Modeling of the Impact of Blood Vessel Flow on the Temperature Distribution during Focused Ultrasound Treatments

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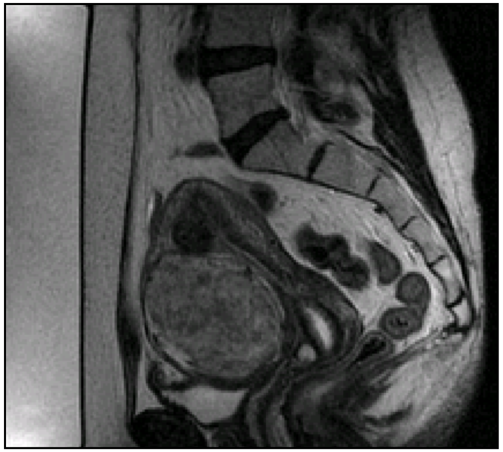
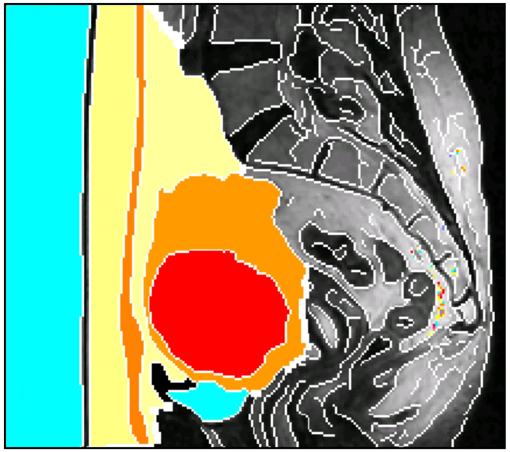
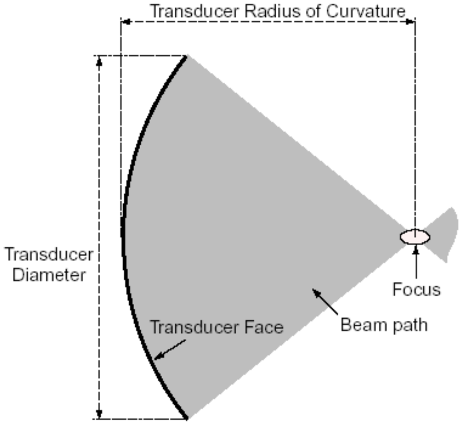
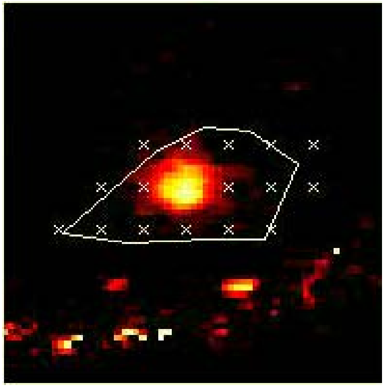
INTRODUCTION

- Hyperthermia (local temperature elevation) has been investigated for the treatment of many kinds of cancer for several years
- Clinical trials have shown that the temperature distributions reached are highly inhomogeneous and it is very difficult to reach the temperature goals required for a successful outcome
- Most beneficial contribution of hyperthermia: enhancing the effectiveness of other treatment modalities such as radiotherapy or chemotherapy
- To overcome the unsatisfactory results caused by technical and temperature control-problems a new generation of focused ultrasound systems have been built for MRI guidance and thermometry

MRI guided Focused Ultrasound Systems

- approved by the Food and Drug Administration for thermal ablation of uterine fibroids (benign tumors of uterus)
- under clinical investigation for ablation of brain, breast, liver tumors palliative of pain caused by bone metastasis
- in preclinical studies investigated to facilitate local drug delivery, control of gene therapy, blood brain barrier disruption



MOTIVATION

- Development of a focused ultrasound treatment planning that models
  (i) power deposition and acoustic energy absorption by the various tissues exposed to focused ultrasound
  (ii) the resulting temperature and thermal dose distributions in the treated volume

- Blood flow is the main factor which determines temperature distribution in tissues

- The bioheat transfer model developed by Lagendijk and co-workers which takes into account discrete blood vessels is employed in the simulations

- Contrary to the more commonly used Pennes bioheat equation, Lagendijk's model can predict more correctly the overall temperature in-homogeneity observed in clinical practice

MATHEMATICAL MODEL

- Transient heat equation solved in the vessel domain

$$\rho_b c_{pb} \frac{\partial T}{\partial t} + \rho_b c_{pb} w \frac{\partial T}{\partial z} + \nabla \cdot \left(k_b \nabla T \right) = P_{FUS}$$

ρ_b = 1060 kg/m^3 density of blood

c_{pb}= *3840* JKg^{-1}K^{-1} specific heat

k_b = 0.6 W m^{-1} K^{-1} thermal conductivity

P_{FUS} focused ultrasound source (density power distribution)

w = axial blood velocity

$$w = 2V_m \left(1 - \frac{r^2}{R^2} \right)$$

V_m mean blood velocity
R vessel radius
r radial coordinate

- Blood incoming temperature: 37 ^{0}C
- Convective flux is assumed at the vessel exit

MATHEMATICAL MODEL

- Transient heat equation solved in the tissue domain

$$\rho_t c_{pt} \frac{\partial T}{\partial t} + \nabla \cdot \left(k_{eff} \nabla T\right) = P_{FUS}$$

ρ_b = 1000 kg/m^3 density of tissue

c_{pb}= *4000* JKg^{-1}K^{-1} specific heat

P_{FUS} focused ultrasound source

k_{eff} = 1.8 W m^{-1} K^{-1} effective thermal conductivity of tissue

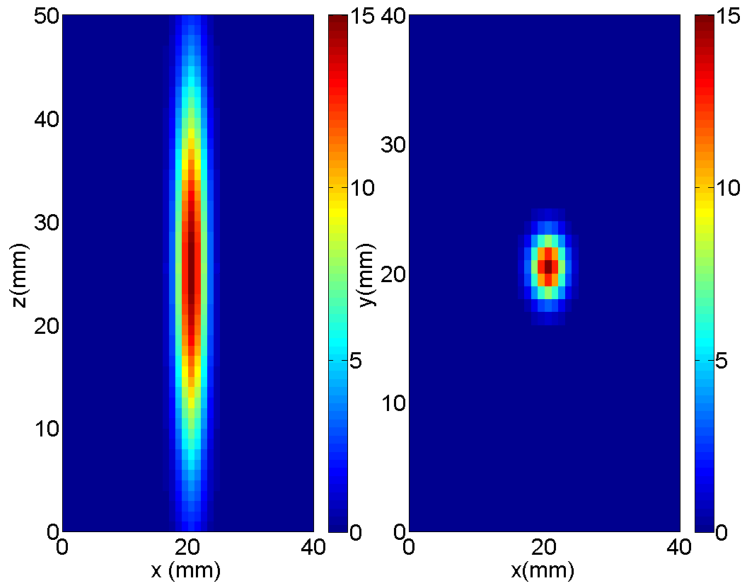
- Fixed heat transfer coefficient simulating a few cm of tissue at the boundary domain

- Initial temperature for both domains: 37 ^{0}C

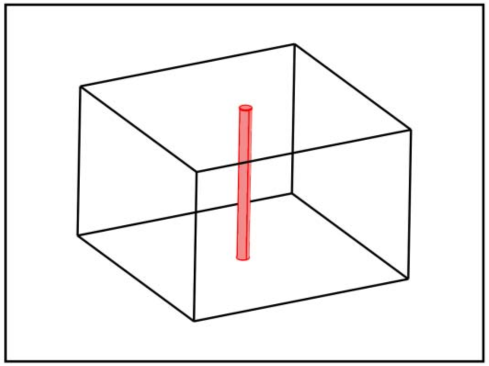
NUMERICAL SIMULATIONS

- Single Artery and Focused Ultrasound

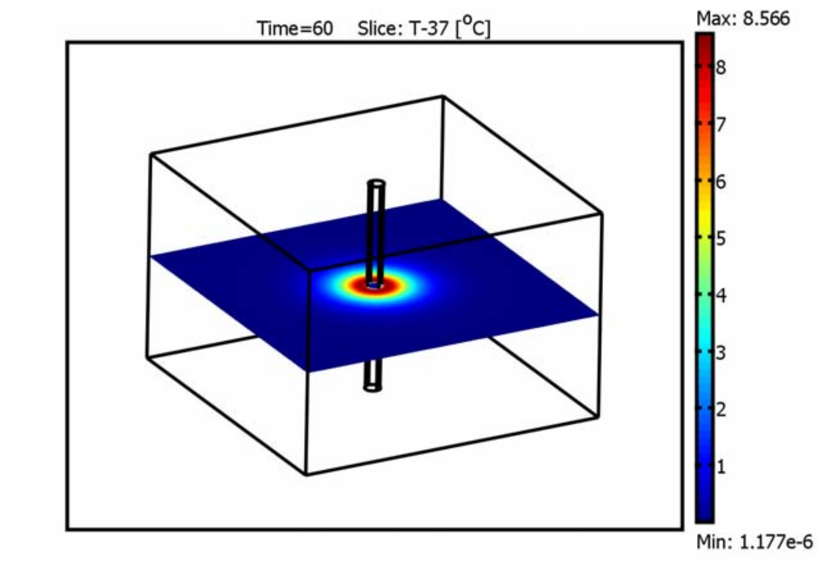
Focused Ultrasound Power
Distribution through the Focus



Focus half-power: width 4 mm, height 30 mm
Peak power density I_0=15 W/ cm^3
Insonation time = 60 s



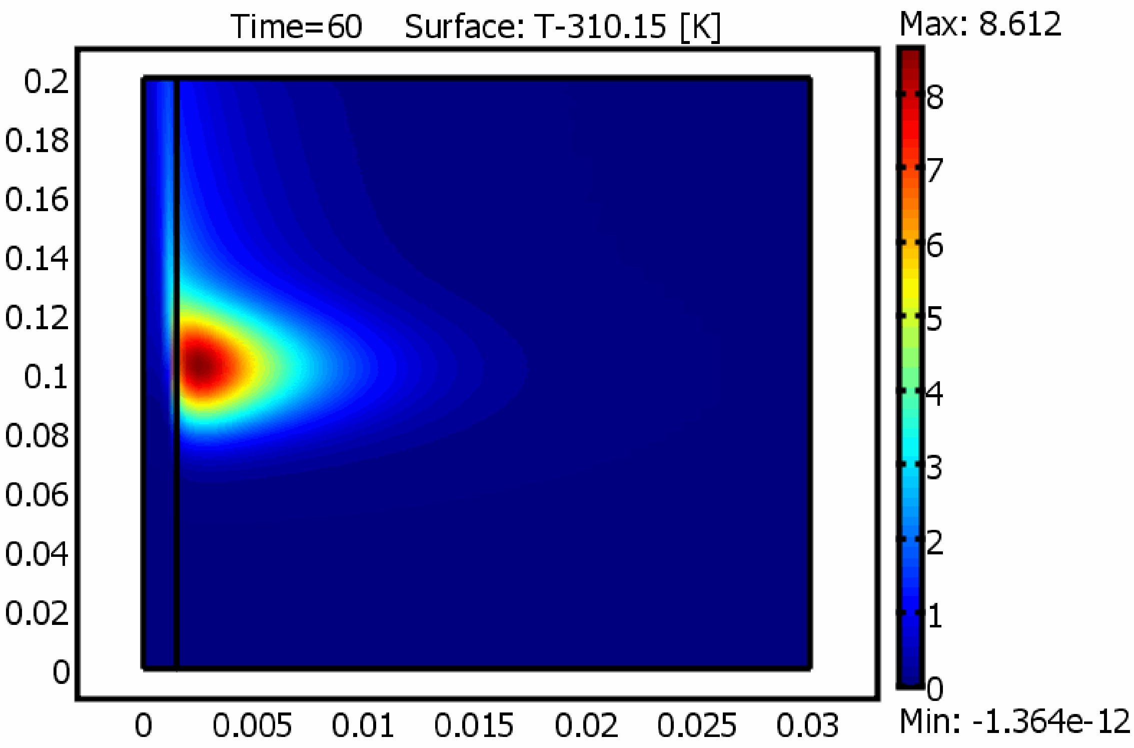
Focus mid-plane of the computational domain at the vessel center



Large Artery and Focused Ultrasound

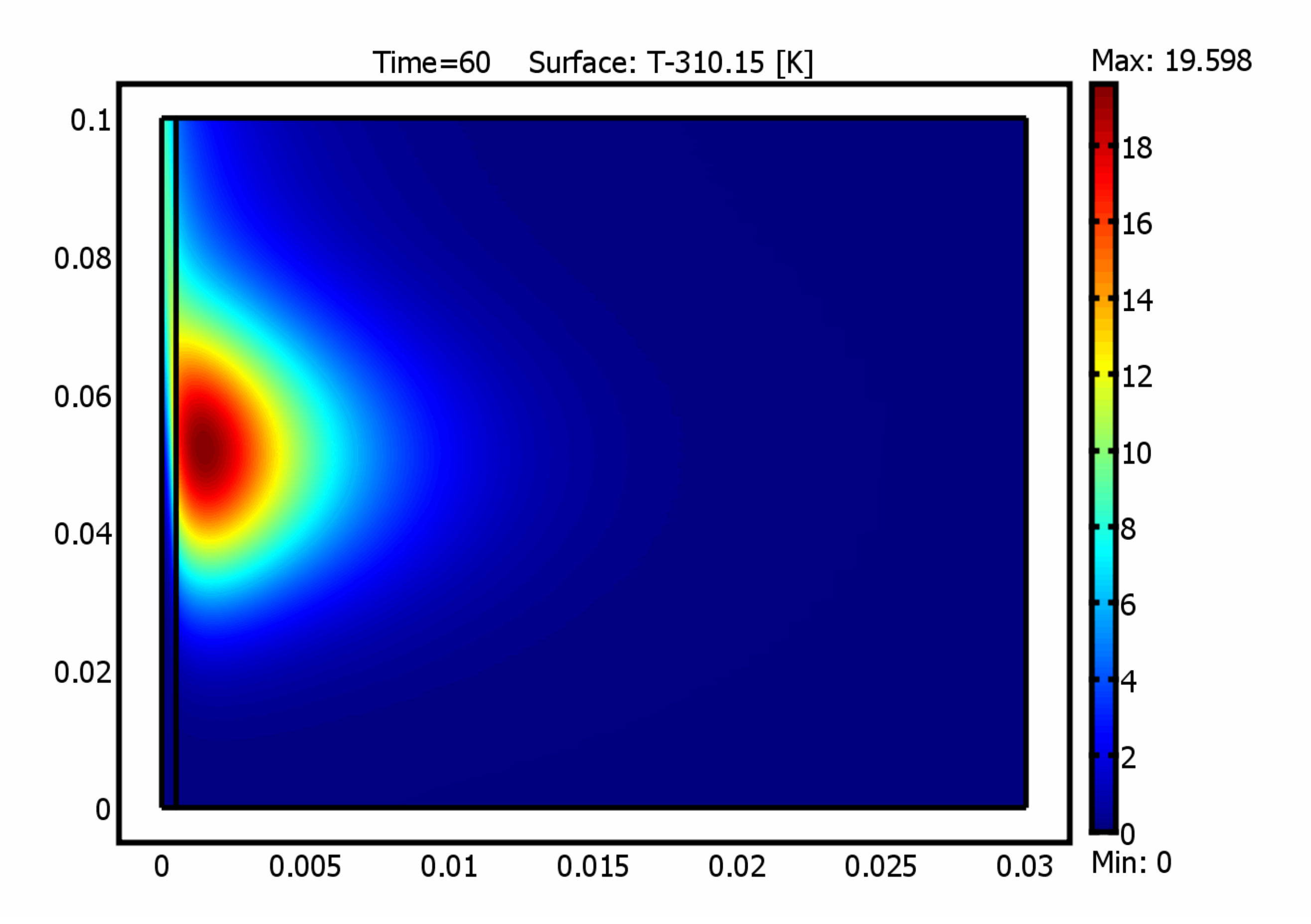
Artery parameters :
radius R=1.5 mm
length L= 200 mm
mean flow velocity V_m= 13 cm s^{-1}

Axial Symmetric Temperature Increase after one minute insonation



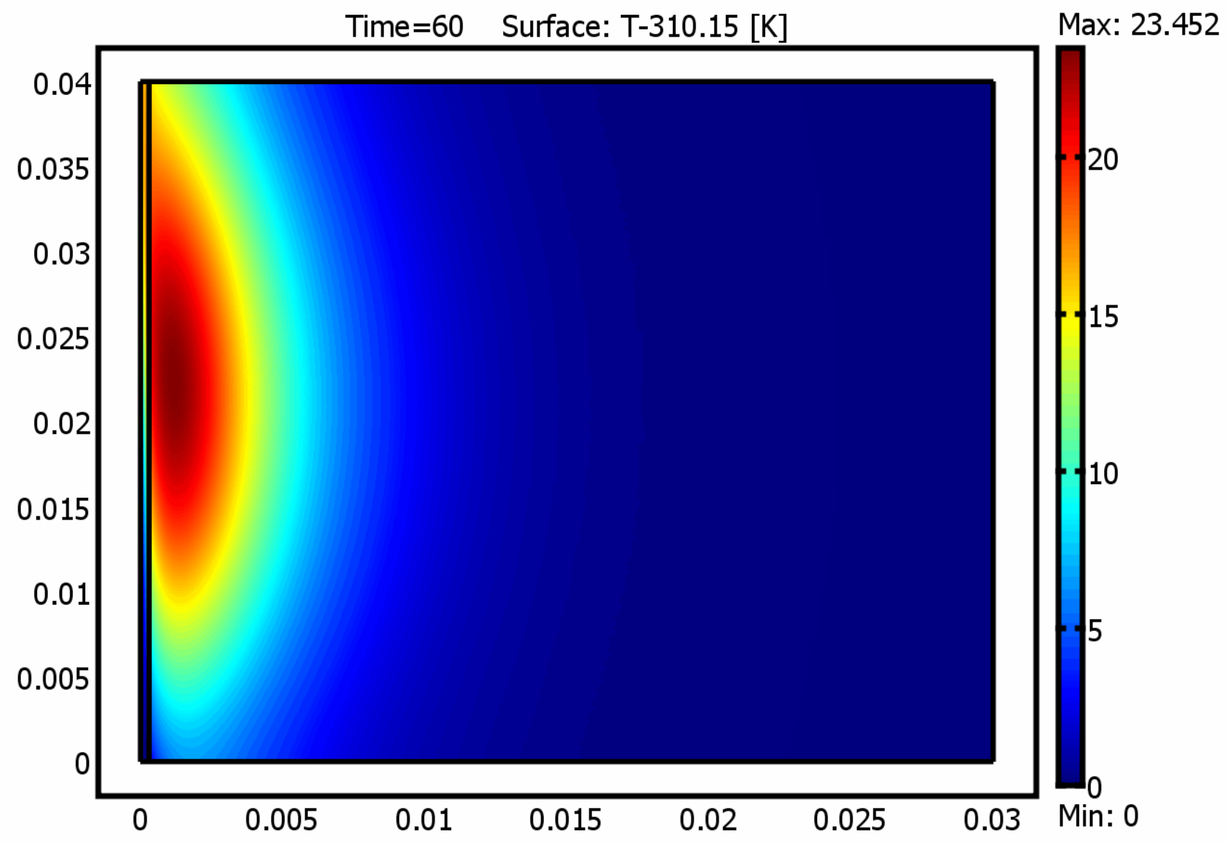
Primary Artery and Focused Ultrasound

Artery parameters :
radius R=0.5 mm
length L= 100 mm
mean flow velocity V_m= 8 cm s^{-1}

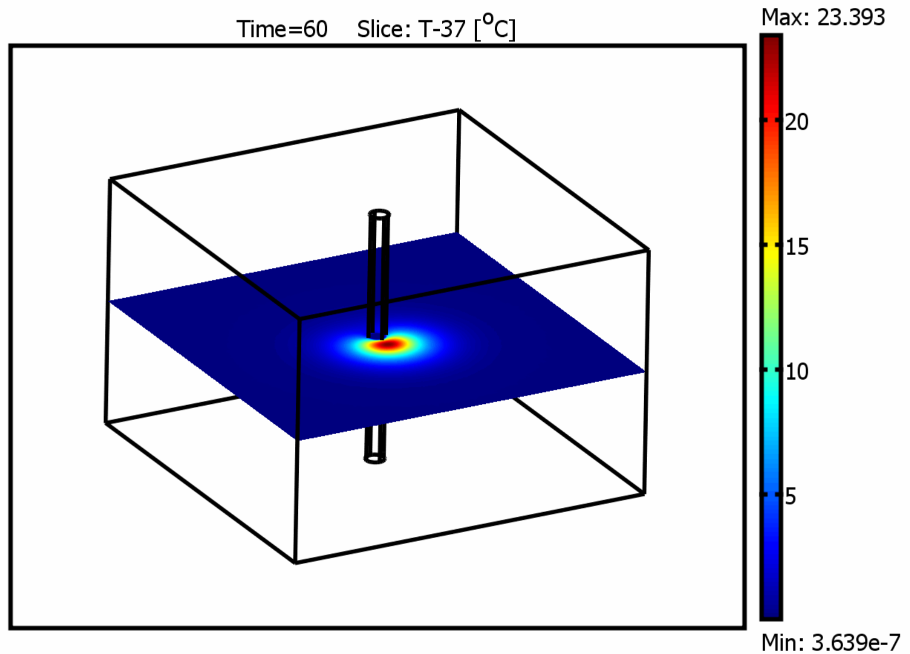


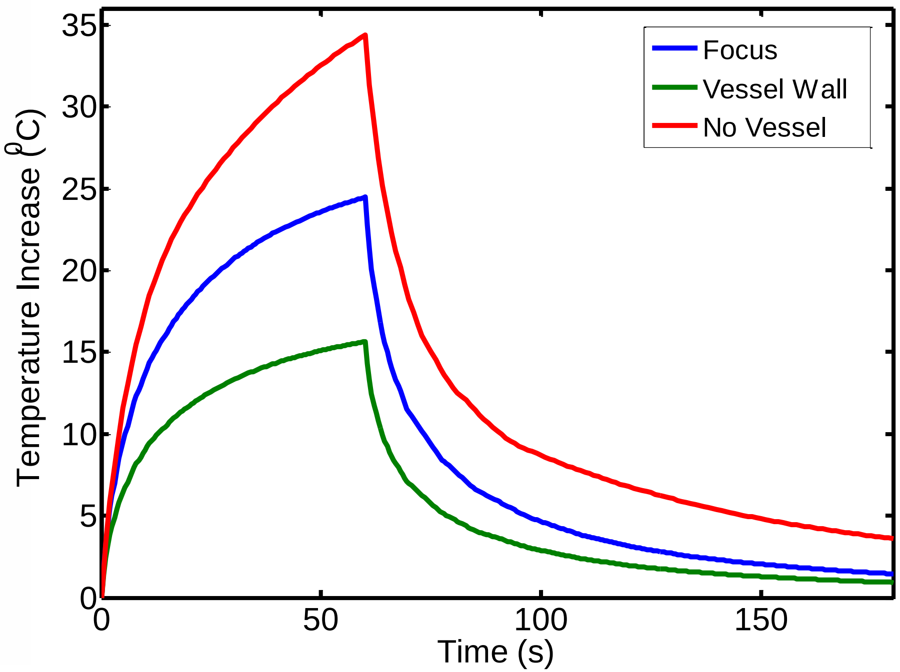
Secondary Artery and Focused Ultrasound

Artery parameters :
radius R=0.3 mm
length L= 40 mm
mean flow velocity V_m= 8 cm s^{-1}



Large Artery - Focus 1 mm away from Vessel Wall

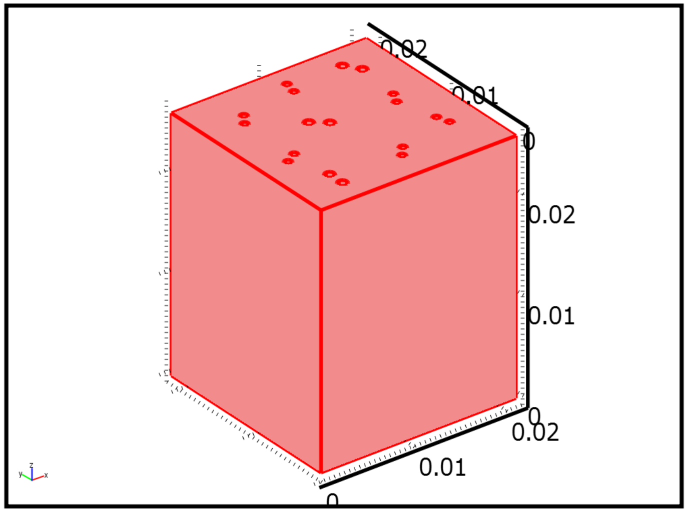




Artery-Vein Pairs and Focused Ultrasound

- Thermally significant vessels run in counter-flow pairs (artery-vein pairs)

- Multiple artery-vein system located in a homogeneous block of muscle-like tissue with dimensions 21x 21x26 mm^3



3 Pairs:
Radius=500 μm
Distance between the artery and vein= 0.8 mm

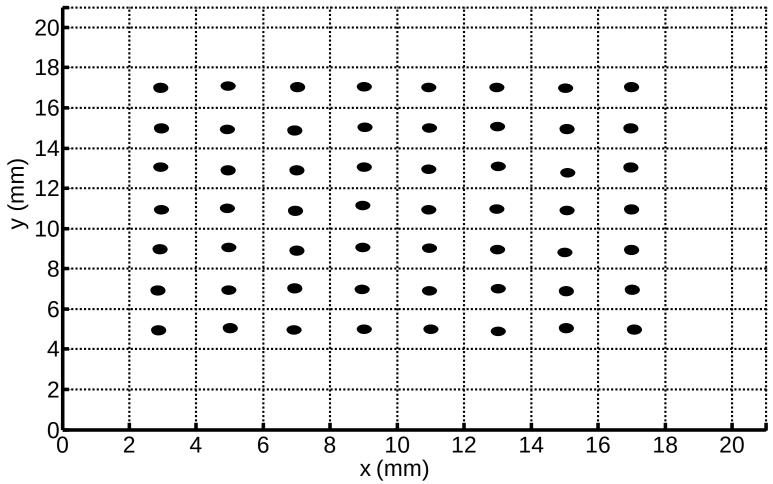
6 Pairs:
Radius: 400 μm
Distance between the artery and vein= 0.6 mm

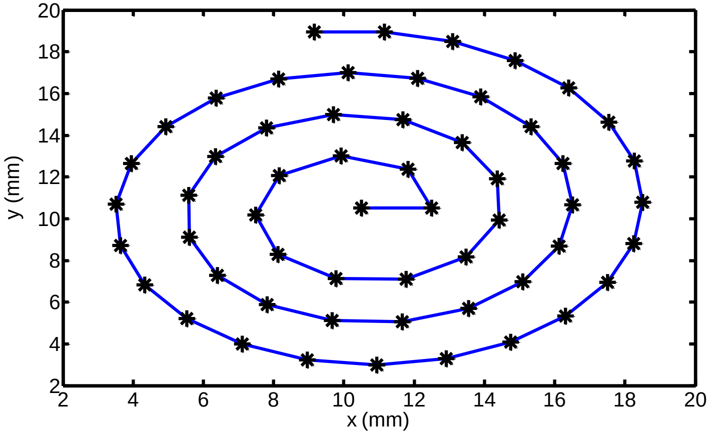
Mean flow velocity: 8 cm/s for all the vessels

Thermal treatment of the multiple-vessel system

- Ultrasound parameters : Focus half-power width 3.2 mm height 24 mm
  Power density varied
  Axial direction of transducer along the vessels

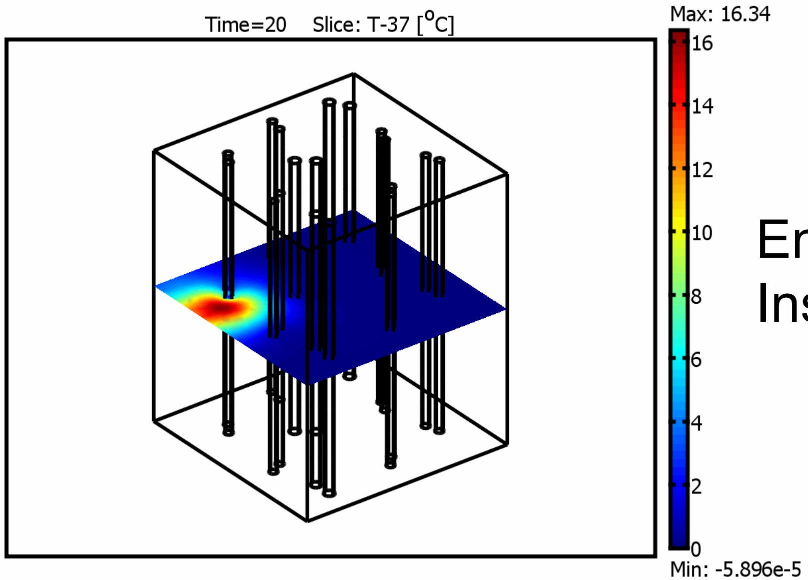
- Ultrasound focus that is stepped through the mid-plane of the computational domain





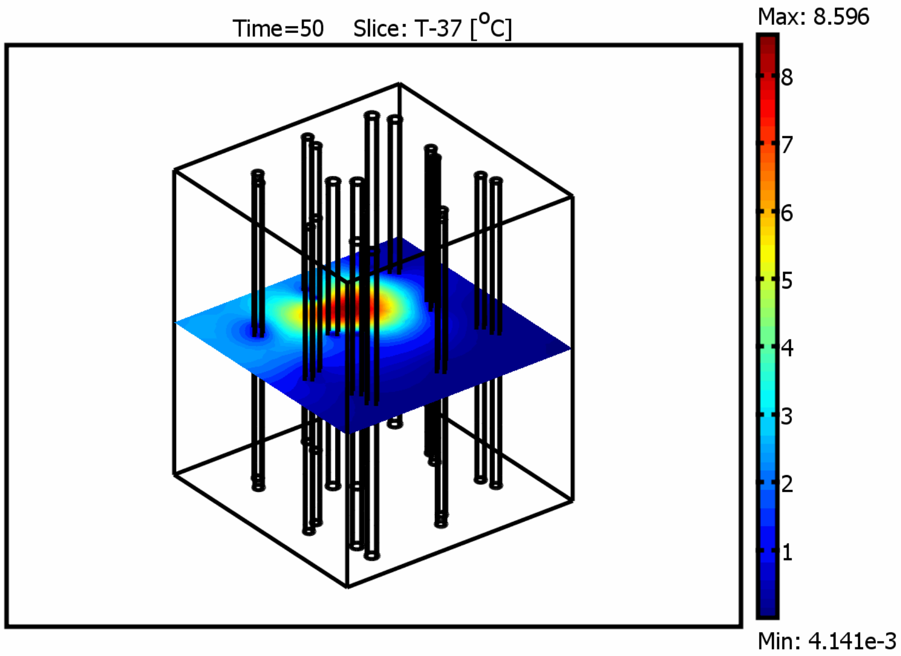
Number of insonations = 56
Duration time for each insonation = 20 s
Cooling period = 5 s
Total Insonation time =1395 s (23 minutes)

Thermal treatment of the multiple-vessel system



Peak power density =16.5 W/cm^3

End of First Insonation Period



End of Second Cooling Period

Thermal Dose Calculation

- The overall performance of the treatments is evaluated by calculating the thermal dose at the mid-plane of the computational domain

$$TD(t) = \int_0^t \mathcal{R}^{43-T(t')} dt' \qquad \mathcal{R} = \begin{cases} 0.25 & T(t) < 43\,^0C \\ 0.5 & T(t) \geq 43\,^0C \end{cases}$$

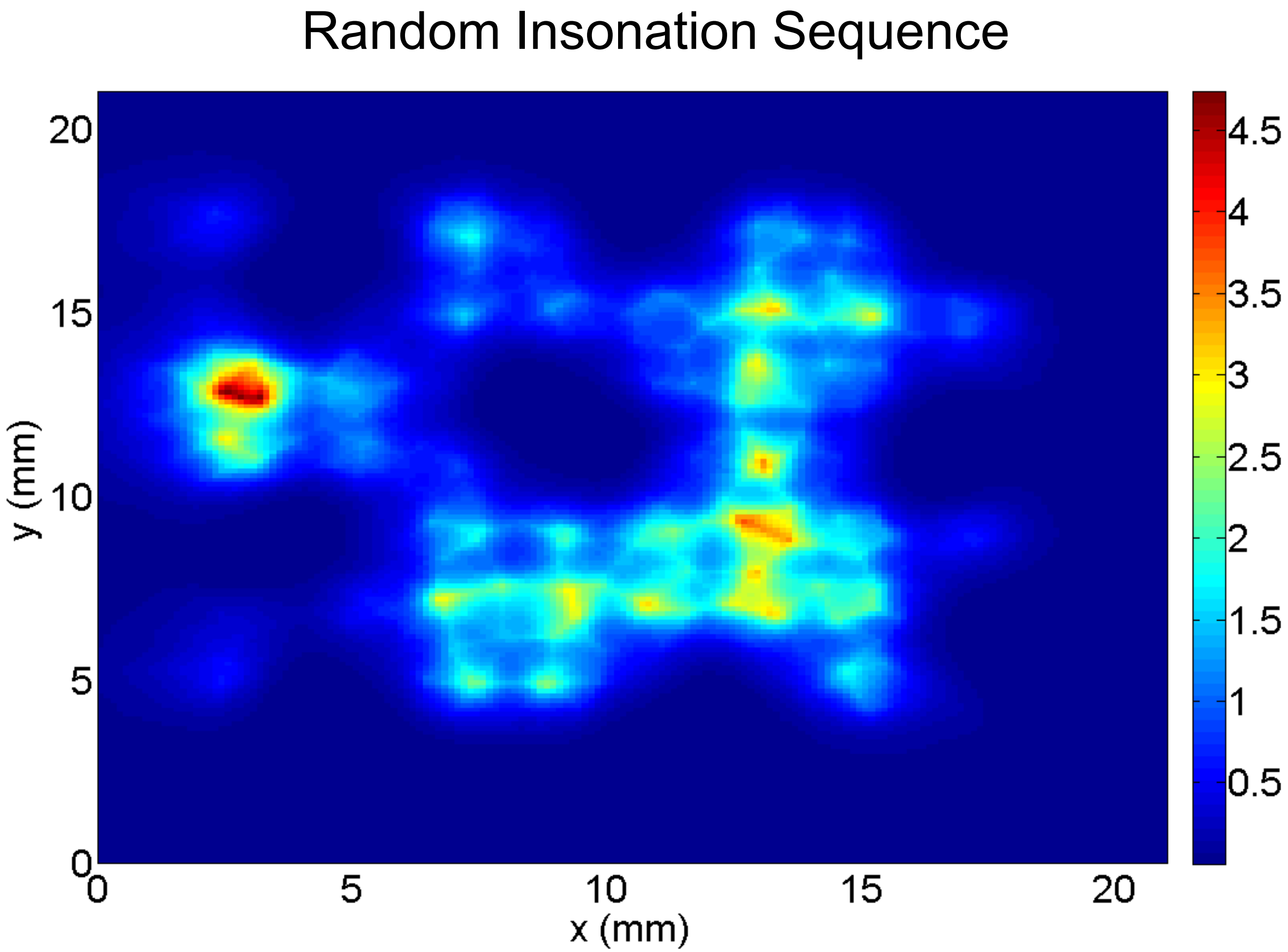
- At 43 ^{0}C, a treatment duration of 240 min has been introduced as a reference for thermal lesion formation

- All thermal dose calculations are normalized to this standard, with a thermal dose of one corresponding to threshold for thermal damage

Thermal Dose in Mid-Plane

- Fixed Power Treatment

Peak Power Density 16.5 W/cm^3



Thermal Dose in Mid-Plane

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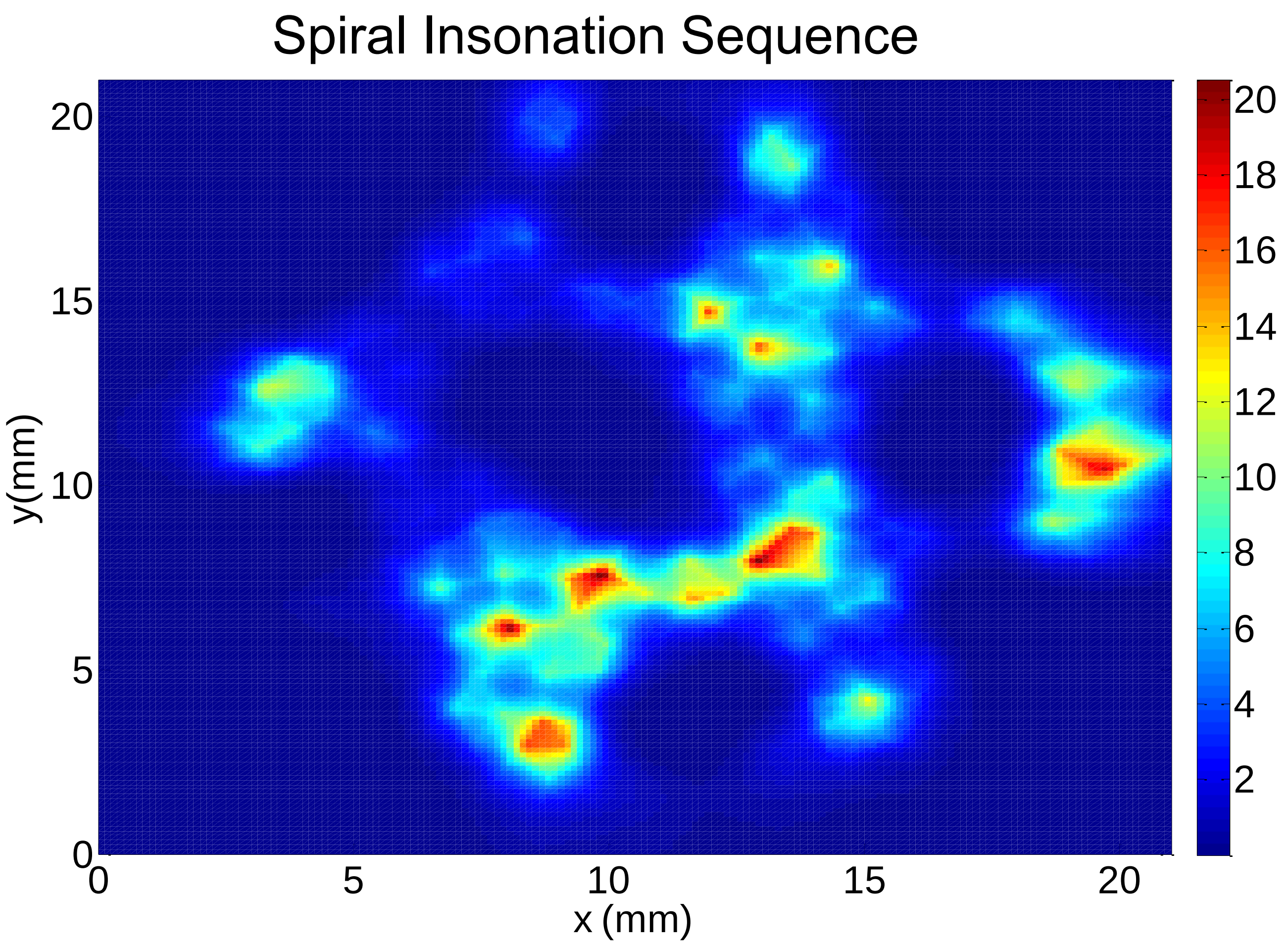
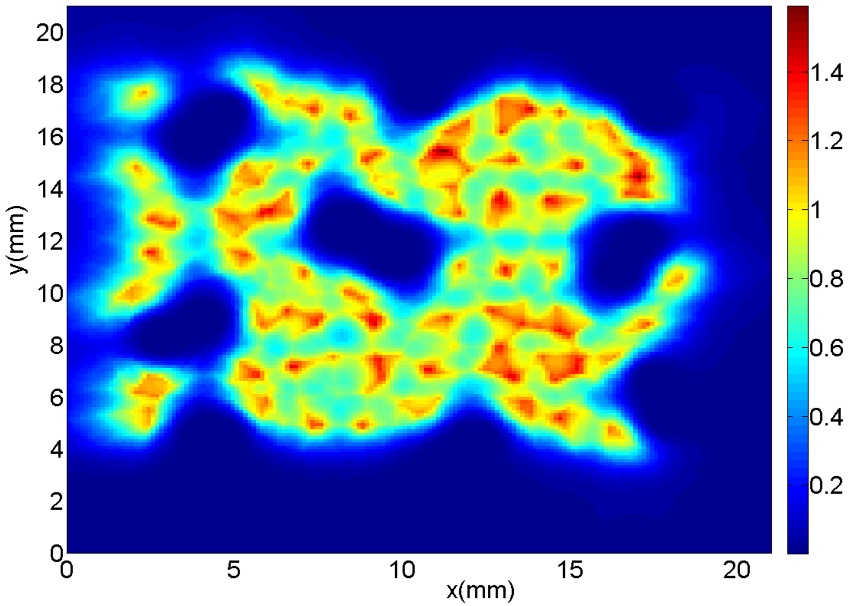


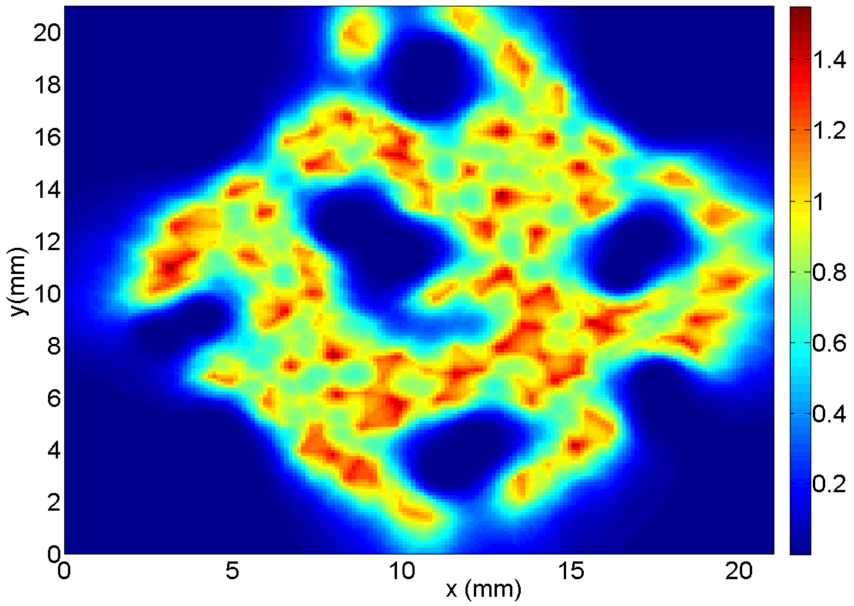
Thermal Dose in Mid-Plane

- Variable power treatment such that the peak thermal dose deposition remains in the range between 1 ±0.04 for each insonation

Random Insonation Sequence



Spiral Insonation Sequence



CONCLUSIONS

- Focused ultrasound has been proposed for a variety of therapeutic applications such as tumor thermal ablation and as a way to increase local drug delivery for cancer treatment
- The clinical limitations and potentials of focused ultrasound hyperthermia can only be understood with the help of an ultrasound treatment planning
- Our results are preliminary and do not take into account the complexity of the real anatomy
- They suggest the importance of a treatment planning that takes into account the presence of blood vessels and blood flow
- They indicate that the overall temperature heterogeneity caused by blood flow could be greatly improved during a treatment provided the availability of blood vessel data and an efficient tailored strategy for delivering the ultrasound treatment