Isogeometric approach to the study of focused ultrasound induced heating in biological tissues

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Motivation

- ▶ When ultrasound passes through a biological tissue the energy of the acoustic field is absorbed by the tissue and transformed into heat.
- ▶ Ultrasound technology has a lot of applications in medicine, surgery: cancer treatment, physical therapy: to improve pain relief, collagen extensibility, muscle and tendon elasticity, ligament repair.
- ► Ultrasound energy is computed from the acoustic pressure, solution of the Helmholtz equation.
- ► Thermal diffusion of ultrasound is modeled with Pennes equation, that relates the distribution of temperature with the absorbed ultrasound energy.

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Goals

- ▶ To compute the ultrasound induced heating of a biological tissue.
- ► To study the influence of parameters of the model in the heating pattern.
- ▶ To solve the problem taking advantages of isogeometric analysis.



The mathematical-physical model

The physical domain



curved transducer emitting acoustic wave of constant amplitude

Two PDE equations:

- ▶ 3 layers tissue: skin, fat, muscle
- ▶ Helmholtz radiation problem, unknown: acoustic pressure
- ▶ Pennes heating problem, unknown: temperature

Acoustic radiation model

u(x, y) acoustic pressure field, solution of Helmholtz equation

$$-\triangle u(x,y) - k^2(x,y)u(x,y) = 0, \quad (x,y) \in \Omega$$

with mixed boundary conditions

$$\begin{array}{rcl} u(x,y) &=& C & \text{on } \Gamma_D \\ \\ \frac{\partial u(x,y)}{\partial \overrightarrow{n}} &=& 0 & \text{on } \Gamma_N \\ \\ \frac{\partial u(x,y)}{\partial \overrightarrow{n}} + \mathrm{i} \, k(x,y) u(x,y) &=& 0 & \text{on } \Gamma_R \end{array}$$

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 Γ_N

C is the amplitude of the ultrasound, i imaginary unit.

Wavenumber

Wavenumber k(x, y) is the complex function

$$k(x,y) = \frac{2\pi f}{c(x,y)} - \mathrm{i}\mu(x,y)$$

where

- f frequency of the pulse emitted by the transducer
- ▶ c(x, y) ultrasound speed propagation and $\mu(x, y)$ attenuation coefficient are piecewise constant functions depending on the tissue.

The solution u(x, y) of the radiation problem is a complex function.

Bioheat transfer model

For $(x, y) \in \Omega$ and $t \in [0, t_f]$, the temperature field T(x, y, t) is solution of Pennes equation

$$\rho(x,y)c_s(x,y)\frac{\partial}{\partial t}T(x,y,t) - k_s(x,y)\Delta T(x,y,t) = \widetilde{Q}(x,y,t)$$

where

- $\widetilde{Q}(x, y, t)$ is the heat source.
- ▶ $\rho(x, y)$ density, $c_s(x, y)$ specific heat, $k_s(x, y)$ thermal conductivity are piecewise constant functions depending on the tissue

Initial condition

$$T(x, y, 0) = T_b, \quad (x, y) \in \Omega$$

Dirichlet boundary condition

$$T(x, y, t) = T_b$$
 for all $(x, y, t) \in \partial \Omega \times [0, t_f]$

where T_b is the blood temperature.

Bioheat transfer model

Assumptions

- The heat source $\widetilde{Q}(x, y, t)$ is derived from the intensity of the acoustic pressure field u(x, y), computed as solution of Helmholtz equation.
- ▶ We assume that the ultrasound is applied in the interval $[0, t_s]$ with $t_s < t_f$, hence

$$\widetilde{Q}(x,y,t) = \left\{ \begin{array}{cc} Q(x,y) & for & 0 \leq t \leq t_s \\ 0 & for & t_s < t \leq t_f \end{array} \right.$$

where

$$Q(x,y) = \mu(x,y) \frac{|u(x,y)|^2}{\rho(x,y)c(x,y)}$$

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So far...

The model: uncoupled system of Helmholtz-Pennes equations

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$$-\triangle u - k^2 u = 0$$
$$\rho c_s \frac{\partial}{\partial t} T - k_s \triangle T = \widetilde{Q}$$

u(x, y) acoustic pressure T(x, y, t) temperature $\widetilde{Q}(x, y, t)$ heat source, computed in terms of u(x, y) $k(x, y), \rho(x, y), c_s(x, y), k_s(x, y)$ are piecewise constant functions

Now...

Numerical solution

► Helmholtz: discretizing spacial variables with isogeometric analysis (IgA).

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▶ Pennes: Lines method with isogeometric analysis.

Isogeometric method

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Isogeometric Analysis, IgA

- ▶ Is an active and relatively new research area introduced in 2005 in the seminal paper of Hughes and co-workers: Isogeometric analysis: CAD, finite elements, NURBS, exact geometry and mesh refinement
- ▶ 2009 appears the first book: Isogeometric analysis: toward integration of CAD and FEA, J.A. Cottrell, T.J. Hughes, Y. Bazilevs.



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Isogeometric Analysis

- ▶ The name Isogeometric Analysis reflects the philosophy of the method: the same basic functions are used to describe the domain geometry and the approximated solution of Partial Differential Equations.
- ▶ IgA can be considered as an extension of the Finite Element Methods (FEM).
- ► FEM and IgA approximate the solution of PDE using piecewise polinomial functions.

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Isogeometric Analysis

- ▶ The name Isogeometric Analysis reflects the philosophy of the method: the same basic functions are used to describe the domain geometry and the approximated solution of Partial Differential Equations.
- ▶ IgA can be considered as an extension of the Finite Element Methods (FEM).
- ► FEM and IgA approximate the solution of PDE using piecewise polinomial functions.

IgA has two basic advantages over classical FEM:

- ▶ The boundary of the physical domain is represented exactly.
- ▶ The approximated solution of the PDE is smoother with one or several continuous derivatives.

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IgA method: B-spline functions

- 1. IgA is based on the use of B-spline functions, which are piecewise polynomial functions.
- 2. The definition of univariate B-splines requires the introduction of an increasing sequence of knots t^{ξ} .
- 3. With sequence of n + k knots t^{ξ} it is possible to define nB-splines functions $B_{i,t^{\xi}}^{k}(\xi), i = 1, ..., n$ of degree k - 1.
- 4. While classical FEM Lagrange functions are only C^0 continuous, B-splines are functions with several continuous derivatives.



Quadratic B-spline functions



IgA method: tensor product B-spline functions

Given two sequences of knots t^{ξ} and t^{η} both in [0, 1], tensor product B-spline functions of degree $k_1 - 1$ in ξ and $k_2 - 1$ in η are defined as:

$$B_{i,j}(\xi,\eta) := B_{i,t^{\xi}}^{k_1}(\xi) B_{j,t^{\eta}}^{k_2}(\eta), \quad 0 \le \xi \le 1, \quad 0 \le \eta \le 1$$
$$i = 1 \dots n, \ j = 1 \dots m$$



IgA method: parametrization of physical domain

The computation of a mesh in FEM is substituted in IgA by the construction of a parametrization of the physical domain Ω:

$$\mathbf{F}(\xi,\eta):\widehat{\Omega}=[0,1]\times[0,1]\to\Omega$$

such that

- **F** transforms $\partial \widehat{\Omega}$ in $\partial \Omega$.
- **F** must be injective.
- ▶ **F** is a tensor product B-spline function

$$\mathbf{F}(\xi,\eta) = \sum_{i=1}^{n_F} \sum_{j=1}^{m_F} \mathbf{P}_{i,j} B_{i,t^{\xi}}^{k_1}(\xi) B_{j,t^{\eta}}^{k_2}(\eta)$$

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where $\mathbf{P}_{i,j}$ are the (unknown) control points.

IgA method: parametrization of physical domain

Current research area: Given Ω , how to compute the control points $\mathbf{P}_{i,j} \in \mathbb{R}^2$ to obtain a "good" parametrization?

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IgA method: parametrization of physical domain

Current research area: Given Ω , how to compute the control points $\mathbf{P}_{i,j} \in \mathbb{R}^2$ to obtain a "good" parametrization?

- The image of a uniform mesh in $[0,1] \times [0,1]$ by parametrization $\mathbf{F}(\xi,\eta)$ defines a (curvilinear) mesh in Ω .
- ► Isoparametric curves of a "good" parametrization $\mathbf{F}(\xi, \eta)$ are almost orthogonal and uniformly distributed in Ω
- Deformations introduced by the map $\mathbf{F}(\xi, \eta)$ affect the accuracy of the approximated solution computed with IgA.

Control points of $\mathbf{F}(\xi, \eta)$





Mesh in Ω defined by $\mathbf{F}(\xi, \eta)$

IgA solution of Helmholtz equation

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Weak formulation

As in FEM, the first step to apply IgA is to obtain the weak formulation of the PDE. Let

$$\mathcal{V}_0^H = \{ v : \Omega \to \mathbb{C}, v \in H^1(\Omega), \ v(x, y) = 0 \ \text{for} \ (x, y) \in \Gamma_D \}$$

Weak formulation of Helmholtz problem: Find $u \in H^1(\Omega)$, with u = C in Γ_D such that,

$$\mathfrak{a}(u,v) = 0, \quad \forall v \in \mathcal{V}_0^H$$

where $\mathfrak{a}(u, v)$ is the sesquilinear form

$$\begin{split} \mathfrak{a}(u,v) &= \int \int_{\Omega} \nabla u(x,y) \cdot \nabla \overline{v}(x,y) - k(x,y)^2 u(x,y) \overline{v}(x,y)) \ d\Omega \\ &+ \operatorname{i} \int_{\Gamma_R} k(x,y) \ u(x,y) \overline{v}(x,y) \ d\Gamma \end{split}$$

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Galerkin discretization

Given the parametrization $(x, y) = \mathbf{F}(\xi, \eta)$ of Ω ,

 \blacktriangleright Define the basis: select n and m and push forward the B-spline functions

$$\phi_{i,j}(x,y) := (B_{i,j} \circ \mathbf{F}^{-1})(x,y), \ i = 1, ..., n, \ j = 1, ..., m$$

Renumerate the B-splines functions defining

$$\psi_r(x,y) := \phi_{i,j}(x,y)$$

with r = (j - 1)n + i and i = 1, ..., n, j = 1, ..., m.

▶ Define the finite dimensional space

$$\mathcal{V}_h^H = \operatorname{span}\{\psi_r(x,y), \ r=1,...,N^H\}$$

where $N^H := n \cdot m$ and

▶ Galerkin: the approximated solution $u_h(x, y) \in \mathcal{V}_h^H$ is given by,

$$u_h(x,y) = \sum_{r=1}^{N^H} \alpha_r \psi_r(x,y)$$

Galerkin discretization

Unknown coefficients $\alpha_r \in \mathbb{R}$ are determined requiring that

$$\mathfrak{a}(u_h, \psi_s) = 0, \text{ for } s = 1, ..., N^H$$

which means that,

$$\sum_{r=1}^{N^H} \alpha_r \int \int_{\Omega} \left(\nabla \psi_r(x, y) \cdot \nabla \psi_s(x, y) - k(x, y)^2 \psi_r(x, y) \psi_s(x, y) \right) d\Omega$$
$$+ i \sum_{r=1}^{N} \alpha_r \int_{\Gamma_R} k(x, y) \psi_r(x, y) \psi_s(x, y) ds = 0, \quad s = 1, ..., N^H$$

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Unknowns coefficients $\alpha_r \in \mathbb{C}$ are computed from the previous equations requiring additionally that $u_h = C$ in Γ_D .

Linear system

Introducing the notation,

$$\begin{split} \mathbf{M} &= (M_{r,s}) = \int \int_{\Omega} k^2 \, \psi_r \psi_s \, d\Omega & \text{mass matrix} \\ \mathbf{S} &= (S_{r,s}) = \int \int_{\Omega} \nabla \psi_r \cdot \nabla \psi_s \, d\Omega & \text{stiffness matrix} \\ \mathbf{E} &= (E_{r,s}) = \int_{\Gamma_R} k \, \psi_r \psi_s \, d\Gamma & \text{Robin matrix} \end{split}$$

for $r, s = 1, ..., N^H$, the previous equations can be written as,

$$A\alpha = b$$

where

$$\mathbf{A} = \mathbf{S} - \mathbf{M} + \mathbf{i}\mathbf{E}$$

 $\boldsymbol{\alpha} = (\alpha_1, ..., \alpha_{N^H})^t$ is the vector of the unknowns.

Properties of matrix \mathbf{A}

- It is large, complex and sparse. Iterative methods are suitable for the solution of the linear system.
- ▶ It is symmetric but it is not Hermitian.
- ▶ It is not positive definite, we solve the system using GMRES.
- ► As k increases A is ill conditioned. This affect the velocity of convergence of GMRES. Hence, it is necessary a preconditioner.
- Complex Shifted Laplacian preconditioner for constant k is given by,

$$\mathbf{A}_{\beta} = \mathbf{A} + \mathrm{i}\beta\,k^2\,\mathbf{M}$$

 $(\beta>0$ parameter) is used to achieve the GMRES convergence.

Spy of \mathbf{A} for bicubic B-spline approximation



IgA solution of Helmholtz equation: remarks

- ▶ Since the solution of Helmholtz eq. is highly oscillatory, in order to obtain a good approximation $u_h(x, y)$, the dimension N^H of approx. space must be large (of order 10⁵).
- If $u_h(x, y)$ and $\hat{u}_h(x, y)$ are the solution of Helmholtz eq. with Dirichlet constants C and $\hat{C} = \lambda C$ respectively then,

$$\widehat{u}_h(x,y) = \lambda \, u_h(x,y)$$

Hence, solving the radiation problem once, the solution corresponding to pulses of different amplitudes are immediately available.

IgA solution of Pennes equation

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Weak formulation of Pennes equation

$$\mathcal{V}_0^P = \{ v : \Omega \to \mathbb{R}, v \in H^1(\Omega), \ v(x,y) = 0, \ \text{for all} \ (x,y) \in \Gamma := \partial \Omega \}$$

Weak formulation of bioheat problem: for any fixed $t \in [0, t_f]$, find $T(x, y, t) \in H^1(\Omega)$ such that $T(x, y, t) = T_b$ on Γ and

$$\mathfrak{b}(T,v) = \mathfrak{q}(v), \quad \forall v \in v \in \mathcal{V}_0^P$$

where $\mathfrak{b}(T, v)$ is a bilinear form and $\mathfrak{q}(v)$ is a linear form

$$\begin{split} \mathfrak{b}(T,v) &= \int \int_{\Omega} \rho(x,y) \, c_s(x,y) \frac{\partial T(x,y,t)}{\partial t} \, v(x,y) \, d\Omega \\ &+ \int \int_{\Omega} k_s(x,y) \, \nabla T(x,y,t) \cdot \nabla \, v(x,y) \, d\Omega \\ \mathfrak{q}(v) &= \int \int_{\Omega} \widetilde{Q}(x,y,t) \, v(x,y) \, d\Omega \end{split}$$

Galerkin discretization

Given the parametrization $(x, y) = \mathbf{F}(\xi, \eta)$ of Ω ,

▶ Define the basis: select \tilde{n} and \tilde{m} and push forward the B-spline functions

$$\phi_{i,j}(x,y) := (B_{i,j} \circ \mathbf{F}^{-1})(x,y), \ i = 1, ..., \widetilde{n}, \ j = 1, ..., \widetilde{m}$$

Renumerate the B-splines functions defining

$$\psi_r(x,y) := \phi_{i,j}(x,y)$$

with r = (j-1)n + i and $i = 1, ..., \tilde{n}, j = 1, ..., \tilde{m}$.

▶ Observation: since the solution T(x, y, t) of Pennes equation is smoother that the solution of Helmholtz equation, a good approximation $T_h(x, y, t)$ can be computed from an approx. space of dimension $N^P := \tilde{n} \cdot \tilde{m}$ much smaller (of order 10³) than N^H .

Galerkin discretization

▶ Define the finite dimensional space

$$\mathcal{V}_h^P = \operatorname{span}\{\psi_r(x,y), \ r=1,...,N^P\}$$

• Galerkin: for any fixed t, the approximated solution $T_h(x, y, t) \in \mathcal{V}_h^P$ is given by,

$$T_h(x, y, t) = \sum_{r=1}^{N^P} \alpha_r(t) \psi_r(x, y)$$

where $\alpha_r(t)$ $r = 1, ..., N^H$ are unknown functions.

• The set of indexes $I = \{1, ..., N^P\}$ is divided in two:

$$I = I_0 \cup I_g$$

 I_0 is the set of indexes of basic functions ψ_r vanishing $\forall (x, y)$ in Γ . $I_g = \{1, ..., N^P\} \setminus I_0$

 Taking into account that B-spline functions define a partition of unity, it is easy to show that boundary condition

$$T_h(x, y, t) = T_b \quad \forall (x, y) \in \Gamma \quad \text{and} \quad t \in [0, t_f]$$

holds, if we assign

$$\alpha_r(t) = T_b, \text{ for } r \in I_g$$

Hence, only remain as unknowns functions $\alpha_r(t)$, $r \in I_0$.

▶ B-splines $\psi_r(x, y)$, $r \in I_0$ are a basis of the subspace of \mathcal{V}_h^P :

$$\mathcal{V}^P_{0,h} = \{ v \in \mathcal{V}^P_h, \text{ such that } v(x,y) = 0 \text{ for all } (x,y) \in \Gamma \}$$

• Galerkin formulation is obtained substituting in the weak formulation v(x, y) by B-splines $\psi_r(x, y)$, $r \in I_0$ and $T_h(x, y, t)$ by $T_h(x, y, t) = \sum_{r=1}^{N^P} \alpha_r(t) \psi_r(x, y)$

Ordinary Differential Equations (ODE) system

The result can be written in matrix form as,

$$\mathbf{M}_0 \, \boldsymbol{\alpha}_0'(t) + \, \mathbf{S}_0 \, \boldsymbol{\alpha}_0(t) = \mathbf{z}(t)$$

where $\boldsymbol{\alpha}_0(t)$ is the vector of unknown functions $\alpha_r(t)$, $r \in I_0$ \mathbf{M}_0 and \mathbf{S}_0 are the stiffness and mass matrices given by,

$$\mathbf{M}_{0} = (M_{qr}) = \int \int_{\Omega} \rho c_{s} \psi_{q} \psi_{r} \, d\Omega, \quad q, r \in I_{0}$$

$$\mathbf{S}_{0} = (S_{qr}) = \int \int_{\Omega} k_{s} \nabla \psi_{q} \cdot \nabla \psi_{r} \, d\Omega, \quad q, r \in I_{0}$$

and $\mathbf{z}(t)$ is a known vector with components $z_r(t)$ that depends on

$$\widetilde{q}_r(t) = \int \int_{\Omega} \widetilde{Q}(x, y, t) \psi_r(x, y) \, d\Omega$$

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Observation: The ODE system can be successfully solved with classical Runge-Kutta 45 method.

Summarizing, IgA solution of Pennes equation is written as:

$$T_h(x, y, t) = \sum_{r \in I_0} \alpha_r(t)\psi_r(x, y) + \sum_{r \in I_g} T_b\psi_r(x, y)$$

where the vector $\boldsymbol{\alpha}_0(t)$ of unknowns with components $\alpha_r(t)$, $r \in I_0$ is computed solving the linear system of Ordinary Differential Equations

$$\mathbf{M}_0 \,\boldsymbol{\alpha}_0'(t) = -\mathbf{S}_0 \,\boldsymbol{\alpha}_0(t) + \mathbf{z}(t)$$

with initial condition

$$\boldsymbol{\alpha}_0(0) = (T_b, ..., T_b)$$

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Numerical Results

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Parameters

In all the numerical experiments the following parameters remain fixed:

- radius of Ω , r = 0.133 m
- curved transducer with semiaperture a = 0.01 m
- ▶ frequency of the pulse f = 1 MHz (in physiotherapy $0.7 MHz \le f \le 3 MHz$).
- the pulse is turn off at $t_s = 30 s$ and $t_f = 60 s$.
- ▶ tissue with 3 layers: skin, fat, muscle

tissue	$\rho(x,y)$	$c_s(x,y)$	$k_s(x,y)$	c(x,y)	$\mu(x,y)$
	density	specific	thermal	ultrasound	attenuation
		heat	conduct.	velocity	
skin	1 200	3590	0.23	1558	24
fat	950	2670	0.19	1478	5.58
muscle	1050	3640	0.55	1547	12.7

IgA solution of a typical problem

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Typical problem: acoustic radiation

amplitude of the pulse $C=0.5\times 10^6$

curvature radius $r_l = 0.0672$

Helmholtz eq. is solved with bicubic B-splines, $N^H = 308502$ dof.



▶ Cyan vertical lines represent the boundary between tissue layers.

- ▶ $\Re e(u_h(0,y))$ and $\Im m(u_h(0,y))$ are highly oscillatory functions.
- ▶ The focused effect produced by the curved lens is observed: the relative maximum of acoustic pressure farthest from the transducer is also the absolute maximum and its value is high (in comparison with the value obtained for a plane transducer).

Typical problem: the heating

Pennes equation is solved with bicubic B-splines, $N^P = 2594$ dof.

Temperature along (a section of) y axis for different times



- ▶ Temperature is shown for points along y axis for fixed times: 5s, 10s, 20s, 25s, 30s
- ▶ The heating pattern is similar for all fixed times, but as time goes by the difference between the temperature of the skin and muscle increases.

Heating induced by ultrasound

amplitude of the pulse $C = 0.5 \times 10^6$ curvature radius $r_l = 0.0672$



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Influence of some parameters in tissue heating

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Influence of pulse amplitude C on acoustic pressure

Fixed curvature radius rl = 0.0674

Absolute value of acoustic pressure along y axis

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- ▶ The number and position of relative extremes of the acoustic pressure are the same for all C.
- The absolute values of acoustic pressure increase with C.

Influence of pulse amplitude C on the temperature

Fixed curvature radius $r_l = 0.0674$

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- \blacktriangleright The temperature field pattern is similar for all selected C .
- The maximum temperature is attained in the skin and the minimum in the fat layer.
- Increasing the pulse amplitude C (from left to right) the temperature increases for the same time.

Influence of lens curvature radius r_l on acoustic pressure

Fixed pulse amplitude $C=5\times 10^5$

Absolute value of acoustic pressure along y axis

Decreasing the curvature radius (from left to right)

► The point of maximum acoustic pressure is moving closer to the transducer.

▶ The maximum acoustic pressure increases substantially.

Influence of lens curvature radius r_l on temperature Fixed pulse amplitude $C = 5 \times 10^5$

- ▶ In all cases the temperature increases as time increases.
- ▶ For small curvature radius (center, right) the maximum temperature is attained at the point of maximum acoustic pressure.
- ▶ For large curvature radius the maximum temperature is attained in the skin.

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Conclusions

For a curved transducer and a 3 layers tissue:

- ► The acoustic pressure field was computed solving Helmholtz equation with IgA.
- ▶ The temperature field induced by the acoustic pressure was computed solving Pennes equation combining the lines method with IgA.
- ► A Matlab code based on the open source software GeoPDEs was implemented.
- ► The influence of parameters of the pulse and the transducer on the heating was studied. Numerical simulations show that:
 - The amplitude C of the ultrasonic pulse doesn't affect the heating pattern. Increasing C the temperature increases mainly in the vertical strip over the transducer.
 - Decreasing the curvature radius of the transducer, the maximum acoustic pressure increases substantially and also the temperature in the vertical strip over the transducer.

▶ To include nonlinear effects in radiation and heating equations.

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- ▶ To include nonlinear effects in radiation and heating equations.
- ► To study the effect of the parametrization of the physical domain in the accuracy of the solution of Helmholtz and Pennes equations.

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- ► To study how the heating depends on the number and time duration of pulse applications.
- ► Adaptation of the model to simulate induced heating in specific physiotherapy applications based on ultrasound.

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