reson 1975



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Patrick Heiler
11/25/2011 | Page 32

Mouse Stroke: ^{23}Na MRI

^{23}Na

Chemical Shift Sodium Imaging (3D-CSI):
TE / TR = 0.34 / 60 ms, ACQ = 3,
0.6 x 0.6 x 1.2 mm^3, 32 min

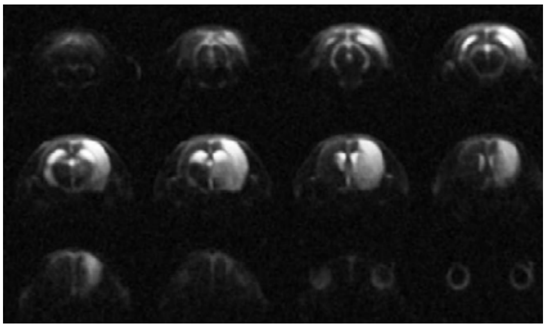
^{1}H

CryoCoil TurboRARE Proton Imaging (2D):
TE / TR = 60 / 2500 ms, ACQ = 4,
0.04 x 0.04 x 0.4 mm^3, 8 min

24h after MCAo

24h after MCAo

Rat Stroke: ^{23}Na 3D-CSI at 9.4 Tesla

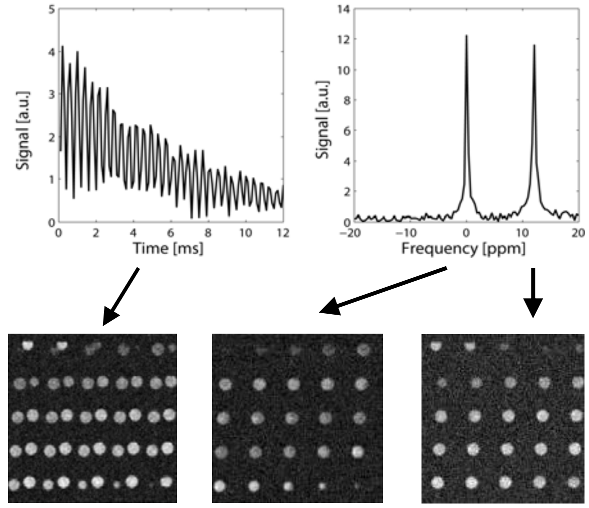


- MCAo (24 hours) of 300 g adult rat
- inductively-coupled ^{23}Na surface coil (anatomically-shaped)
- ^{23}Na 3D-CSI sequence: TE / TR = 0.34 / 40 ms, 3 averages, 0.9 x 0.9 x 1.8 mm^{3}, 19 min

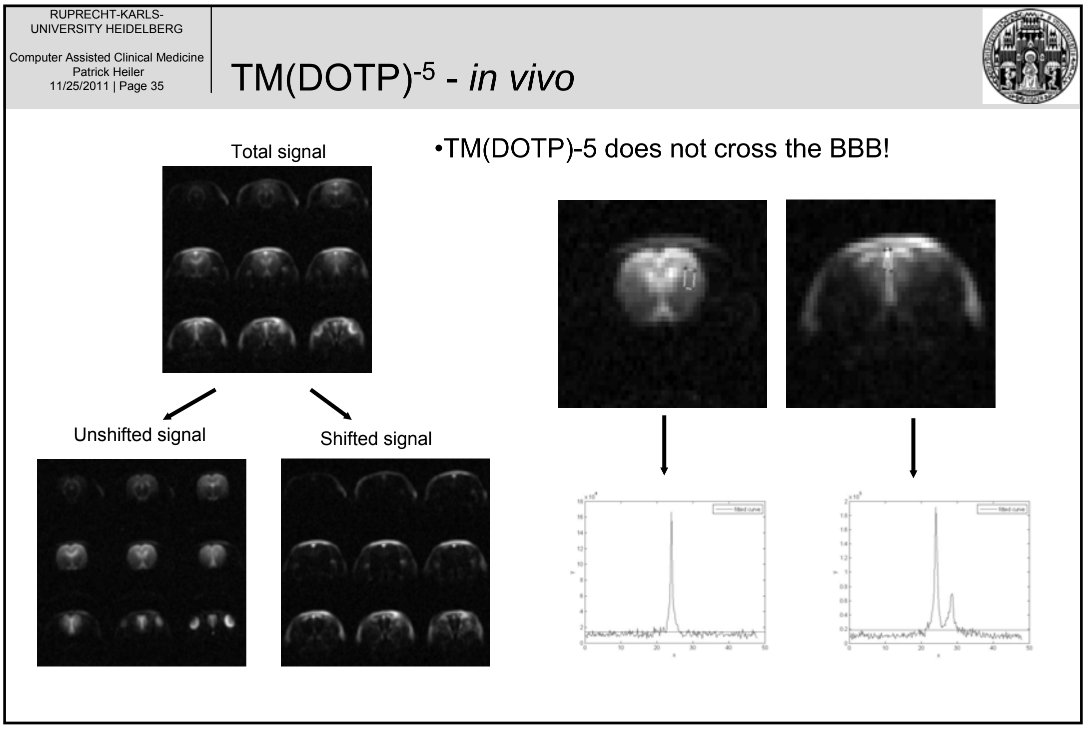
ROI	Stroke ROI						Contralateral ROI					
	T2*	Δ	M0	Δ	const	Δ	T2*	Δ	M0	Δ	const	Δ
1	10,2	0,3	7	0,1	0	0,1	7,2	1,5	1,9	0,1	0,4	0,2
2	10,8	1,1	7,8	0,3	0	0,7	6,1	1,2	1,6	0,1	0,4	0,2
3	7,6	0,5	3,8	0,1	0	0,2	5,2	1,2	0,8	0,1	0,5	0,1
4	8,1	0,4	5,6	0,1	0	0,2	5,1	0,8	0,9	0,1	0,4	0,1
5	6,8	0,3	4,8	0,1	0	0,1	5,4	0,7	0,8	0,1	0,5	0,1

TM(DOTP)$^{-5}$ Phantom Measurement

- TM(DOTP)$^{-5}$ shifts the resonance frequency of neighboring sodium ions!



Phantom
- two vials filled with saline solution (0.9 %)
- left vial was additionally doped with 10 mM TM(DOTP)$^{-5}$.



TM(DOTP)$^{-5}$ - *in vivo*

Total signal

Unshifted signal

Shifted signal

- TM(DOTP)-5 does not cross the BBB!