Investigation of Inertial Cavitation of Sonosensitive and Biocompatible Nanoparticles in Flow - Through Tissue-Mimicking Phantoms Employing Focused Ultrasound

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Motivation – Efficient chemotherapy

Systemic chemotherapy

- Small amount of cytostatic drug (CD) can be accumulated inside tumour
- Dosage is limited due to side effects

→ Drug-Delivery concepts
- Reduce side effects
- Increase dosage of CD inside the tumorous tissue

I. Development of sonosensitive and biocompatible nanoparticles
   - Carrier of the CD
   - Initiation of drug release via focused ultrasound → Inertial Cavitation

II. Investigation of suited ultrasound signals
   - Consideration of diagnostic limit value (Mechanical Index $MI$)
     \[
     MI = \frac{\hat{p}_{\text{neg}}}{\text{MPa}} \leq 1.9 \sqrt{\frac{f}{\text{MHz}}}
     \]
   - Setup for measurements
Motivation – Drug release

Sphere: Polymer + CD
~110 nm
Capsule: Polymer + Oil + CD
~200 – 250 nm

Drug release - Cavitation

1. p
2. Longitudinal wave – Bubble dynamics
   \[|p_{\text{neg}}| < p_{\text{Tr}}\]
3. Bubble collapse - Implosion
   Fluid jet close to surface of nanocarrier
   Drug release and destruction of nanocarrier

FUS transducer
nano-capsules
tumour
blood vessel (diameter \(\phi d_C\))
Motivation – Challenge

Blood vessels
\( \phi d_C = 0.6 \text{ mm} - 2.4 \text{ mm} \)

Focal zone / Focal volume \( V_F(f) \)

Sound field parameters

- Sound pressure \( \hat{p}_{PRFP \text{max}} = 1.85 \text{ MPa} \)
- Sound intensity \( I_{\text{max}} \approx 1.23 \frac{W}{m^2} \)
- Focal diameter \( \phi d_F - 1 \text{dB} \approx 1 \text{ mm} \)
Experimental – PVA-Phantom

3D-View

Section A-A

Dimensions

- $h_p = 100\,\text{mm}$
- $h_{ps} = 50\,\text{mm}$
- $w_p = 61 - 63\,\text{mm}$
- $\phi d_c = 1 - 3\,\text{mm}$

Sound impedance

- $Z_{\text{PVA}} \approx 1.60 - 1.65 \cdot 10^6 \text{kgm}^{-2}\text{s}^{-1}$
- $Z_{\text{blood}} \approx 1.68 \cdot 10^6 \text{kgm}^{-2}\text{s}^{-1}$
- $Z_{\text{muscle}} \approx 1.65 \cdot 10^6 \text{kgm}^{-2}\text{s}^{-1}$
Experimental – Setup

Computer

Transmitter unit

Receiver unit

Water basin

PVA - Phantom

Temperature controller unit

Beaker Magnet stirrer

Multifunction- I/O device

Collector

Peristaltic pump
Experimental - Settings

Ultrasound signal
- Burst signal \( m \)
- \( f = 550 - 950 \) kHz
- \( \hat{p}_{PRFP} (MI = 1.4; f) \approx 1.04 - 1.36 \) MPa
- \( T_B = 0.6 \) ms
- \( T_P = 2 \) s
- \( m = 1, \ldots, M \)
- \( M = 50 \)

Additional parameters
- Water temperature \( T = 30 \) °C
- Flow velocity \( v_f(\varnothing d_C = 1 \text{ mm}) = 50 \text{ mm/s} \)

Sine burst
- \( u_s(t) \)

Cavitation → Noise

Broadband signal \( u_{Bm}(t) \)
- \( U_m(i) \)

\[
S_{rm} = \sqrt{\sum_{i=i_S}^{i_E} U_m(i)^2 / B}
\]

\[
S_{RM} = \frac{1}{M} \sum_{m=1}^{M} S_{rm}
\]
Results – Nanocapsules; $\phi d_C = 1$ mm; $MI = 1.4$
Results – Nanocapsules – Inertial cavitation

Inertial cavitation is a necessary effect for drug release

Indicator: Implosion of bubbles during positive pressure phase (PPP) → Noise energy in PPP > Noise energy in NPP

1. Determine $t_{IC}$
2. Model and shift signal $u_M(t)$
3. Calculate energy $E_{pos}$ & $E_{neg}$ of $u_{Bm}(t)$ in pressure phases

\[ E_{PPP, NPP}(MI) = \sum_{m=1}^{M} \int_{t_{IC}}^{t_{IC}+T_B} |u_{Bm}(t)|^2 dt \]
### Results – Nanocapsules – Inertial cavitation

IC vanishes with an increasing frequency as well as an increasing $MI$ (pressure)

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$E_{PPP} > E_{NPP}$
## Results – Nanocapsules – Inertial cavitation

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IC vanishes with an increasing frequency as well as an increasing MI (pressure)

$E_{PPP} > E_{NPP}$
Conclusion

- Investigation of IC of the nanocapsules under realistic conditions
- By calculating the voltage spectral density, the focal volume should be considered
- Calculation of the energy of the noise signal gives a hint, if cavitation is either stable or inertial
Outlook

- PVA-Phantom employing a more complex vascularisation
- Coupling unit to investigate clinical application
Thank you for your attention

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