UNIVERSITY OF AMSTERDAM

heat transport in tissue

bioheat equation
thermal properties
vascular cooling

Hans Crezee

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Location University of Amsterdam
[2]*Cancer Center Amsterdam*
The Netherlands

Thermal therapy

Hyperthermia

- Heating tumor to 40-43°C for 1h
- Combined with radiotherapy and/or chemotherapy
- Tumor-selective radiosensitization

Thermal therapy

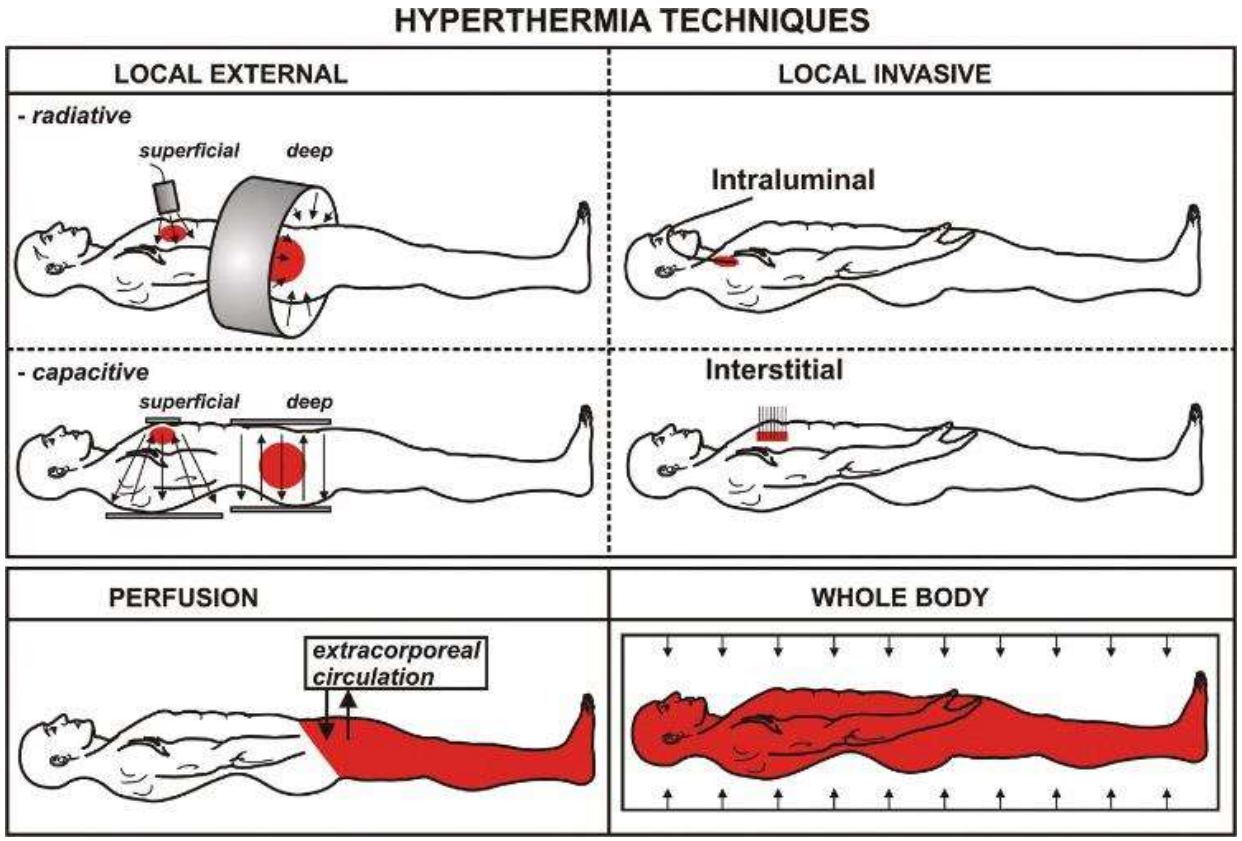
Hyperthermia

- Heating tumor to 40-43°C for 1h
- Combined with radiotherapy and/or chemotherapy
- Tumor-selective radiosensitization

Thermal ablation

- Heating tumor to 80-100°C for few minutes
- Direct tissue ablation

Thermal therapy



Heated volume differs strongly

Van der Zee et al *Int J Hyperthermia* 2008;24:111-22

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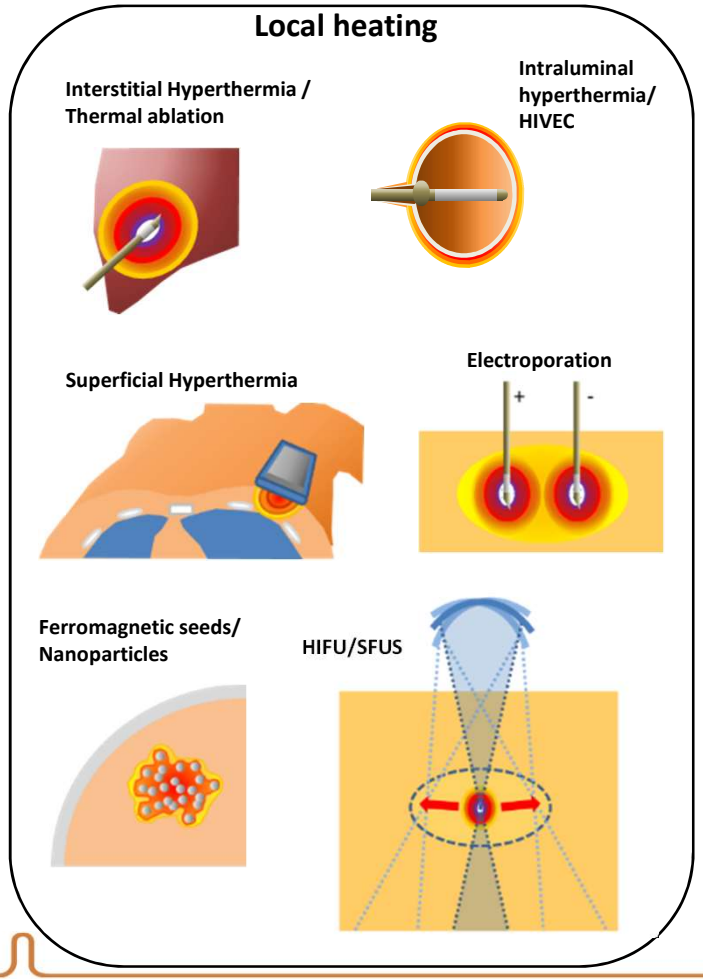
Thermal therapy



Heated volume differs strongly

- 1-4 cm

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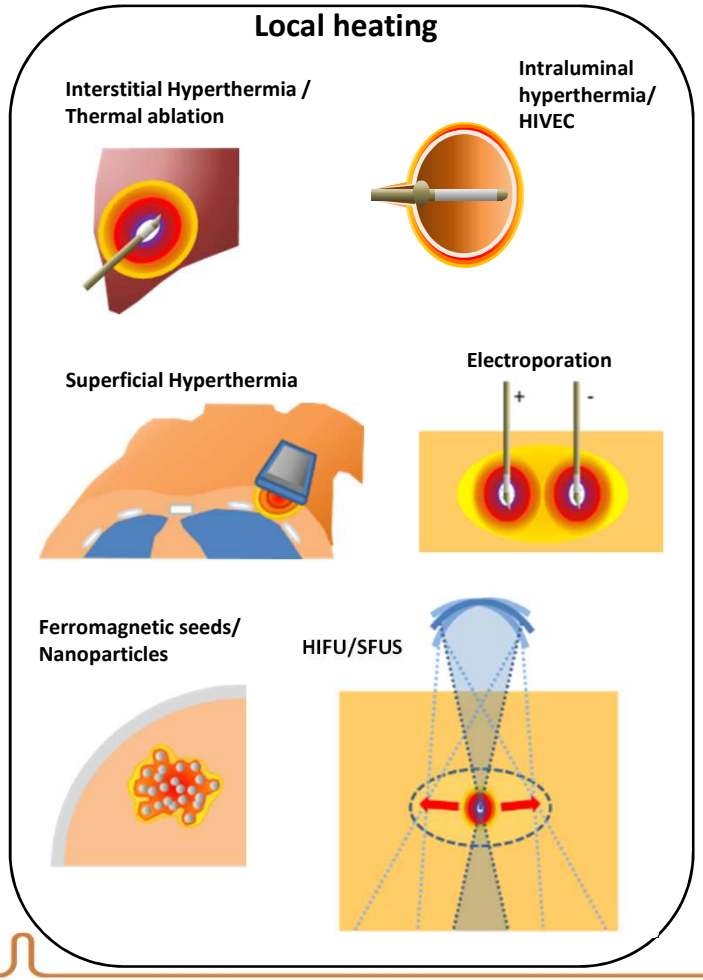
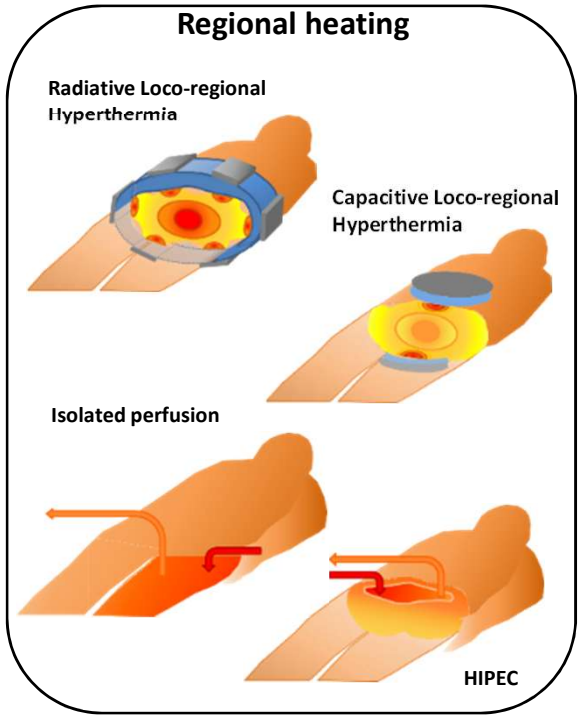
Kok et al *Int J Hyperthermia* 2020;37(1):711-741

Thermal therapy





Heated volume differs strongly

- 1-4 cm
- 10-20 cm

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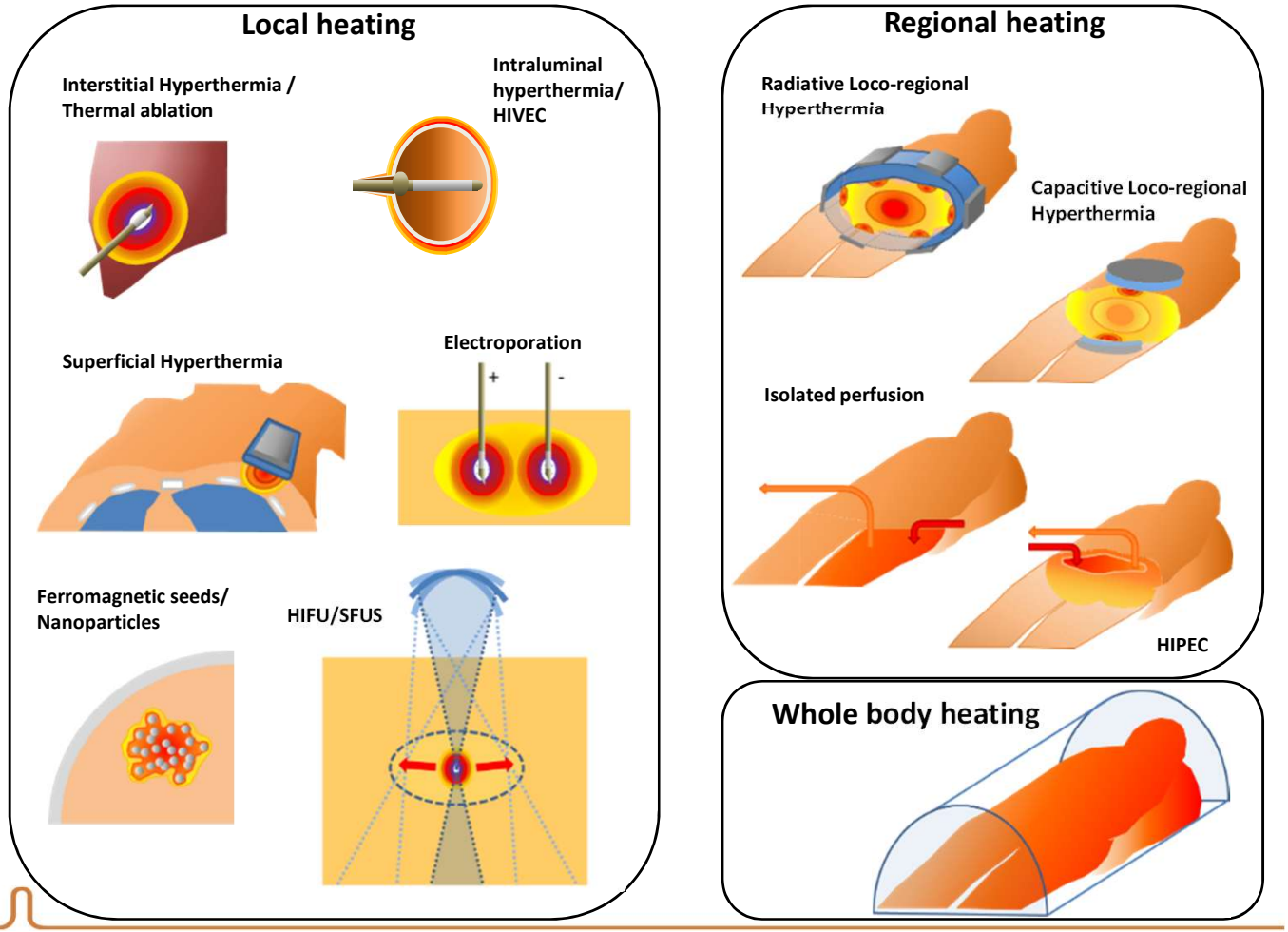
Thermal therapy



Heated volume differs strongly

- 1-4 cm
- 10-20 cm
- Whole body

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Kok et al *Int J Hyperthermia* 2020;37(1):711-741

Modeling heat transport in tissue

Modeling heat transport in tissue

- Bio-heat equation
- Thermal properties of tissues
- Vascular cooling

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Modeling heat transport in tissue

- Bio-heat equation
  - Different models used
    - Pennes bio heat equation
    - Effective conductivity
    - Discrete vessels

Modeling heat transport in tissue

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Modeling heat transport in tissue

- Pennes bio-heat equation
  - Describes heat transport in tissue by
    - Conduction
    - Blood flow

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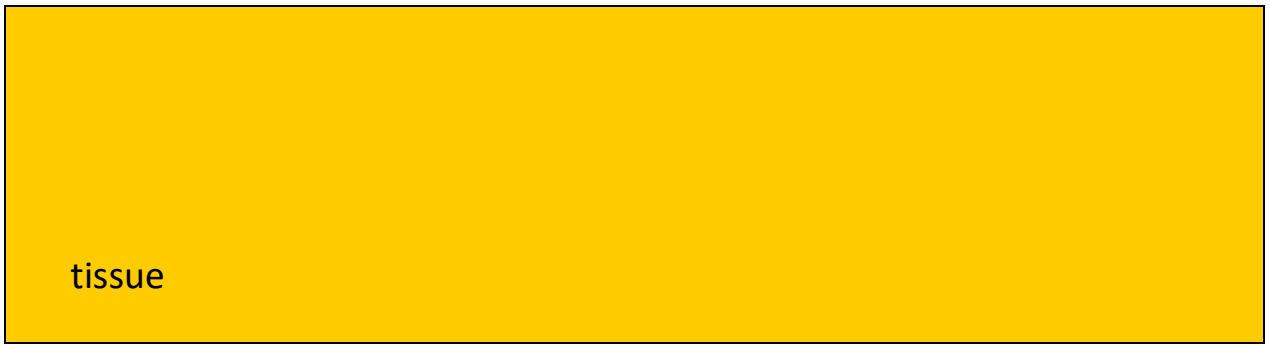
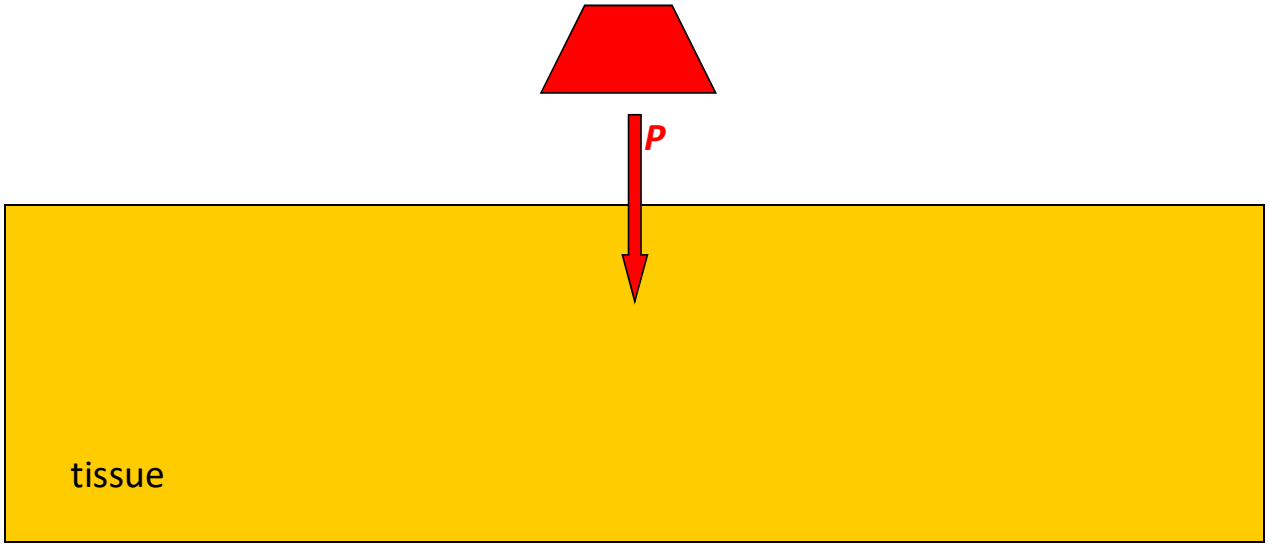
Heat transport by conduction

- A volume of non-perfused material



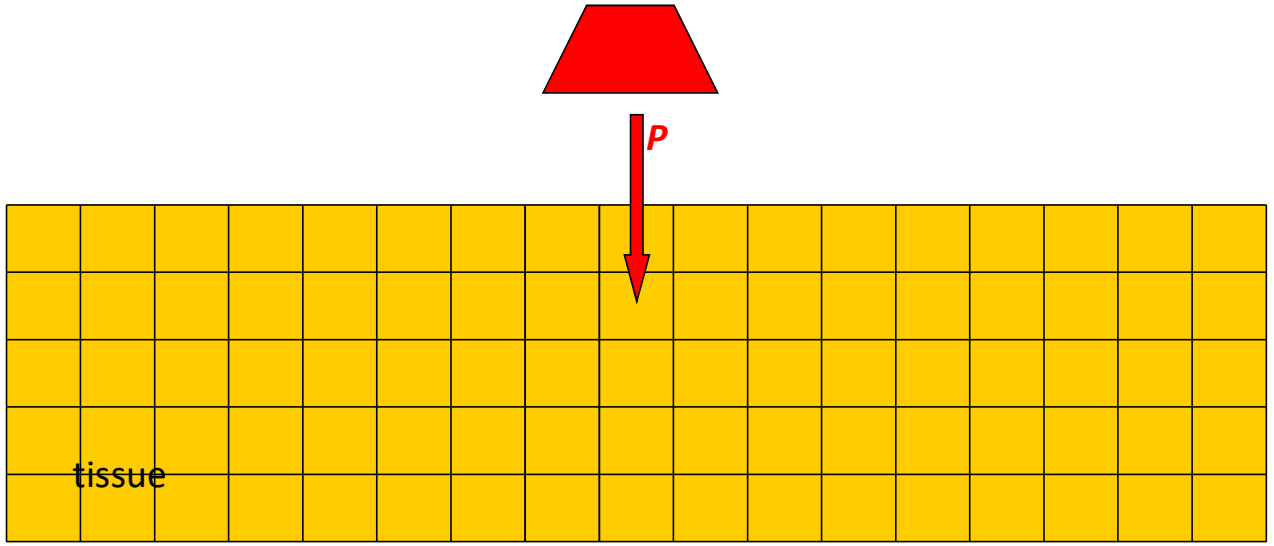
Heat transport by conduction

- Applicator depositing power



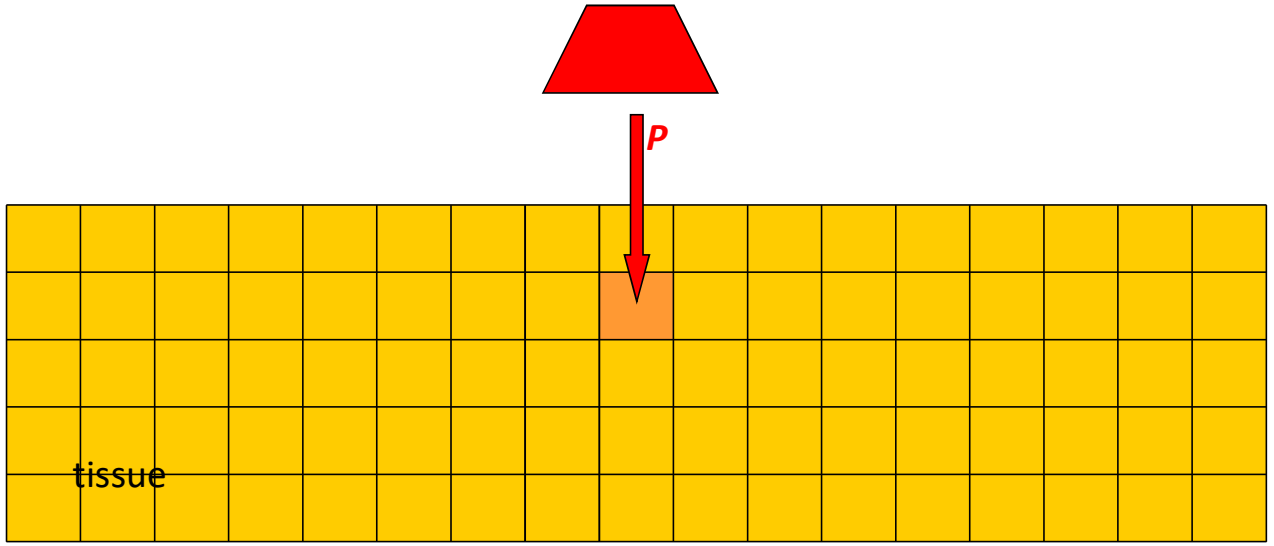
Heat transport by conduction

- Division into subvolumes: voxels



Heat transport by conduction

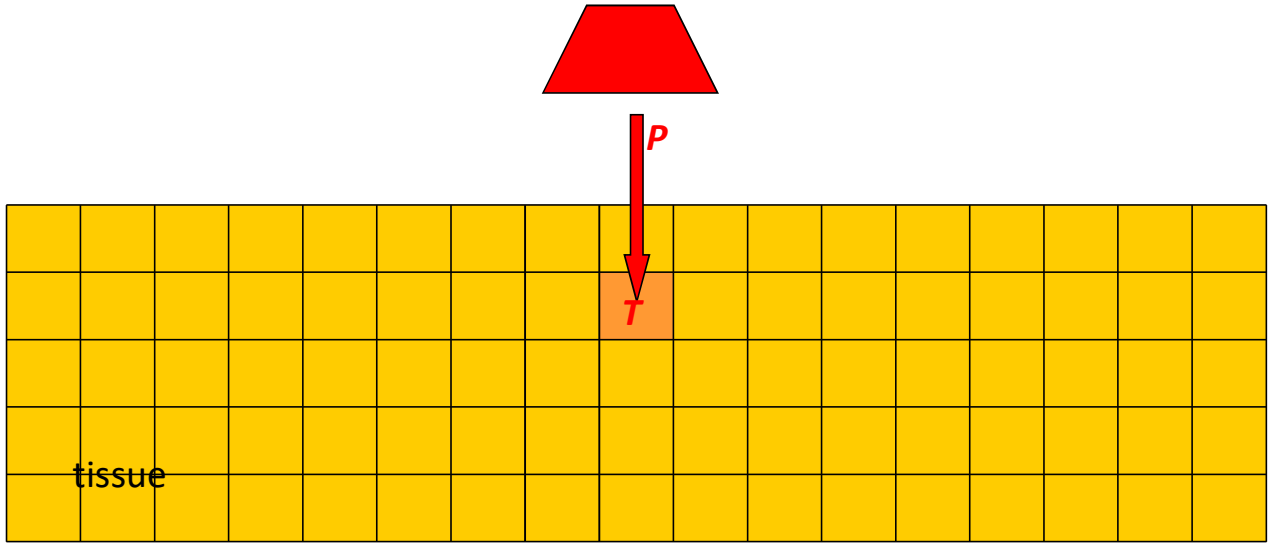
- heat balance for one voxel



Heat transport by conduction

$$c\rho\frac{\partial T}{\partial t} = \nabla\cdot\left(k\nabla T\right) + P$$

Energy balance equation



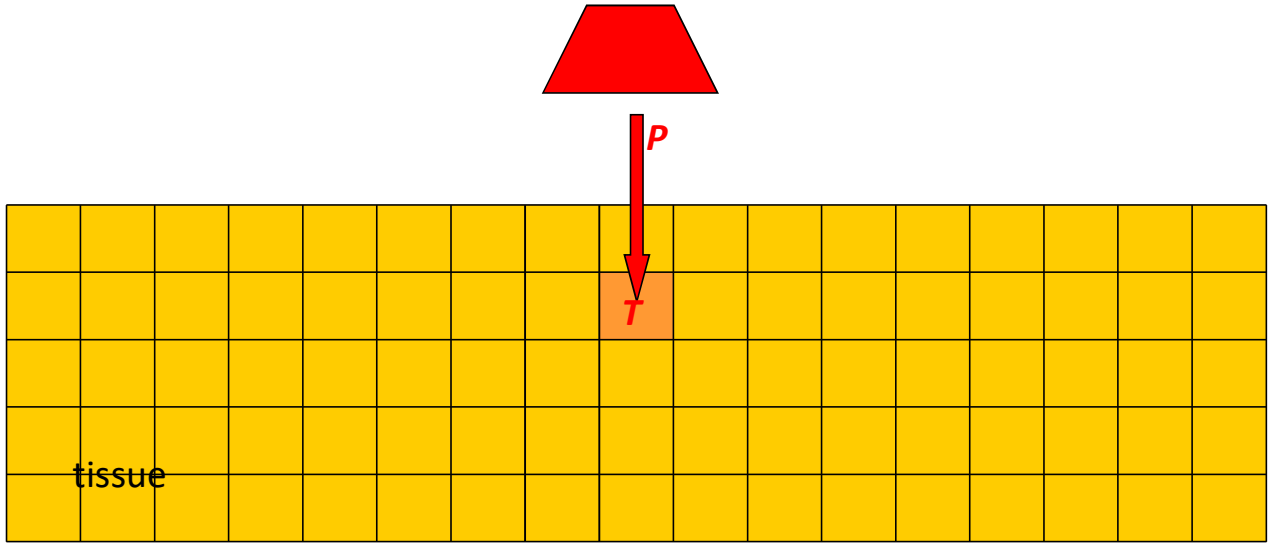
Heat transport by conduction

$$c\rho\frac{\partial T}{\partial t} = \nabla\cdot\left(k\nabla T\right) + P$$

- Temperature change $c\rho\frac{\partial T}{\partial t}$

  ρ tissue density

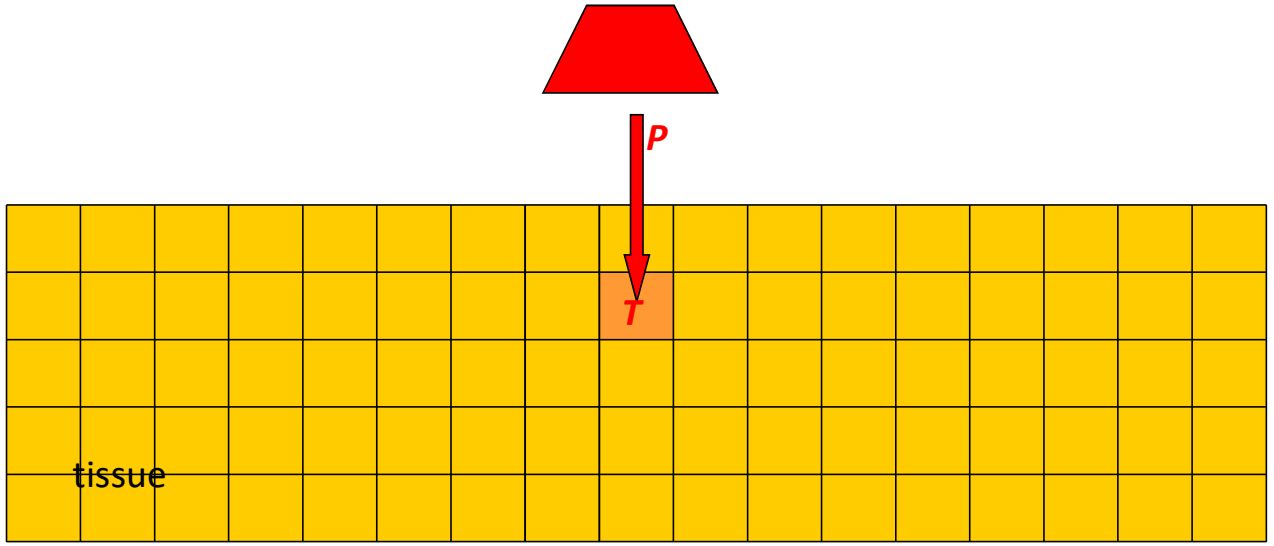
  c tissue heat capacity



Heat transport by conduction

$$c\rho\frac{\partial T}{\partial t} = \nabla\cdot\left(k\nabla T\right) + P$$

- Temperature change $c\rho\frac{\partial T}{\partial t}$
- Power density *P*

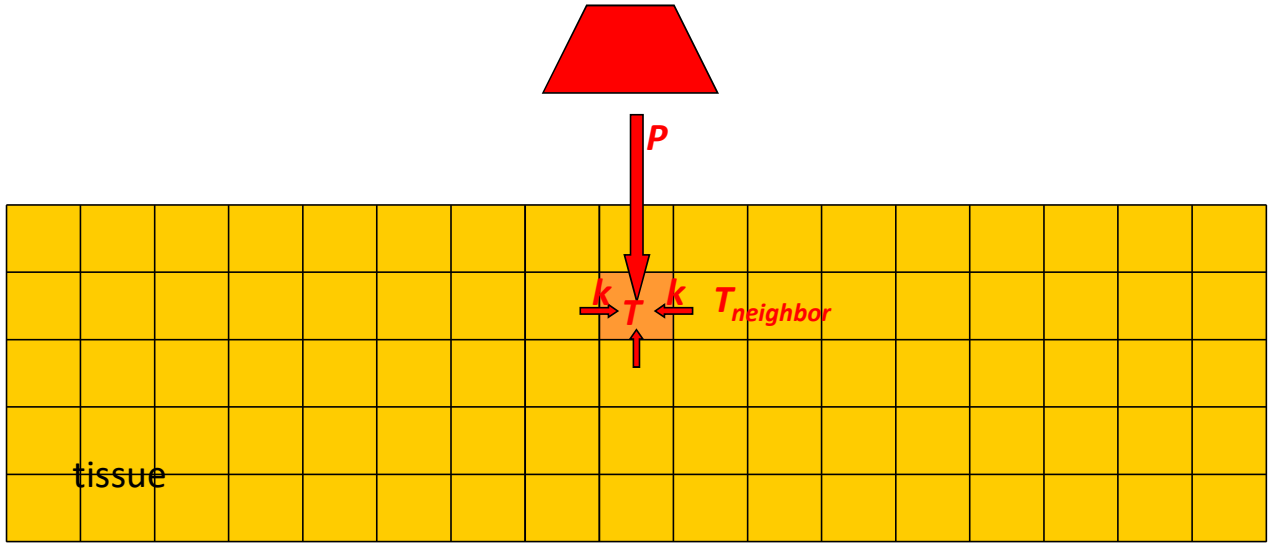


Heat transport by conduction

$$c\rho\frac{\partial T}{\partial t} = \nabla\cdot\left(k\nabla T\right) + P$$

- Temperature change $c\rho\frac{\partial T}{\partial t}$
- Power density *P*
- Conduction $\nabla\cdot\left(k\nabla T\right)$

  k tissue conductivity



Heat transport by conduction

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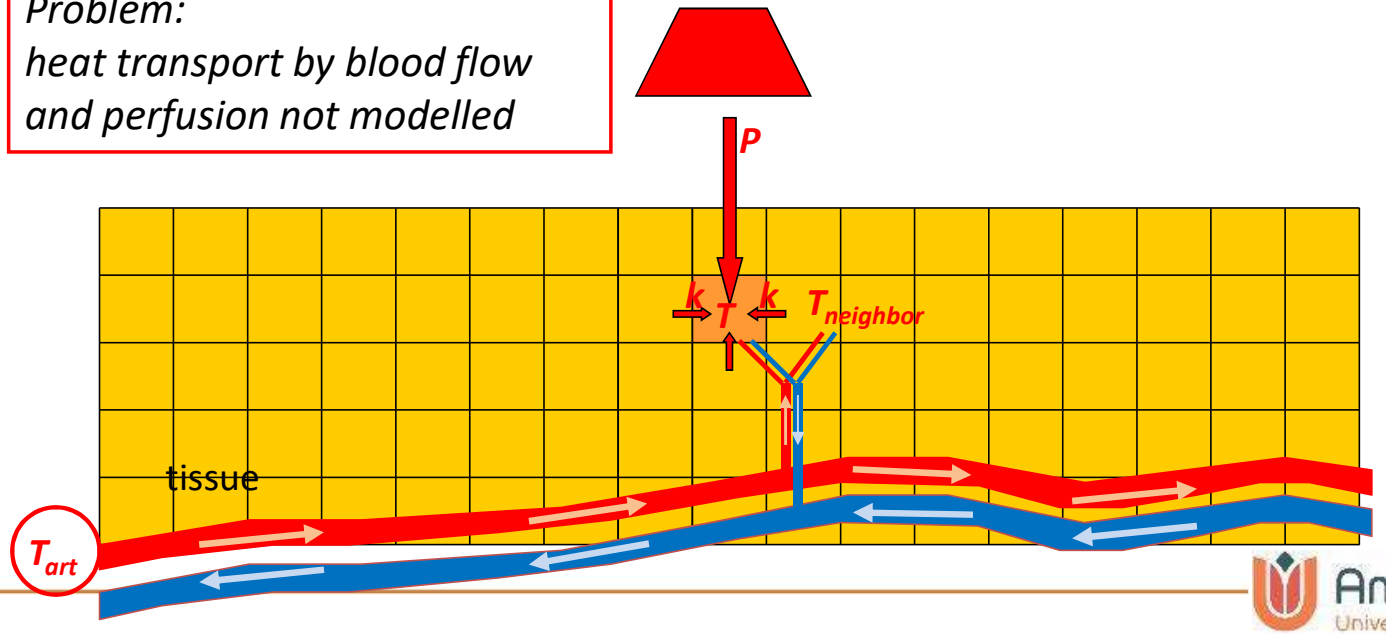
- Temperature change $c\rho\frac{\partial T}{\partial t}$
- Power density *P*
- Conduction $\nabla\cdot\left(k\nabla T\right)$

Problem:
heat transport by blood flow and perfusion not modelled



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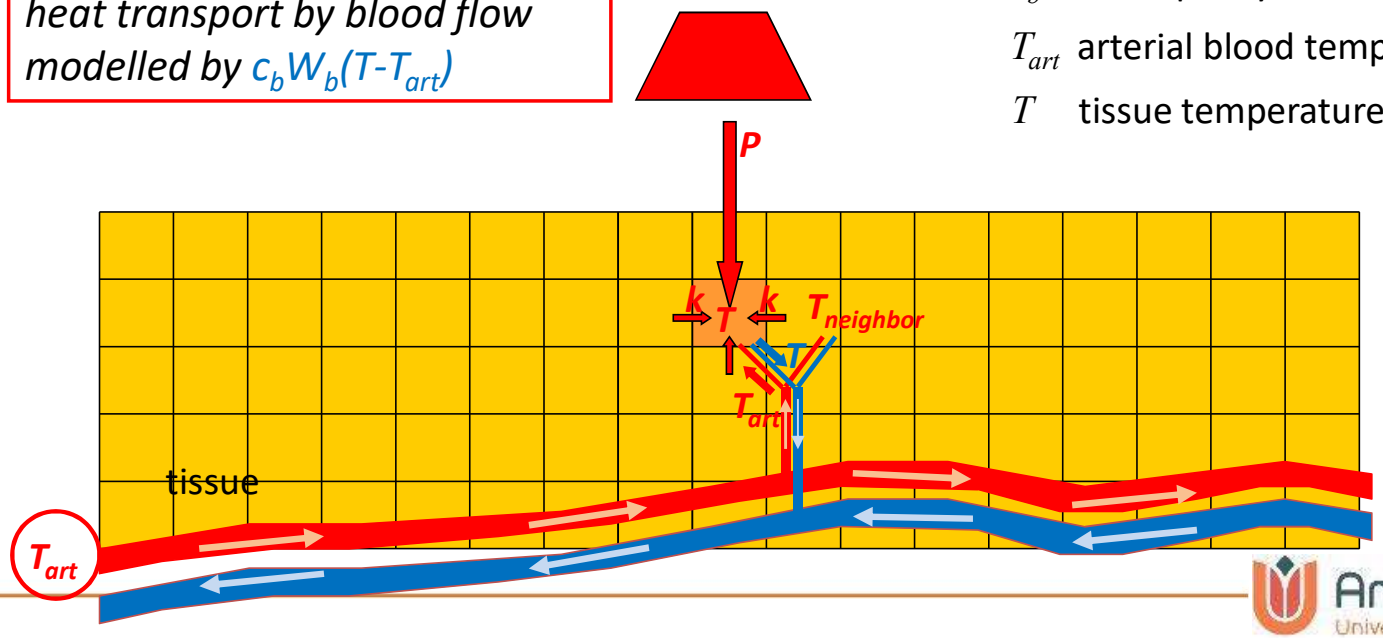
Pennes bio heat equation

$$c\rho\frac{\partial T}{\partial t} = \nabla\cdot\left(k\nabla T\right) - c_b W_b (T - T_{art}) + P$$

- Temperature change $c\rho\frac{\partial T}{\partial t}$
- Power density *P*
- Conduction $\nabla\cdot\left(k\nabla T\right)$
- Perfusion W_b
  - c_b heat capacity of blood
  - T_{art} arterial blood temperature
  - T tissue temperature

heat transport by blood flow modelled by $c_b W_b (T-T_{art})$



Pennes HH, *J Appl Physiol*. 1 93-122 (1948)

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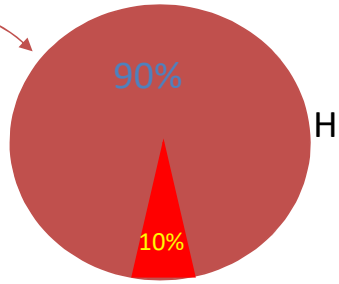

Heat removal

Perfusion is the dominant heat removal mechanism

Pennes bio heat equation

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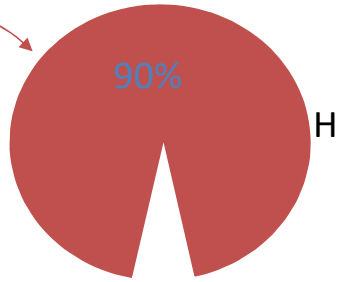

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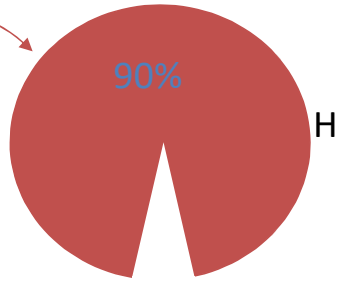

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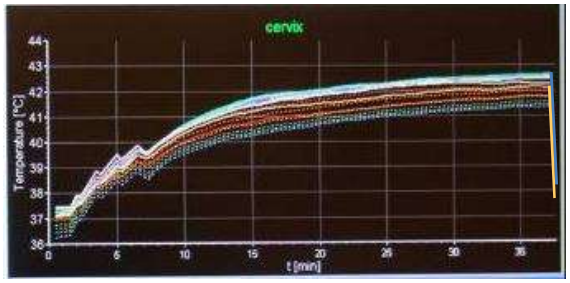
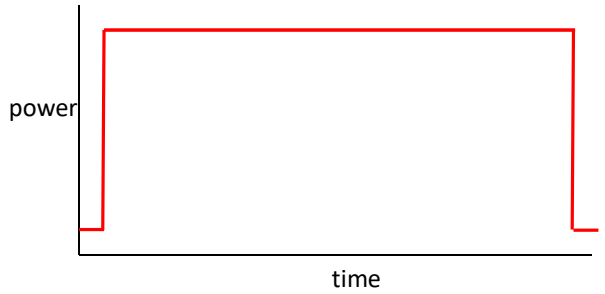


This equation simplifies interpretation of data:



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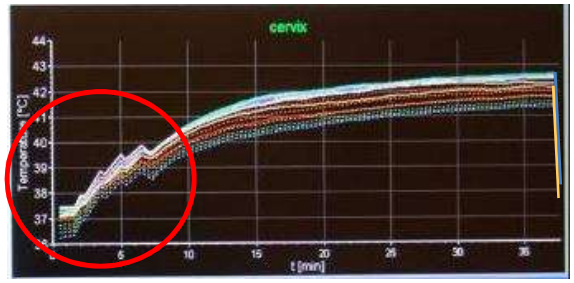
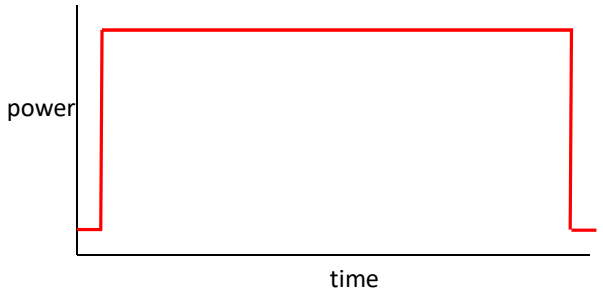


This equation simplifies interpretation of data:

- At the start of treatment



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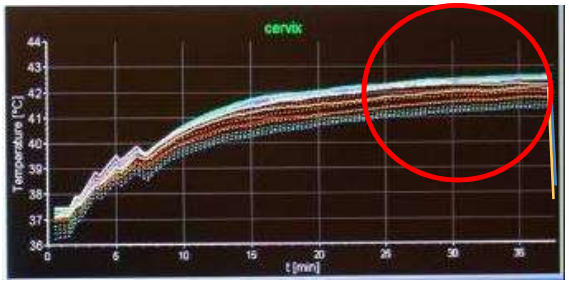
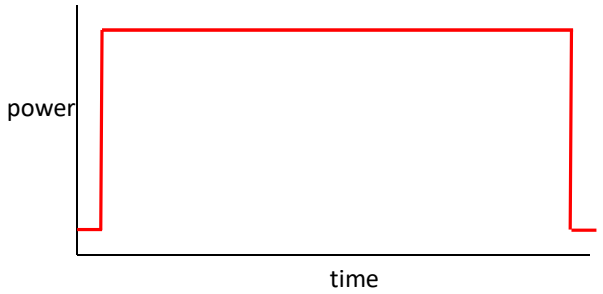


This equation simplifies interpretation of data:

- At the start of treatment
- During steady state



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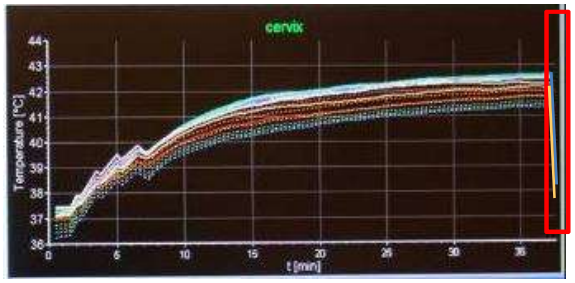
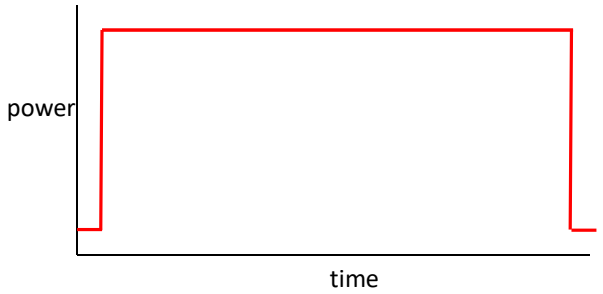


This equation simplifies interpretation of data:

- At the start of treatment
- During steady state
- After power off



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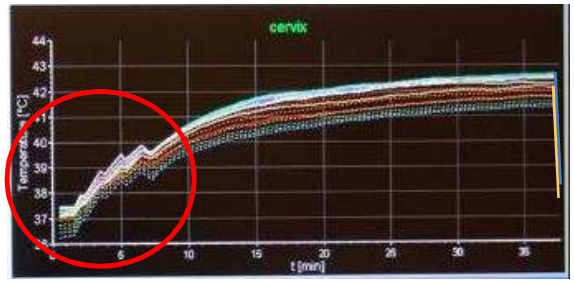
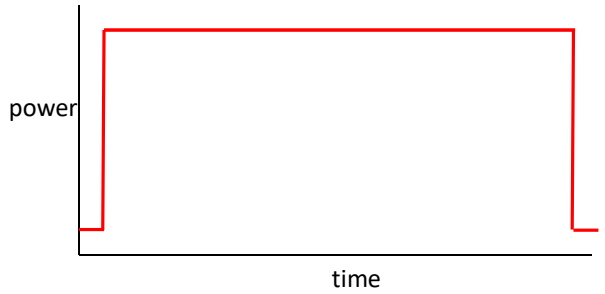
Pennes bio heat equation

$$c\rho\frac{\partial T}{\partial t} = -c_b W_b (T - T_{art}) + P$$

At the start of treatment $T = T_{art}$:





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Van Haaren et al, *Int J Hyperthermia* 23: 303-314 (2007)

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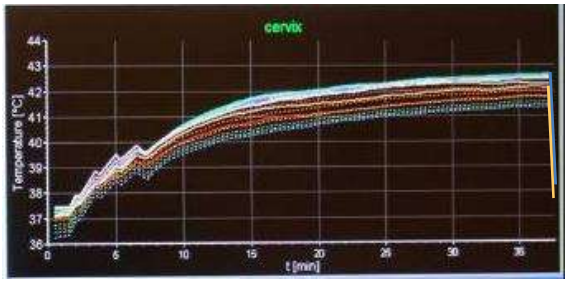

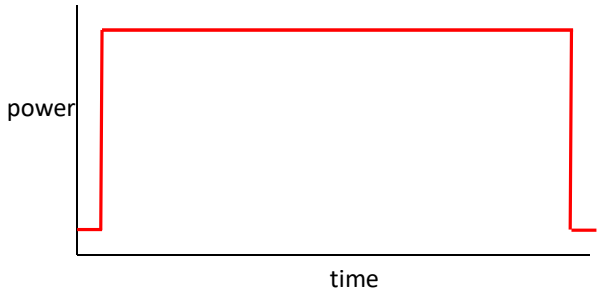

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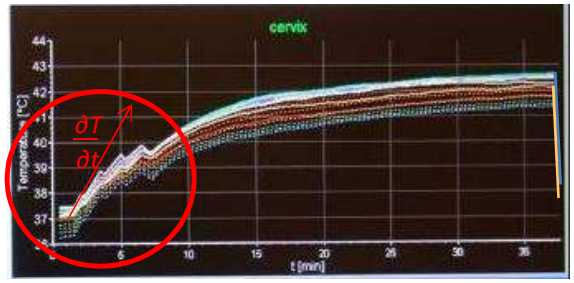
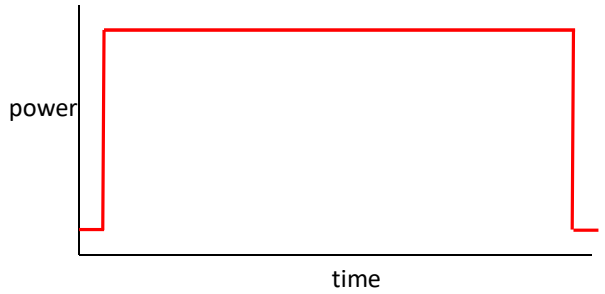


At the start of treatment $T = T_{art}$:

$$c\rho\frac{\partial T}{\partial t} = P$$



At start of treatment:
rate of temperature rise is proportional to absorbed power *P*

Van Haaren et al, *Int J Hyperthermia* 23: 303-314 (2007)

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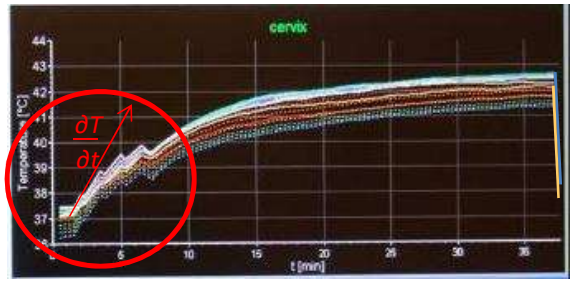

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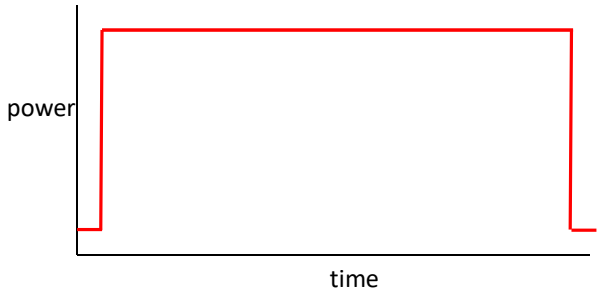

At start of treatment:
rate of temperature rise is proportional to absorbed power *P*

Temperature rise after 60 sec power pulse indicative for *P* distribution

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Van Haaren et al, *Int J Hyperthermia* 23: 303-314 (2007)

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$$c\rho\frac{\partial T}{\partial t} = -c_b W_b (T - T_{art}) + P$$

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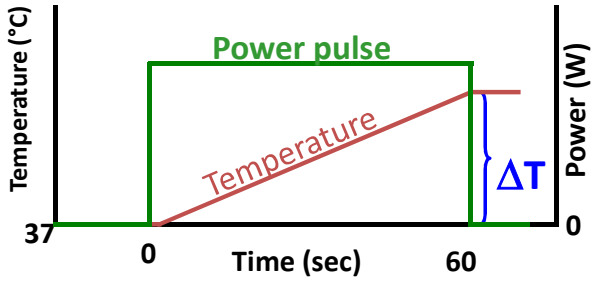

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Temperature rise after 60 sec power pulse indicative for *P* distribution

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Pennes bio heat equation

Power pulse procedure prescribed in 1989 ESHO QA guidelines

6. Characterization of applicators

6.1. The effective field size (EFS) of an applicator is defined by the 50% SAR contour measured at a depth of 10 mm from the surface of a plane homogeneous phantom with the dielectric properties of muscle. The penetration depth (PD) is defined as the distance below 10 mm at which the SAR is 50% of that at 10 mm depth. Measurements to determine the penetration depth must be made from the position of maximum SAR at 10 mm depth.

6.2. Both EFS and PD must be measured with the applicator arranged as the 'clinical set-up', including a bolus if appropriate. If a bolus is used, then its temperature should be equal to the initial temperature of the phantom.

6.3. EFS and PD should be determined by measuring the changes in temperature resulting from a brief pulse of high power. If non-perturbing E-field probes, thermographic imaging or liquid-crystal sheet imaging are used to determine SAR distributions, such measurements should be corroborated by measurements obtained using the power pulse technique.

6.4. If either a radiofrequency capacitive technique or a multi-element array of applicators is used, the EFS can depend critically on the particular geometry involved. Additional characterization of these techniques should be attempted using geometrically realistic phantoms.

6.5. When using the power pulse technique, measurements to determine the EFS and PD must be made within 60 seconds of the start of the pulse to minimize artefacts caused by thermal conduction within the phantom.

6.6. The plane muscle phantom used for determining EFS and PD must be 10 cm thick and must extend at least 5 cm beyond the physical dimensions of the applicator and bolus. In the case of radiofrequency capacitive electrodes, the thickness of the phantom should be equal to that of the tissue between the electrodes in the clinical set-up.

Temperature rise after 60 sec power pulse indicative for *P* distribution

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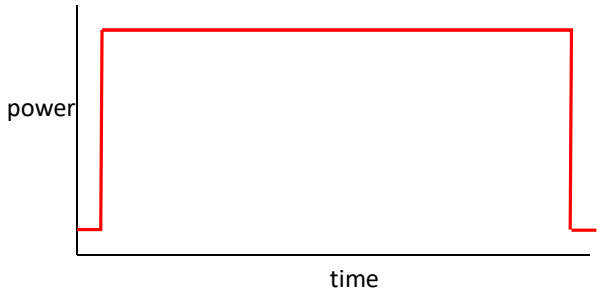
Hand et al, *Int J Hyperthermia* 5: 421-428 (1989)

Pennes bio heat equation

$$c\rho\frac{\partial T}{\partial t} = -c_b W_b (T - T_{art}) + P$$

At steady state $c\rho\frac{\partial T}{\partial t} = 0$:



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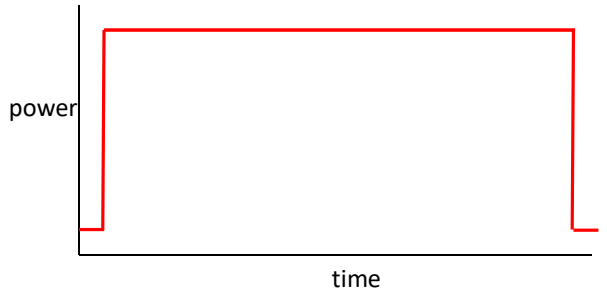
$$\cancel{c\rho\frac{\partial T}{\partial t}} = -c_b W_b (T - T_{art}) + P$$

At steady state $c\rho\frac{\partial T}{\partial t} = 0$:



Pennes bio heat equation

$$\cancel{c\rho\frac{\partial T}{\partial t}} = -c_b W_b (T - T_{art}) + P$$

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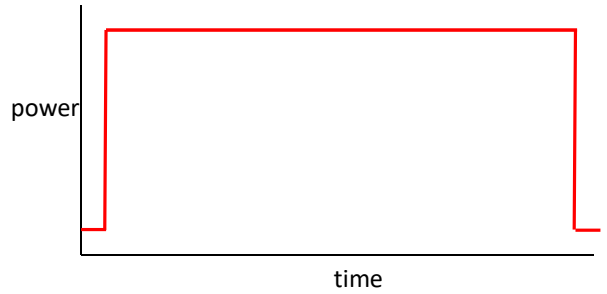

During steady state:
Temperature rise T-T_{art} is proportional to absorbed power P

Pennes bio heat equation

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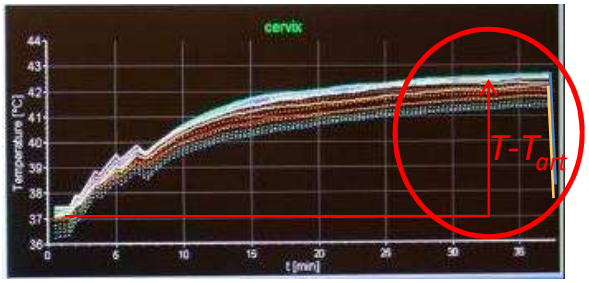

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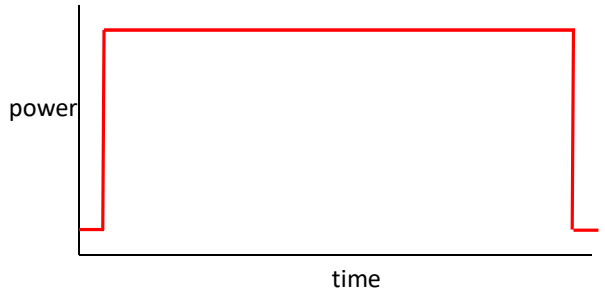

During steady state:
Temperature rise T-T_{art} is proportional to absorbed power P

Absorbed power distribution indicative for temperature distribution

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Pennes bio heat equation

measurement of Absorbed Power distribution prescribed to characterise applicators in 1989 ESHO QA guidelines

6. Characterization of applicators

6.1. The effective field size (EFS) of an applicator is defined by the 50% SAR contour measured at a depth of 10 mm from the surface of a plane homogeneous phantom with the dielectric properties of muscle. The penetration depth (PD) is defined as the distance below 10 mm at which the SAR is 50% of that at 10 mm depth. Measurements to determine the penetration depth must be made from the position of maximum SAR at 10 mm depth.

6.2. Both EFS and PD must be measured with the applicator arranged as the 'clinical set-up', including a bolus if appropriate. If a bolus is used, then its temperature should be equal to the initial temperature of the phantom.

6.3. EFS and PD should be determined by measuring the changes in temperature resulting from a brief pulse of high power. If non-perturbing E-field probes, thermographic imaging or liquid-crystal sheet imaging are used to determine SAR distributions, such measurements should be corroborated by measurements obtained using the power pulse technique.

6.4. If either a radiofrequency capacitive technique or a multi-element array of applicators is used, the EFS can depend critically on the particular geometry involved. Additional characterization of these techniques should be attempted using geometrically realistic phantoms.

6.5. When using the power pulse technique, measurements to determine the EFS and PD must be made within 60 seconds of the start of the pulse to minimize artefacts caused by thermal conduction within the phantom.

6.6. The plane muscle phantom used for determining EFS and PD must be 10 cm thick and must extend at least 5 cm beyond the physical dimensions of the applicator and bolus. In the case of radiofrequency capacitive electrodes, the thickness of the phantom should be equal to that of the tissue between the electrodes in the clinical set-up.

Absorbed power distribution indicative for temperature distribution

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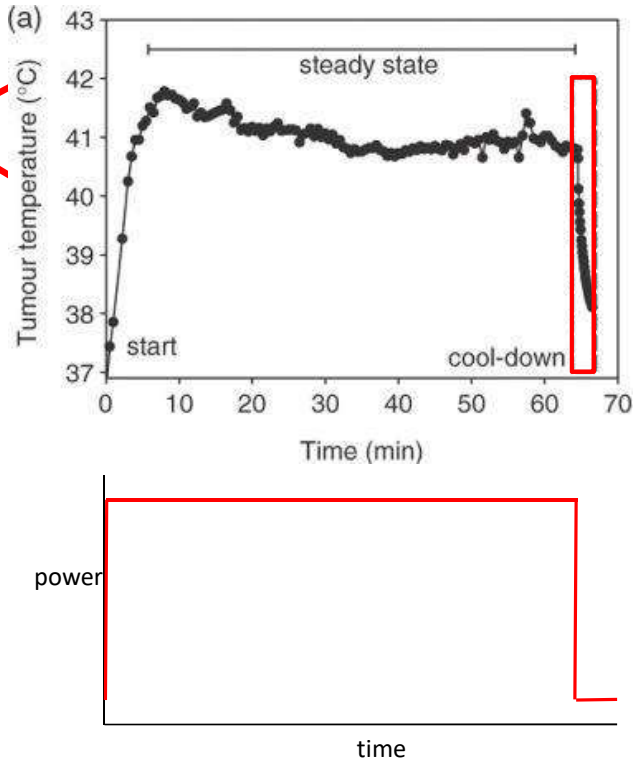
Hand et al, *Int J Hyperthermia* 5: 421-428 (1989)

Pennes bio heat equation

$$c\rho\frac{\partial T}{\partial t} = -c_b W_b (T - T_{art}) + P$$

After power off: $P = 0$



Van Haaren et al, *Int J Hyperthermia* 24: 663-674 (2008)

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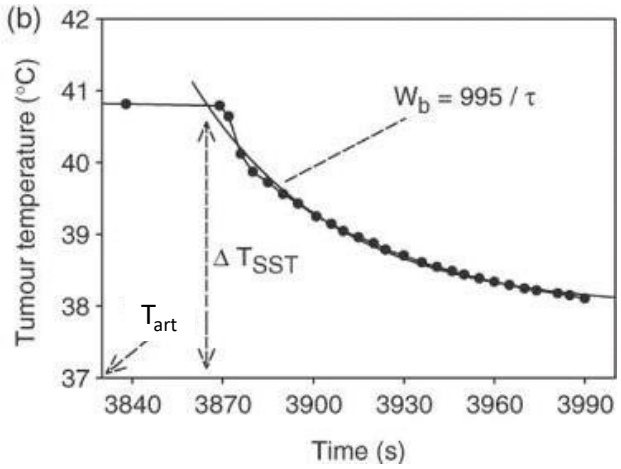
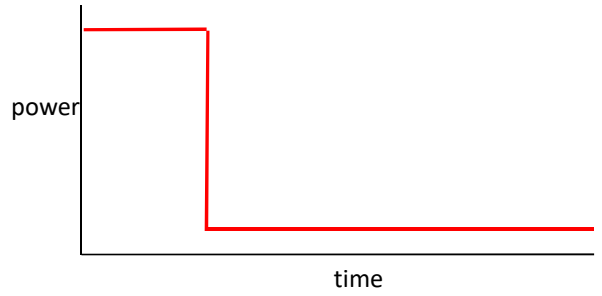
Pennes bio heat equation

$$c\rho\frac{\partial T}{\partial t} = -c_b W_b (T - T_{art})$$

fit an exponential function:

$$T(t) = T_{art} + \Delta T_{SST} \cdot \exp(-t/\tau)$$





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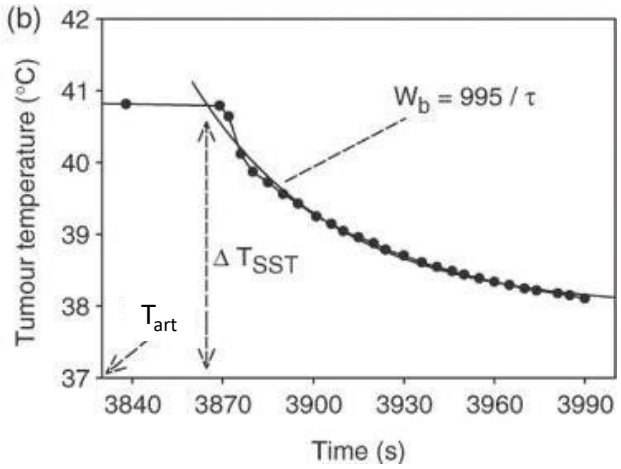

fit an exponential function:

$$T(t) = T_{art} + \Delta T_{SST} \cdot \exp(-t/\tau)$$

yields:

$$\rho_t c_t \cdot \frac{-\Delta T_{SST}}{\tau} \cdot \exp(-t/\tau) = -c_b W_b \cdot \Delta T_{SST} \cdot \exp(-t/\tau)$$

$$W_b = \frac{\rho_t c_t}{c_b \tau}$$

Van Haaren et al, *Int J Hyperthermia* 24: 663-674 (2008)

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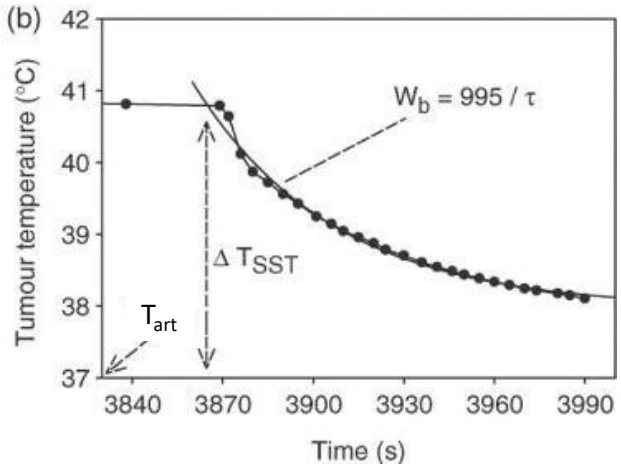

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Perfusion W_b can be derived from decay time

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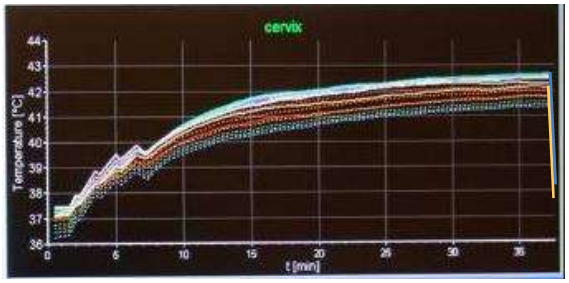
Van Haaren et al, *Int J Hyperthermia* 24: 663-674 (2008)

Pennes bio heat equation

$$c\rho\frac{\partial T}{\partial t} = -c_b W_b (T - T_{art}) + P$$



This simple equation allows us to derive parameters from measured *T* data:

- power density *P*
- tissue perfusion W_b

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Pennes bio heat equation

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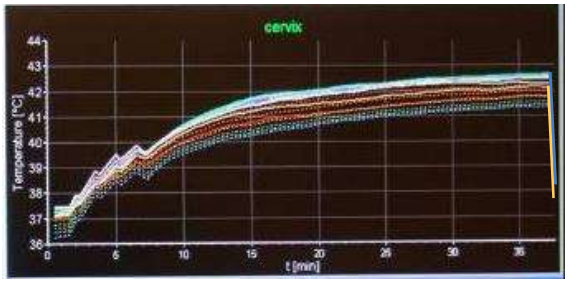

This simple equation allows us to derive parameters from measured *T* data:

- power density *P*
- tissue perfusion W_b

But is this correct?

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Heat transport in tissue

- Bio-heat equation
  - Different models used
    - Pennes bio heat equation
    - Effective conductivity
    - Discrete vessels

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Review: Kok *et al*. *Int J Hyperthermia* 29: 336 – 345 (2013)

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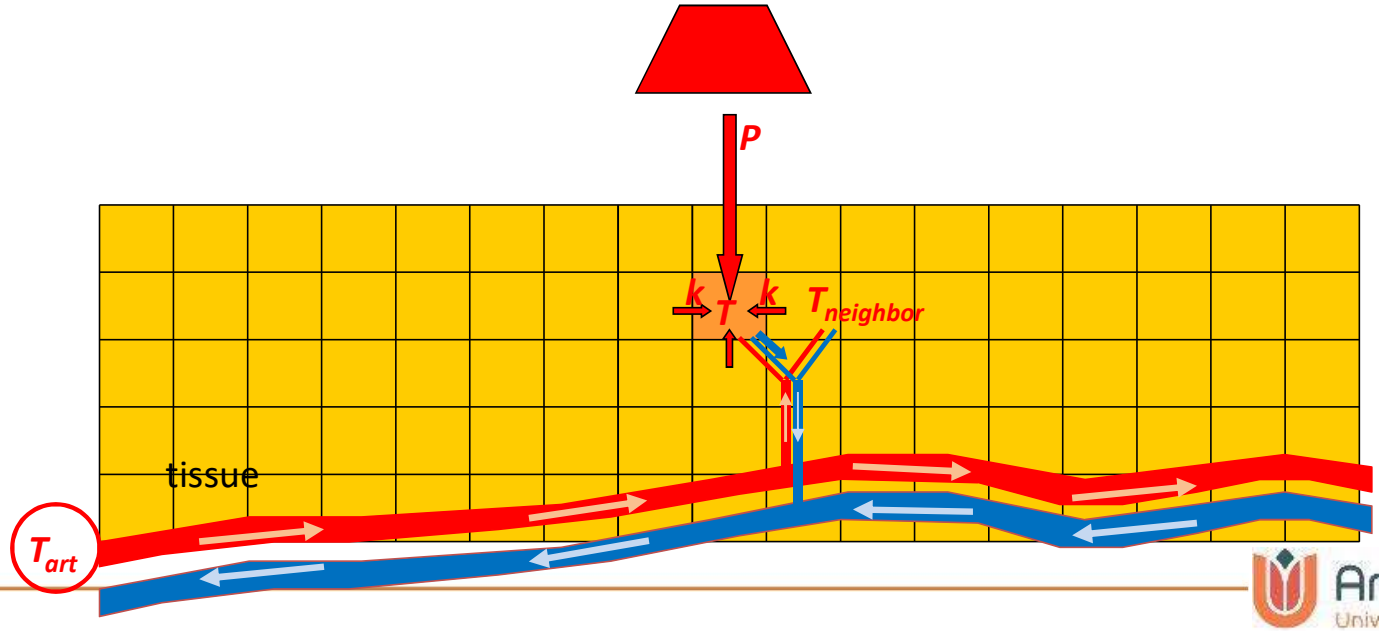
Review: Kok *et al*. *Int J Hyperthermia* 29: 336 – 345 (2013)

Heat transport in tissue

$$c\rho\frac{\partial T}{\partial t} = \nabla\cdot(k\nabla T) - c_b W_b (T - T_{art}) + P$$

- T_{art} = 37°C



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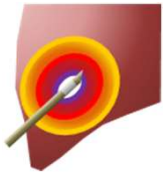
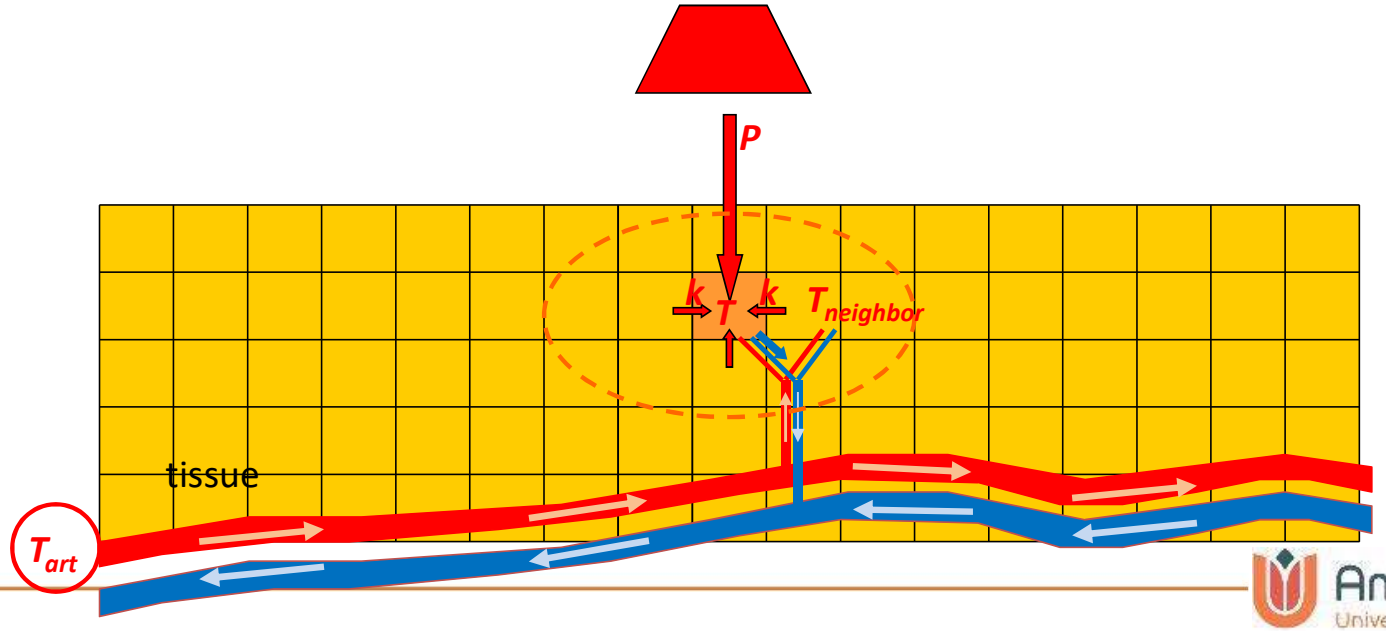
Heat transport in tissue

$$c\rho\frac{\partial T}{\partial t} = \nabla\cdot(k\nabla T) - c_b W_b (T - T_{art}) + P$$

- T_{art} = 37°C
- Validity assumption:
  - small heated volume ☺





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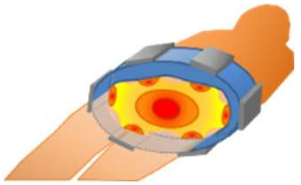

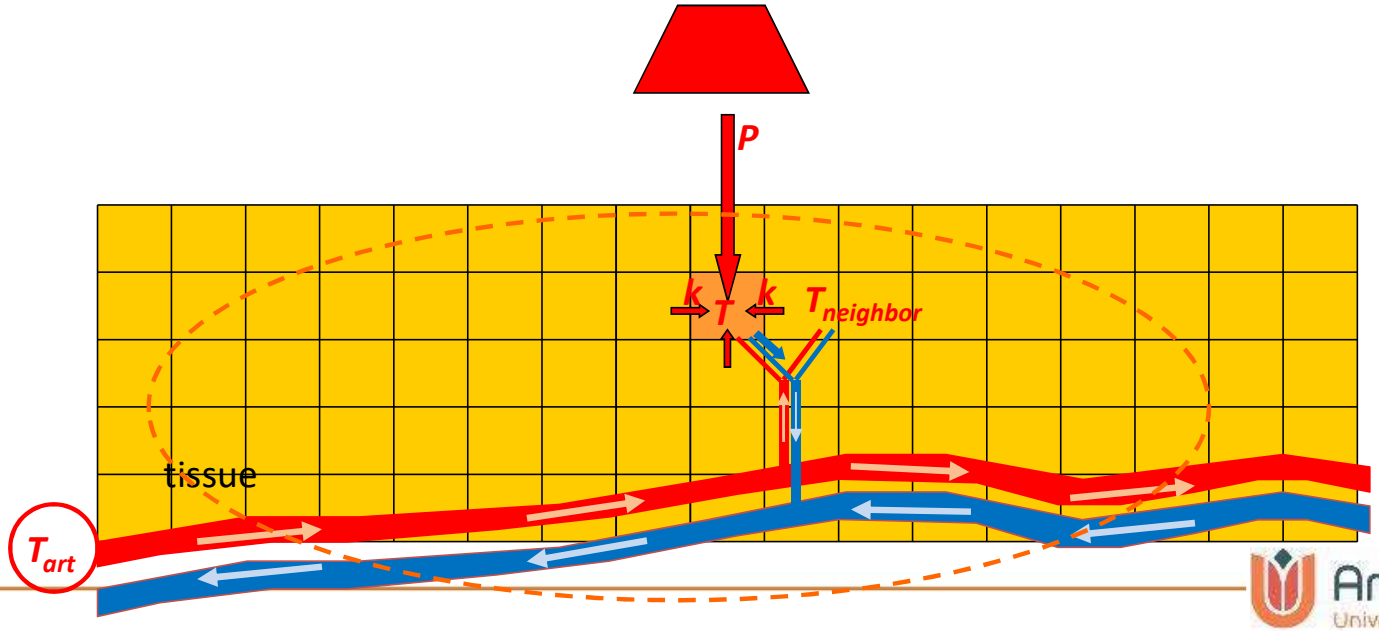

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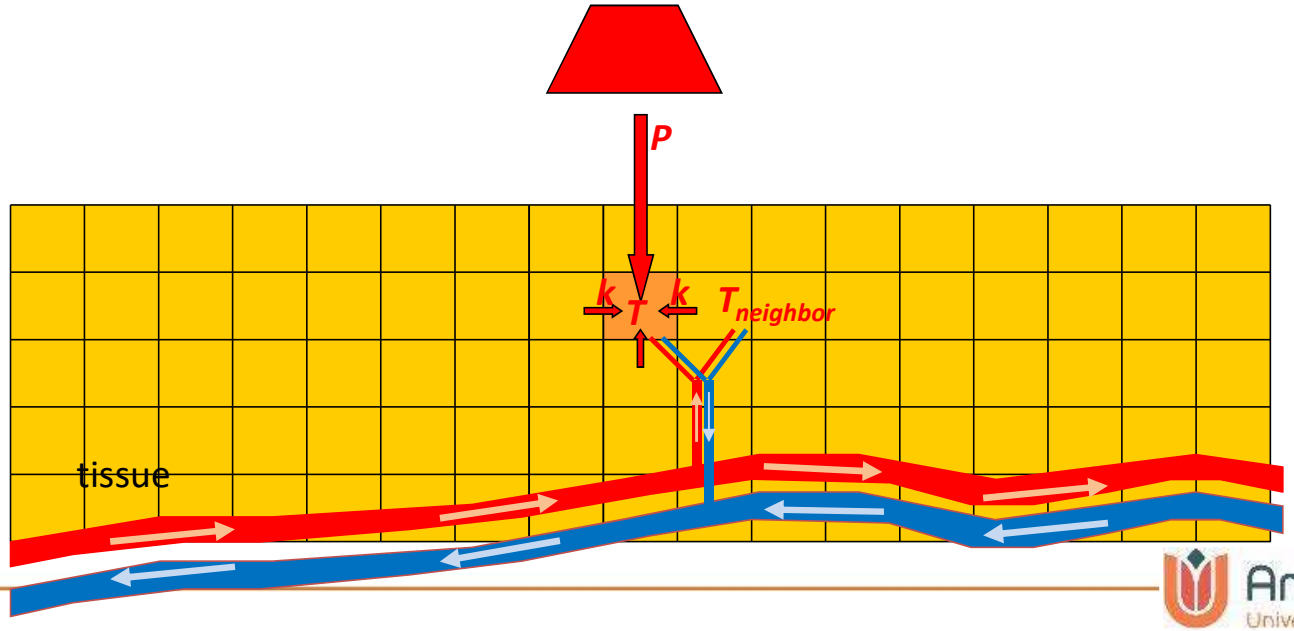
Heat transport in tissue

$$c\rho\frac{\partial T}{\partial t} = \nabla\cdot\left(k\nabla T\right) + P$$

- Temperature change $c\rho\frac{\partial T}{\partial t}$
- Power density *P*
- Conduction $\nabla\cdot\left(k\nabla T\right)$



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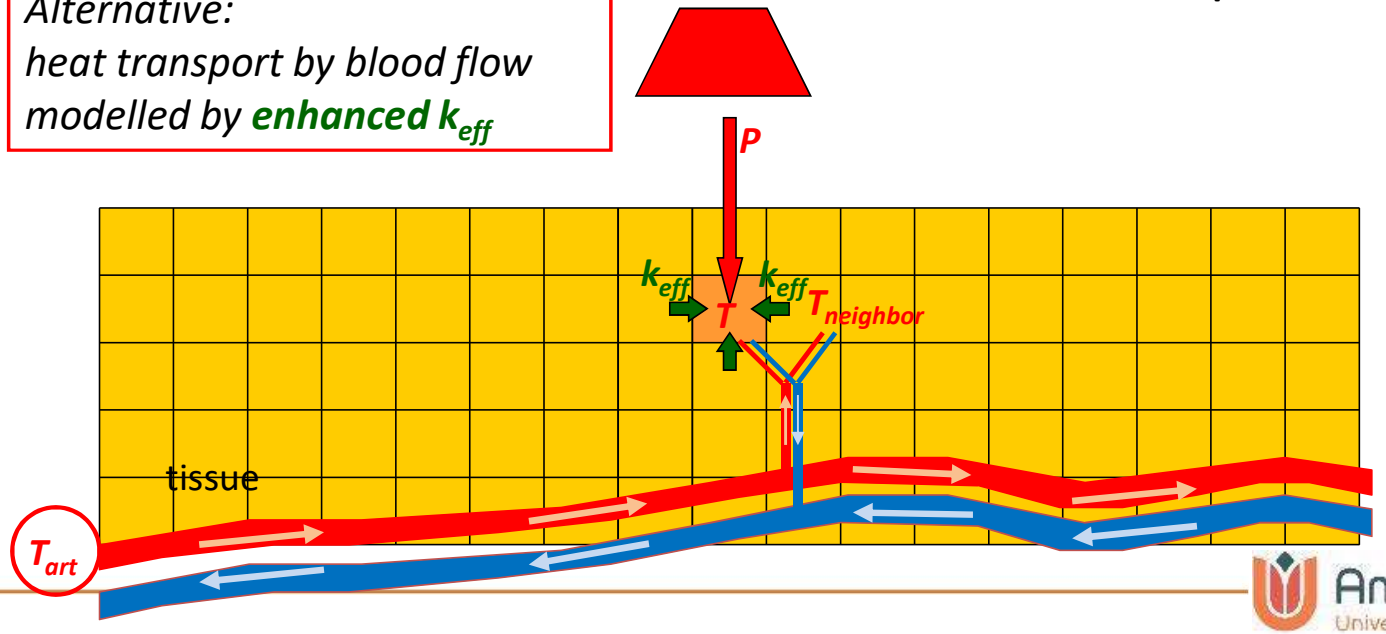
Heat transport in tissue

$$c\rho\frac{\partial T}{\partial t} = \nabla\cdot\left(k_{eff}\nabla T\right) + P$$

- Temperature change $c\rho\frac{\partial T}{\partial t}$
- Power density *P*
- Conduction $\nabla\cdot\left(k_{eff}\nabla T\right)$

Represents **conduction** and **perfusion**

Alternative:
heat transport by blood flow modelled by ***enhanced*** k_{eff}



Crezee et al *Phys Med Biol* 39 813-822 (1994)

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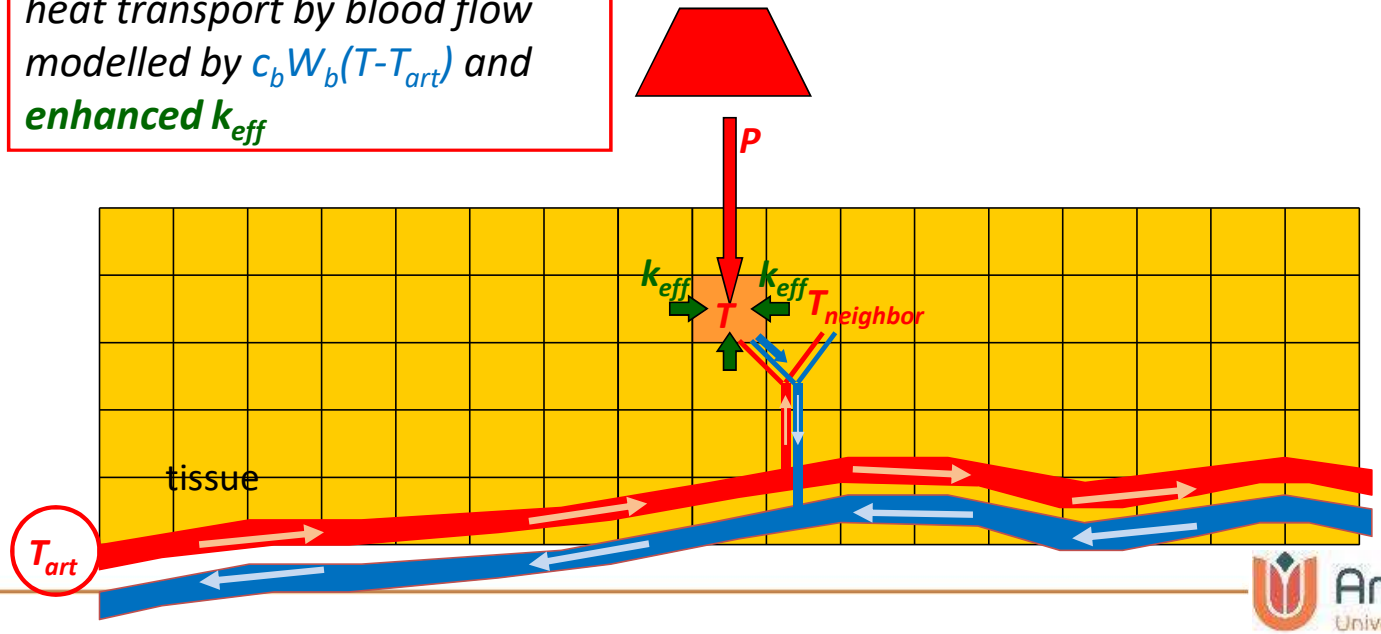
Heat transport in tissue

$$c\rho\frac{\partial T}{\partial t} = \nabla\cdot\left(k_{eff}\nabla T\right) - c_b W_b (T - T_{art}) + P$$

- Temperature change $c\rho\frac{\partial T}{\partial t}$
- Power density P
- Conduction $\nabla\cdot\left(k_{eff}\nabla T\right)$
- Perfusion W_b

heat transport by blood flow modelled by $c_b W_b (T-T_{art})$ and ***enhanced k_{eff}***



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Crezee et al *Phys Med Biol* 39 813-822 (1994)

Heat transport in tissue

- Bio-heat equation
  - Different models used
    - Pennes bio heat equation
    - Effective conductivity
    - Discrete vessels

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Review: Kok *et al*. *Int J Hyperthermia* 29: 336 – 345 (2013)

Heat transport in tissue

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Discussed later

Review: Kok *et al*. *Int J Hyperthermia* 29: 336 – 345 (2013)

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Heat transport in tissue

- Bio-heat equation
- Thermal properties of tissues
- Vascular cooling

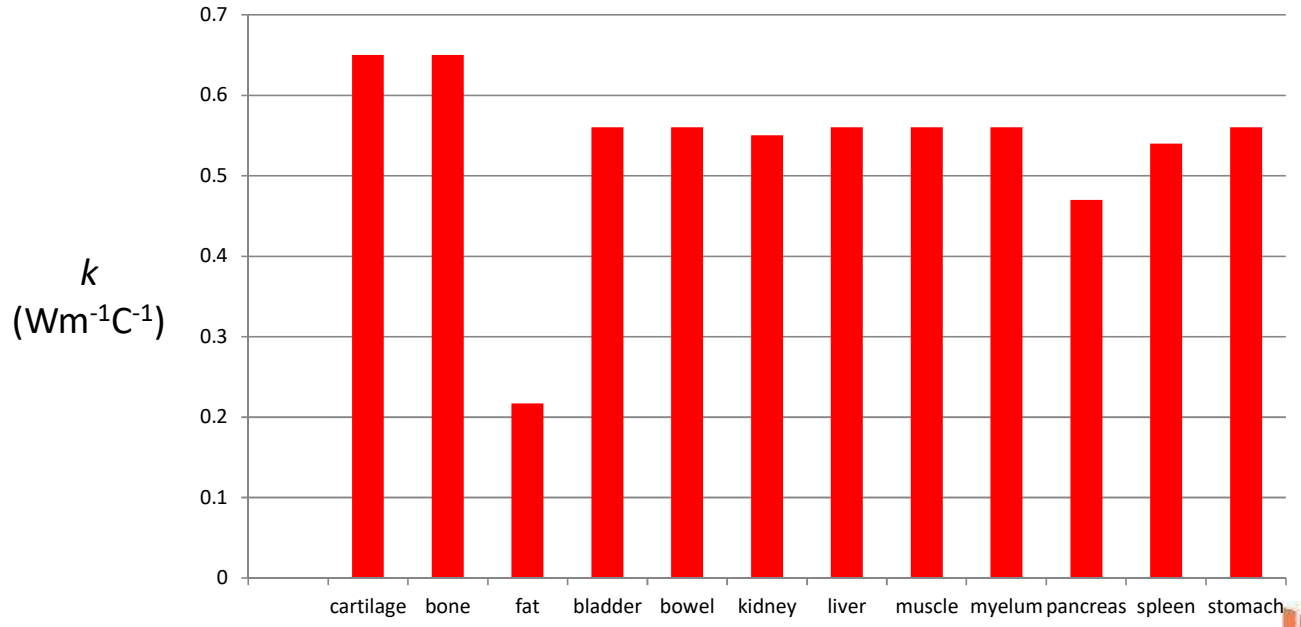
Thermal properties of tissue

Relevant thermal properties:

- Conduction
- Blood flow

Thermal properties of tissue

Thermal conduction:



ESHO task group committee *Treatment planning and modelling in hyperthermia* (1992)

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Thermal properties of tissue

Thermal conduction:

ESHO task group committee *Treatment planning and modelling in hyperthermia* (1992)

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Thermal properties of tissue

Blood flow depends on:

- Tissue type

Thermal properties of tissue

Blood flow depends on:

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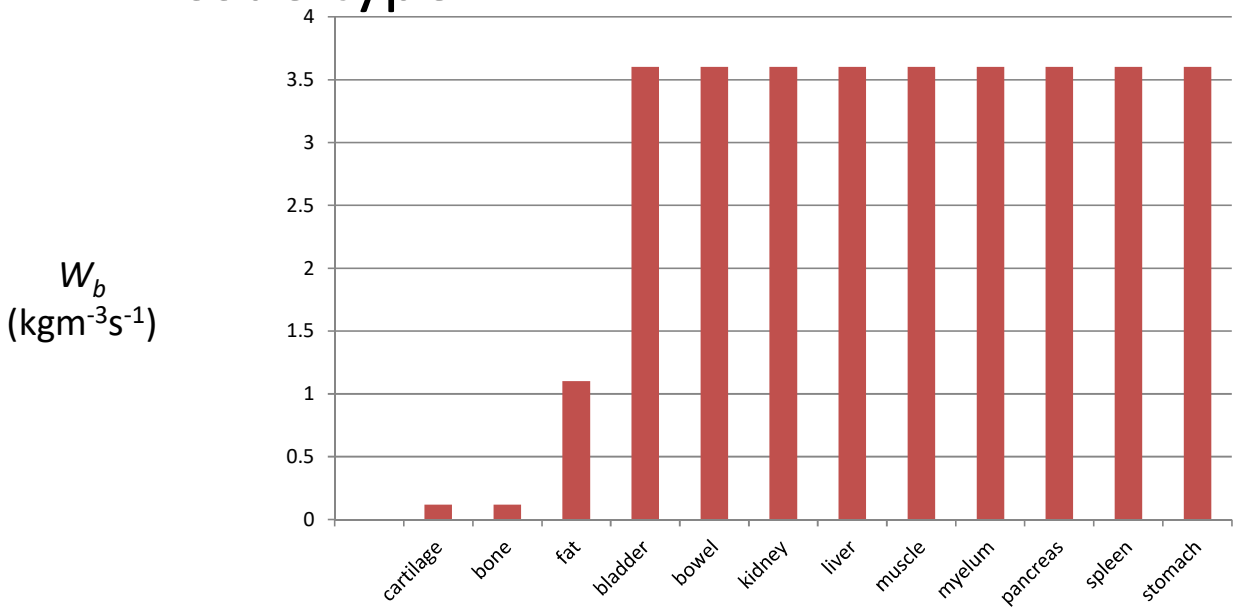

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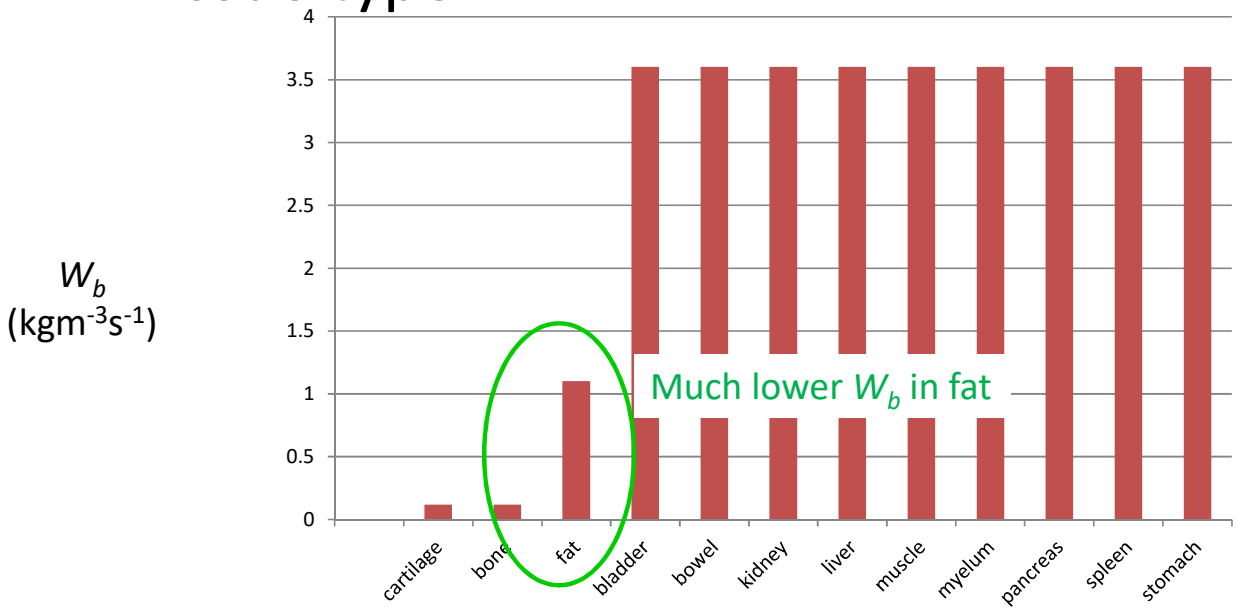

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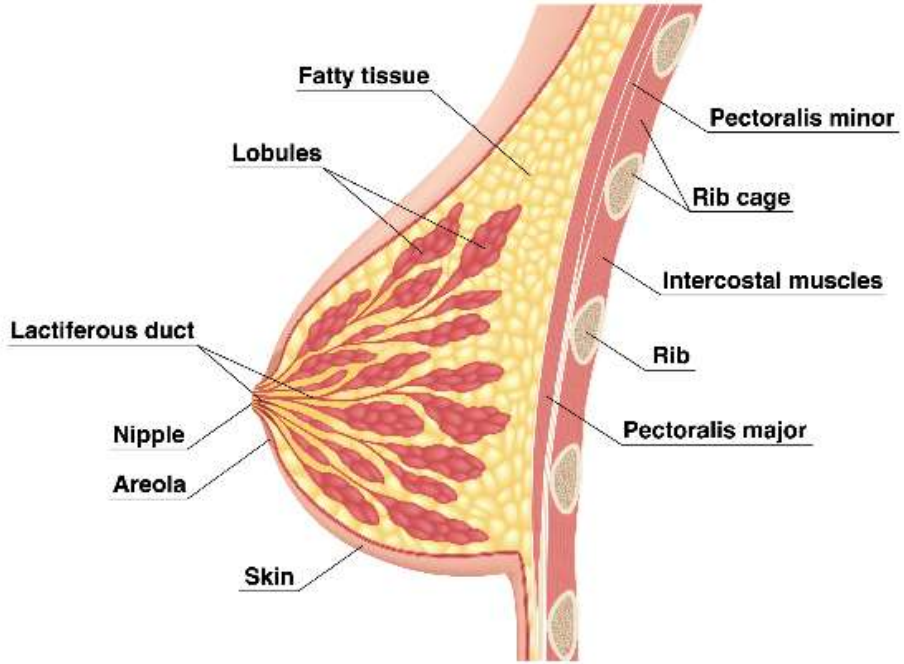
ESHO task group committee *Treatment planning and modelling in hyperthermia* (1992)

Thermal properties of tissue

Blood flow depends on:

- Tissue type
- Detailed data in recent reviews



ω_t (kg/s/m^3) of healthy and tumour breast tissue.

Fibroglandular	Fat	Tumour Tissue
Min. Max.	Min. Max.	Min. Max.
0.189-0.754	0.014-8.798	0.530-22.260

Said Camilleri et al, *Sensors (Basel).* 2022;22:3894

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Thermal properties of tissue

Blood flow depends on:

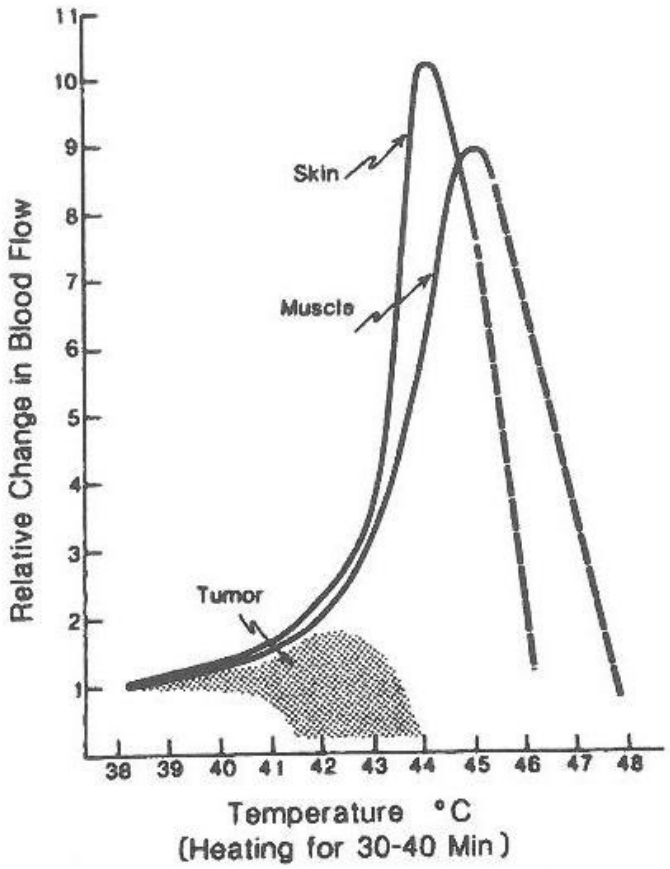
- Tissue type
- Detailed data in recent reviews
  - ITIS database popular

https://itis.swiss/virtual-population/tissue-properties/database/

Thermal properties of tissue

Blood flow depends on:

- Tissue type
- Temperature



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Song *Cancer Res* vol 44 4721s-4730s 1984

Thermal properties of tissue

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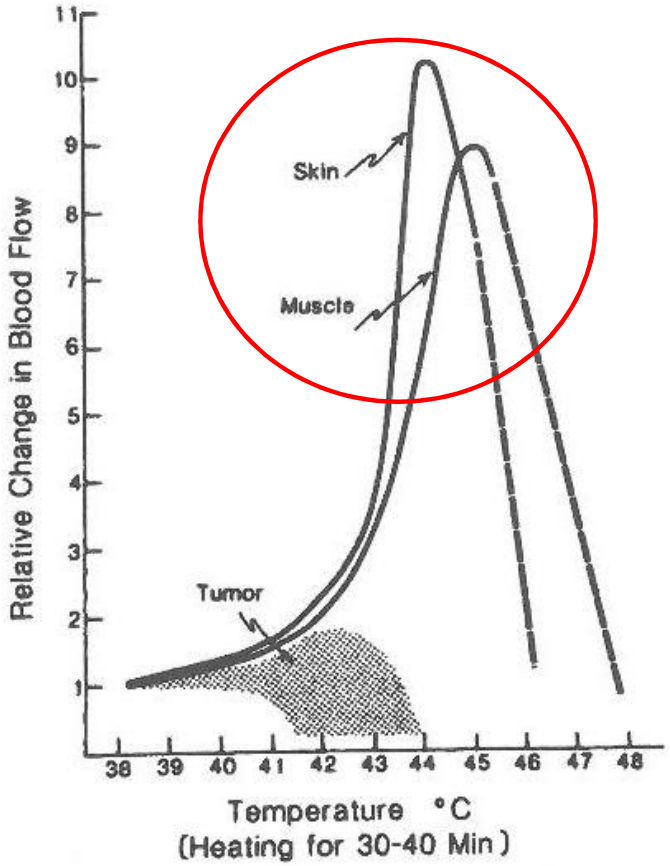

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Song *Cancer Res* vol 44 4721s-4730s 1984

Thermal properties of tissue

Blood flow depends on:

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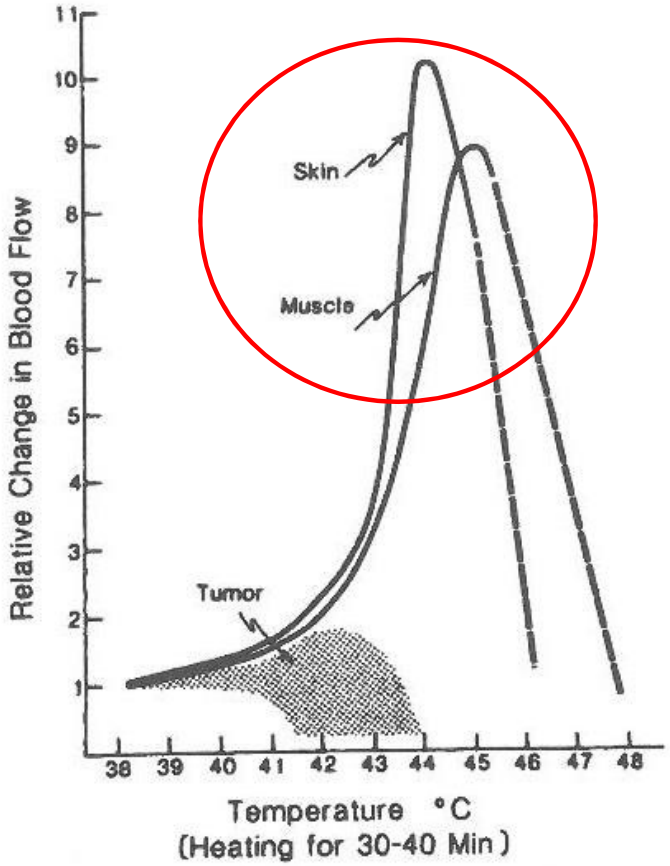
published perfusion data are generally valid under normothermic conditions



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Song *Cancer Res* vol 44 4721s-4730s 1984

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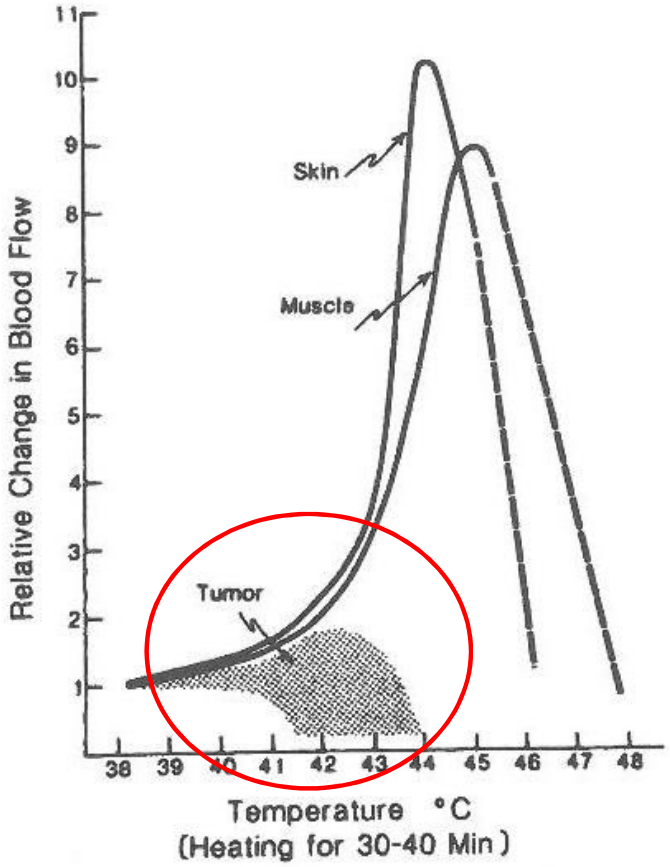

Song *Cancer Res* vol 44 4721s-4730s 1984

Thermal properties of tissue

Blood flow depends on:

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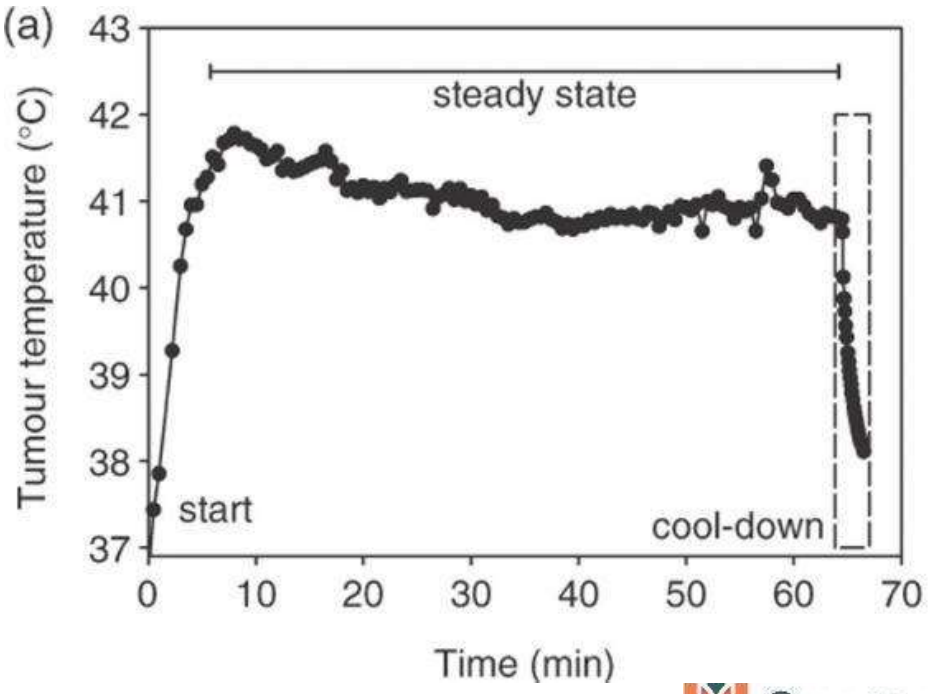

Van Haaren et al, *Int J Hyperthermia* 24: 663-674 (2008)

Thermal properties of tissue

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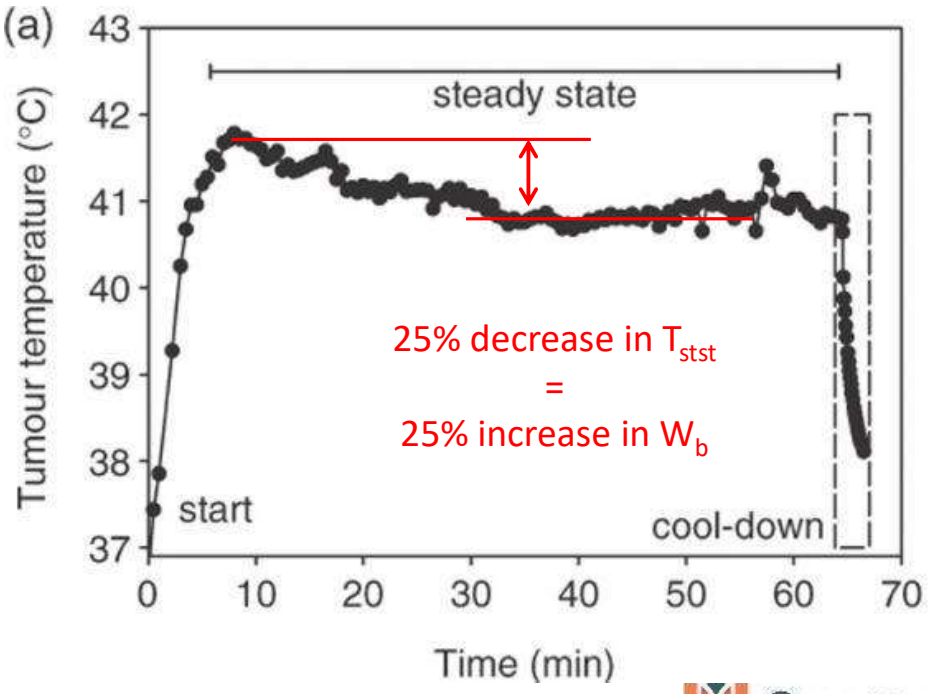

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Van Haaren et al, *Int J Hyperthermia* 24: 663-674 (2008)

Heat transport in tissue

- Bio-heat equation
- Thermal properties of tissues
- Vascular cooling

Vascular cooling

Impact of blood flow depends on vessel size:

Vascular cooling

Impact of blood flow depends on vessel size:

- **Small vessels**:
  - (almost) in thermal equilibrium with tissue
  - Modelled collectively with bio-heat equation

Vascular cooling

Impact of blood flow depends on vessel size:

- **Small vessels**:
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    - Pennes bio-heat equation
    - Effective tissue conductivity

Vascular cooling

Impact of blood flow depends on vessel size:

- **Small vessels**:
  - (almost) in thermal equilibrium with tissue
  - Modelled collectively with bio-heat equation
- **Large vessels**:
  - Arteries cause cold tracks in tissue
  - Modelled individually

Vascular cooling

Cold track along large, unequilibrated vessels

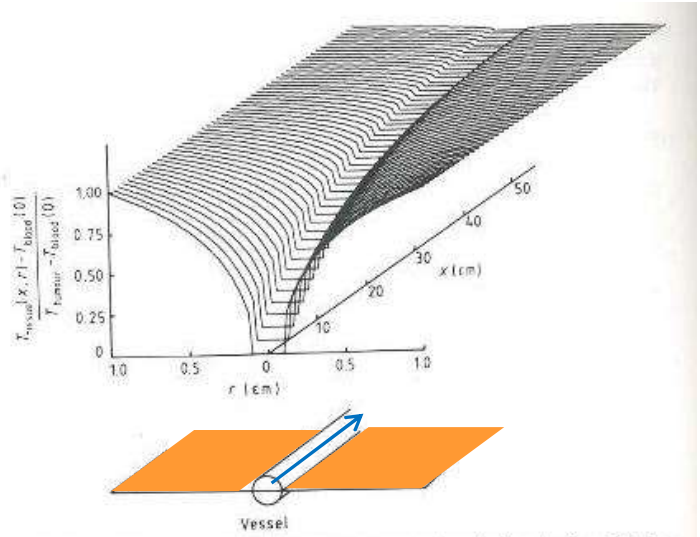
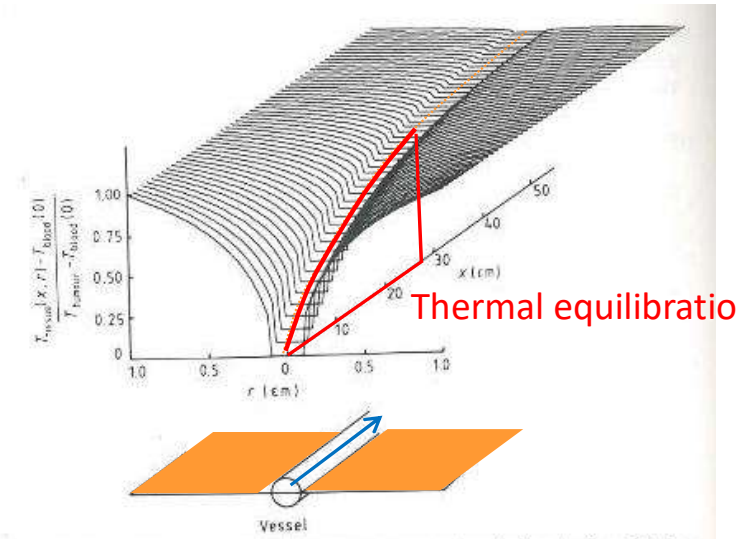


Figure 3. Two-dimensional plot of the temperature distribution in a plane through the axis of vessel 2 along the x-axis. Note the difference in scale between the x-axis and the r-axis (length x-axis 0.5 m).

Lagendijk *Phys Med Biol* 27 17-23 (1982)

Vascular cooling

Cold track along large, unequilibrated vessels



Thermal equilibration length

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Lagendijk *Phys Med Biol* 27 17-23 (1982)

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Vascular cooling

Thermal equilibration length

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Main branches	1	10	8	6×10^2	23	1.3	19
Secondary branches	0.6	4	8	10^3	14	0.5	6.7
Tertiary branches	0.14	1.4	3.4	7.6×10^4	1	0.01	0.16
Terminal branches	0.05	0.1	2	1×10^6	0.3	0.001	0.012
Terminal arteries	0.03	0.15	0.4	1.3×10^7	0.03	0.000 06	0.000 8
Arterioles	0.02	0.2	0.3	4×10^7	0.02	0.000 02	0.000 3
Capillaries	0.008	0.1	0.07	1.2×10^9	0.002	0.000 000 7	0.000 01
Vernules	0.03	0.2	0.07	8×10^7	0.006	0.000 01	0.000 15
Terminal branches	0.07	0.15	0.07	1.3×10^7	0.014	0.000 06	0.000 8
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Secondary veins	1.5	4	1.3	1.8×10^3	6	0.5	6.8
Main veins	2.4	10	1.5	6×10^2	10	1.4	20
Large veins	6	20	3.6	4×10	60	22	300
Vena cava	12.5	40	33	1	1200	860	12 000

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not in thermal equilibrium

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modelled individually

Discrete vessels

not in thermal equilibrium

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near thermal equilibrium

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continuum model

Pennes or k_{eff}

near thermal equilibrium

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Impact of blood flow depends on vessel size:

- **Small vessels**:
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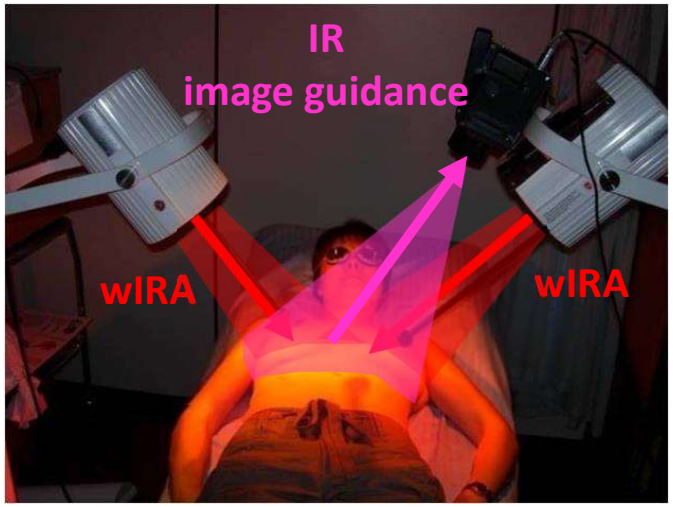
Vascular cooling



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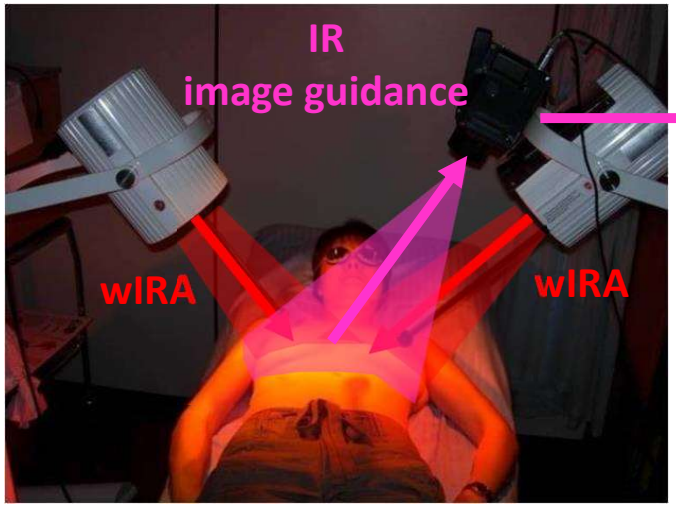

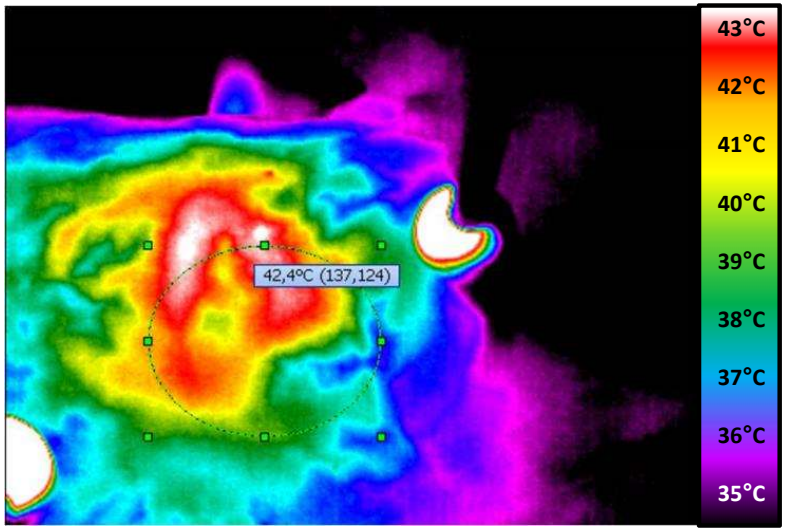

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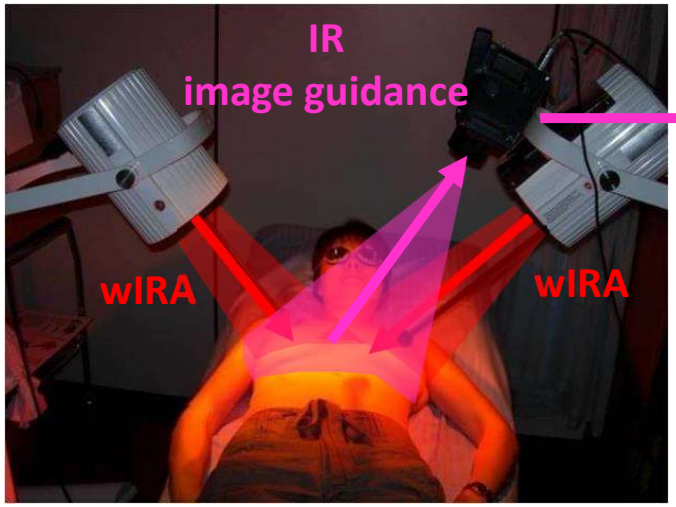

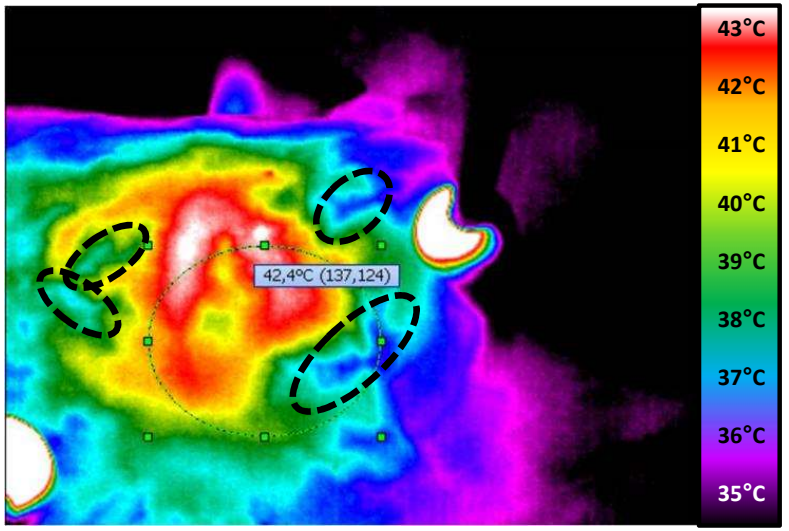

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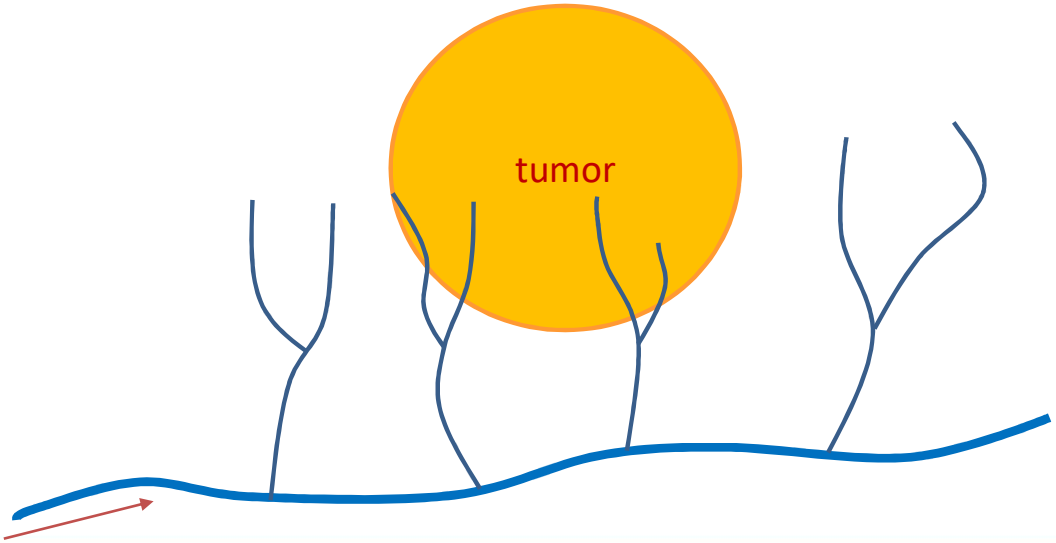
Pre-heat arteries by heating
Large margin around tumor

Vascular cooling

Preheating arterial blood flow



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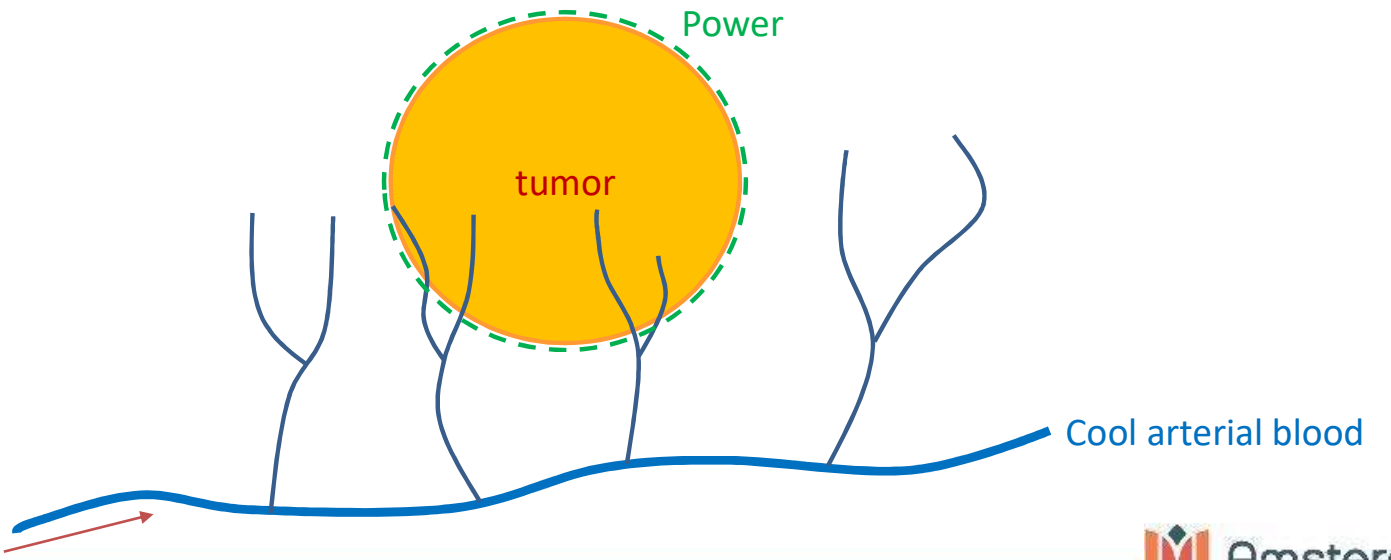
Vascular cooling

Preheating arterial blood flow



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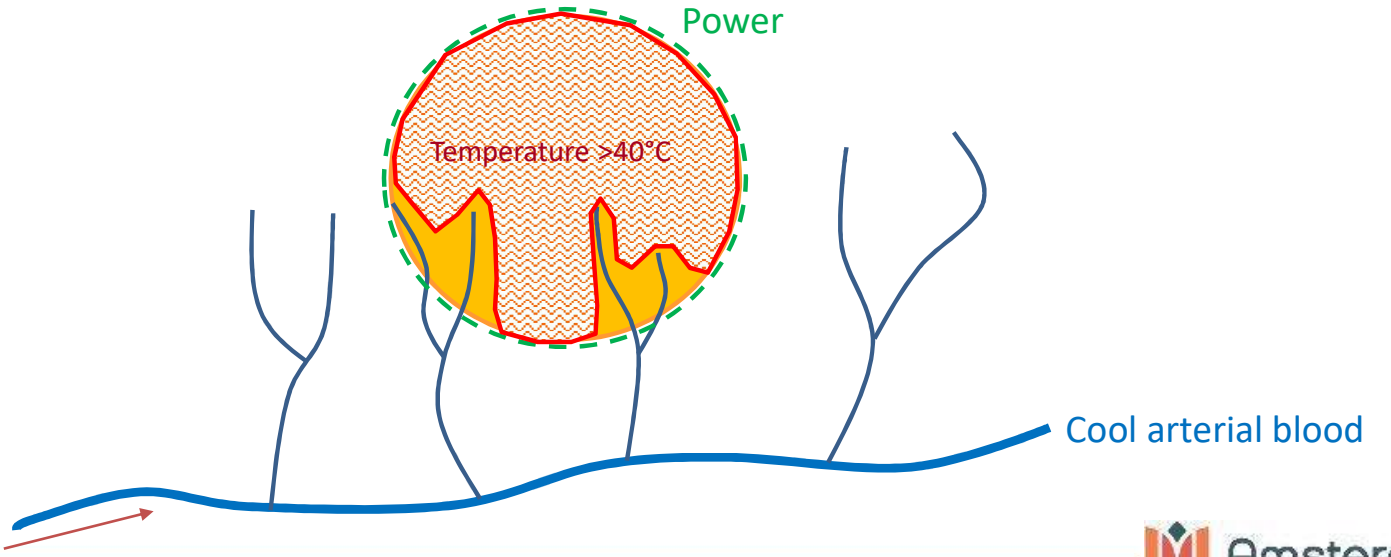

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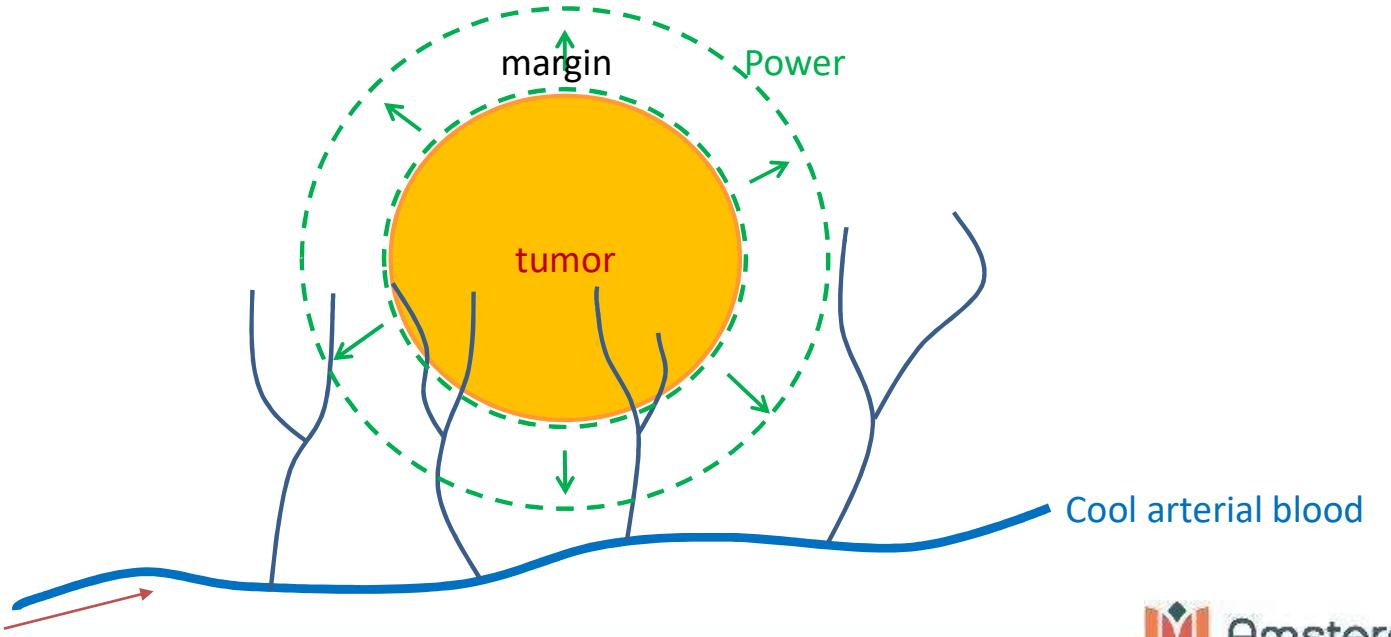

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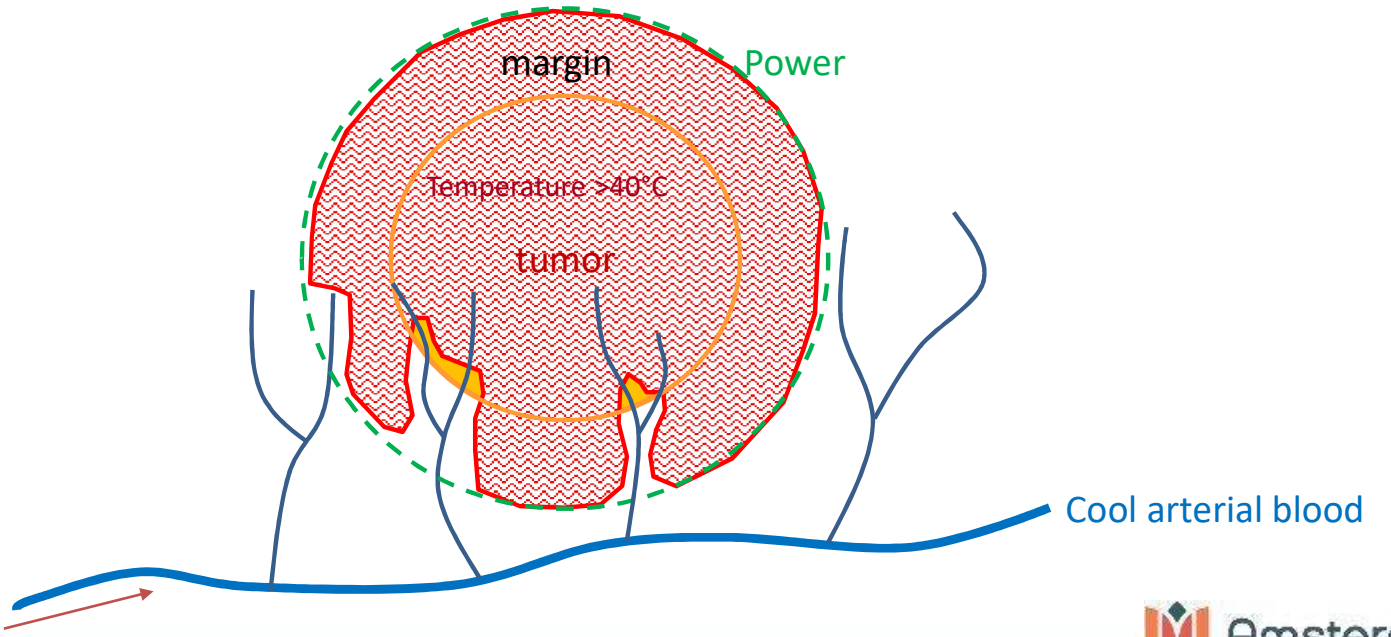

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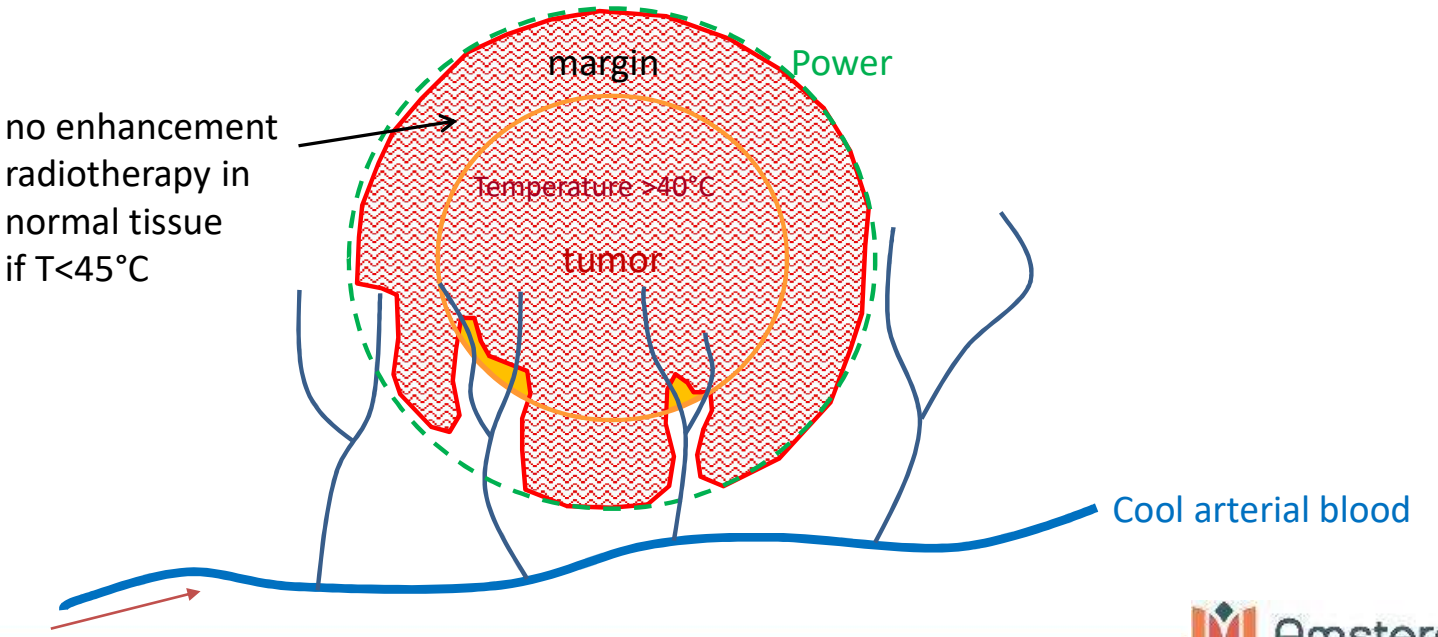
Vascular cooling

Preheating arterial blood flow



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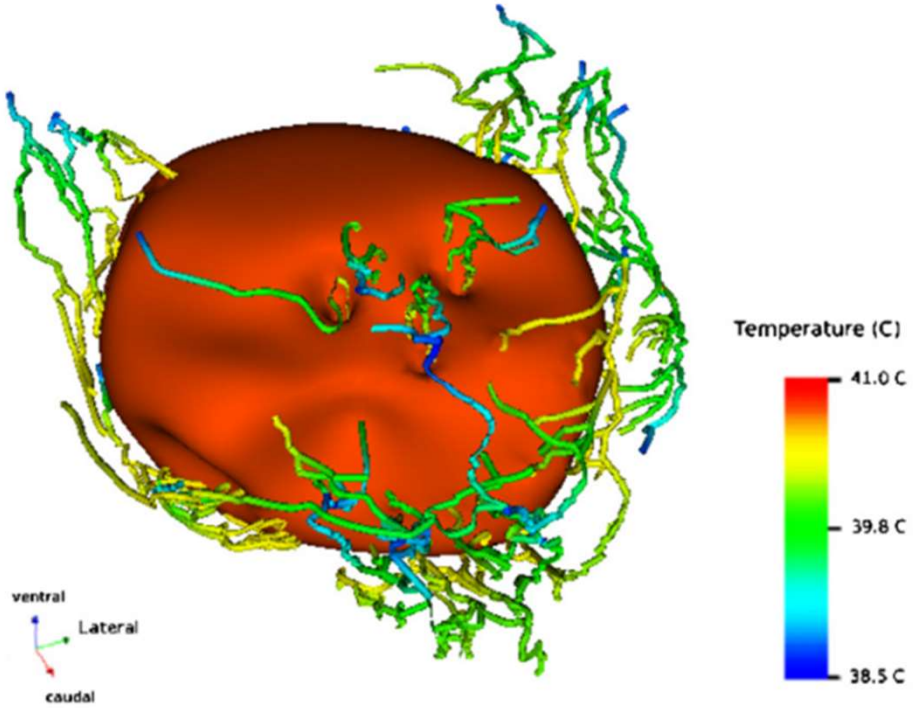
Vascular cooling

Example: locoregional hyperthermia of prostate



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Van den Berg *et al. Phys Med Biol*. 2006; 51: 809-825

Heat transport in tissue

- Bio-heat equation
- Thermal properties of tissues
- Vascular cooling

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Conclusion: bio heat transfer is a complex and challenging topic, with limited accuracy for Pennes equation

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Tomorrow:

modeling heat transport in treatment planning

Heat transport in tissue

Thank you for your attention!

Questions?

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