ULTRASONIC ASSESSMENT OF PERFUSION CONDITIONS IN THE BRAIN AND IN THE KIDNEY

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Introduction

Contrast Agent Imaging Modes

Non-Destructive Modes

- detection of non-linear scattering
- advantages: high frame rate
- disadvantages: low SNR
  - high blood / tissue contrast → low transmit power (tissue harmonics)
  - high bandwidth → reduced transducer sensitivity
- possible solution
  - specialized transducers
  - longer pulse sequences
- applications
  - organs affected by motion artifacts
  - low – moderate attenuation / depth

Destructive Modes

- destruction of microbubbles by ultrasound
- advantages: high SNR & contrast
  - transmit and receive bandwidth match transducer bandwidth
  - destruction → high transmit power, pulse sequences
  - time-variance analysis / "wall filters" → high blood / tissue contrast
- disadvantages: low frame rate, tradeoff between time resolution, spatial resolution, SNR
  - long pulses → effective destruction, poor resolution
  - long sequences → high SNR, increased sensitivity to motion
  - ECG triggering → less motion artifacts, increased acquisition time
- possible solution
  - complex pulse sequences, e. g. destruction + imaging pulses (time-multiplex or frequency multiplex)
- applications
  - high attenuation → brain

Perfusion Imaging

Perfusion Imaging in the Brain

Key Issue

- high attenuation of bone window
  - destructive imaging mode
  - "fragile" contrast agent: Levovist®
  - bolus injection, qualitative evaluation of time-intensity curves

In Vivo Experiments

- time-variance imaging (TVI), 2.5 MHz phased array, Siemens Sonoline® Elegra
- acquisition time: 1 – 2 min, 0.5 fps
- model-based evaluation of time-intensity curves (TICs)

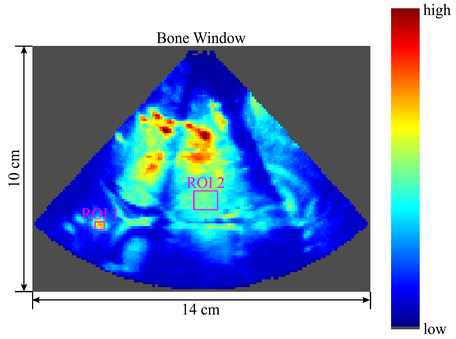

Fig. 1: Peak intensity image of a human brain.

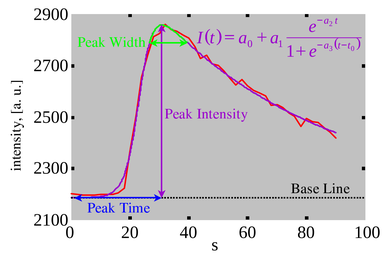

Fig. 2: Least square fit of the model function to the measured TIC.

- model (Fig. 2.) considers characteristics of typical TICs
  - offset: a_0
  - step-function: $\frac{1}{1+e^{-a_3(t-t_0)}}$
    slope: a_3, position in time: t_0
  - exponential fall-off $e^{-a_2 t}$
  - scaling factor: a_1

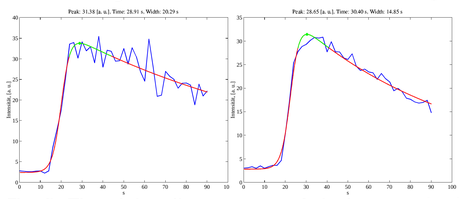

Fig. 3: Time-intensity curves. Anterior cerebral artery (left), perfused brain tissue (right). In the artery, the maximum intensity is reached earlier and the peak width is wider.

Results

- evaluation of TICs for 1 mm x 1 mm ROIs → parameter images (Fig. 1)
- model-based parameter extraction facilitates interpretation of TICs (Fig. 3)
- superior performance of destructive imaging techniques in the brain were confirmed in experiments with healthy volunteers (data for Levovist®)

Perfusion Imaging in Other Selected Organs (Kidney, Liver)

Key Issue

- motion artifacts
  - high frame rate → non-destructive imaging mode
  - short acquisition time → fast method for perfusion imaging required

Fast Method for Perfusion Imaging

- "phase inversion"-based harmonic imaging technique
- frames rates of 1 – 20 fps
- infusion of the contrast agent or acquisition during the peak of a bolus
- acquisition of typically 10 – 40 images

Model for the Concentration as a Function of Insonations

- at the very first acquisition, the concentration of microbubbles in a sample volume is given by

$$c(1) = c_0,\ c_0 = c_{\text{blood pool}} \frac{V_{\text{blood in sample}}}{V_{\text{sample}}}$$

- some destruction of microbubbles will occur due to the insonation
- compared to the time interval between frames, destruction is instantaneous
- due to perfusion, blood is exchanged (wash-out / wash-in) between frames following an exponential function so that

$$\lim_{\Delta t \to \infty} c(n+1) = c_0$$

- change in concentration from insonation to insonation

$$c(n+1) = c(n) \cdot e^{-d} \cdot e^{-p \cdot \Delta t}_{\text{wash-out}} + c_0 \cdot (1 - e^{-p \cdot \Delta t})_{\text{wash-in}},$$

$$n = \text{number of insonation},\ \Delta t = \frac{1}{\text{frame rate}},$$

$$d = \text{destruction coefficient},$$

$$p = \text{perfusion coefficient}$$

- closed form solution

$$c(n) = c_0 \cdot \left(x^{n-1} + y \cdot \frac{x^{n-1} - 1}{x - 1} \right),$$

$$x = e^{-d} \cdot e^{-p \cdot \Delta t},$$

$$y = (1 - e^{-p \cdot \Delta t})$$

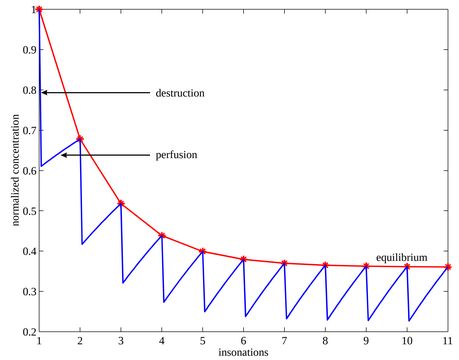

Fig. 4: Model for the concentration of microbubbles in a sample volume as a function of insonations (blue line). Red stars indicate the concentration observed in the ultrasound images. The "measured" TIC (red line) corresponds to the above equation.

Using the Model

- preconditions
  - image intensity must be converted to a parameter that is proportional to the concentration of microbubbles
  - the assumption that destruction is instantaneous may not apply to all contrast agents
- least square fit of the model to the measured curve yields c_0, d, p

In Vivo Experiments / Results

Fig. 5: Images of a rabbit kidney. Ensemble Contrast Imaging (ECI, "phase inversion"). Images 1, 2, 4, 8. Infusion of Imagent®.

We scanned a normal kidney of an anaesthetized rabbit. Imagent® was infused to keep the concentration of microbubbles in the blood pool constant. A series of 16 images was then acquired at a frame rate of 5 fps.

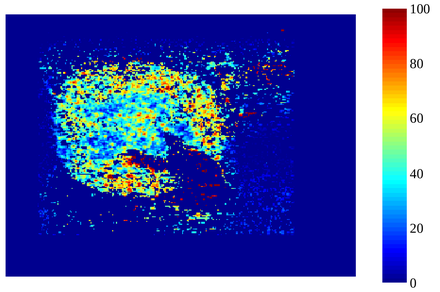

Fig. 6: Parameter image of c_0 (arbitrary concentration units). c_0 is a measure of blood volume per sample volume. Inside the renal vein and the renal artery, the concentration of microbubbles does not change. Therefore, c_0 cannot be calculated.

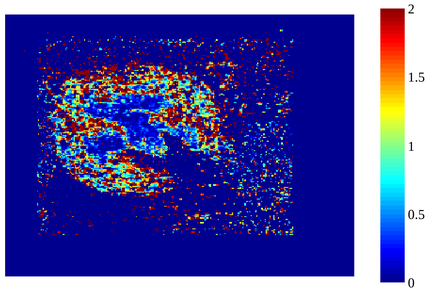

Fig. 7: Parameter image of p, i. e. a measure of perfusion. As explained above, also p cannot be calculated inside bigger vessels.

Conlusions

- suitable combinations of
  - imaging modes,
  - contrast agents,
  - contrast administration methods,
  - post processing techniques

  enable the assessment of perfusion
  - in the brain,
  - in the kidney and other organs
- the proposed techniques offer qualitative perfusion images
- clinical trial will be necessary (in progress for "brain perfusion")

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