# *Hyperthermia Treatment Planning*

## *Principles, application and future perspectives*

**Petra Kok**

*Department of Radiation Oncology*
*Amsterdam University Medical Centers*
*University of Amsterdam*
*Cancer Center Amsterdam*
*The Netherlands*

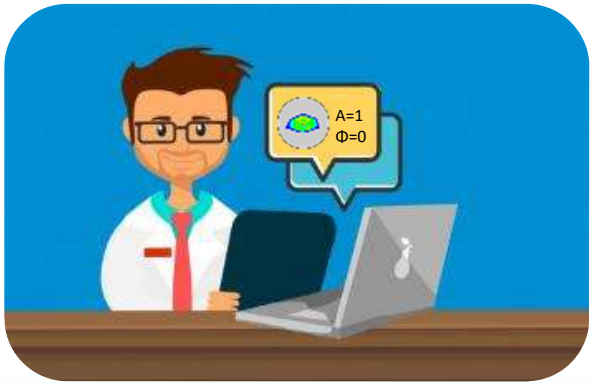
# Hyperthermia treatment planning

***Principles***

# Hyperthermia treatment planning

***Application of computer simulations to estimate SAR/temperature distributions in patients***

*Supportive to optimize treatment quality*



## Hyperthermia treatment planning

- Hyperthermia treatment planning
  - Wide variety of applications

Kok et al. *IEEE JERM*; 2021; 5(3): 214-222

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## Hyperthermia treatment planning

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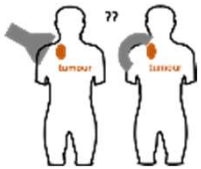
**Evaluation of treatment strategies**

**Applicator selection**



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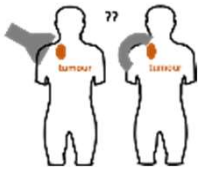
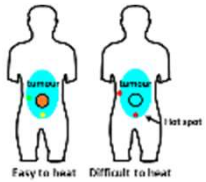


**(Pre-)treatment evaluation**

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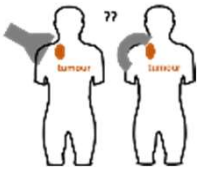

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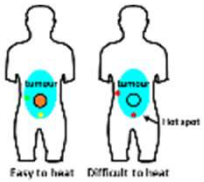
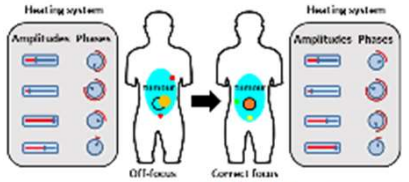



**Evaluation of steering strategies**

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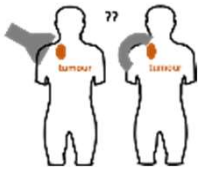

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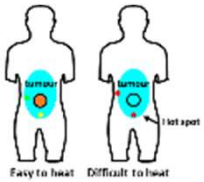


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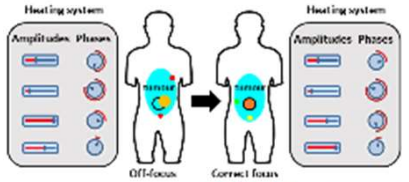


**Device design**

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## Hyperthermia treatment planning

- Process/ workflow
  - Create dielectric patient model

Kok et al. *Int. J. Hyperthermia*; 2017; 33(6): 593-607

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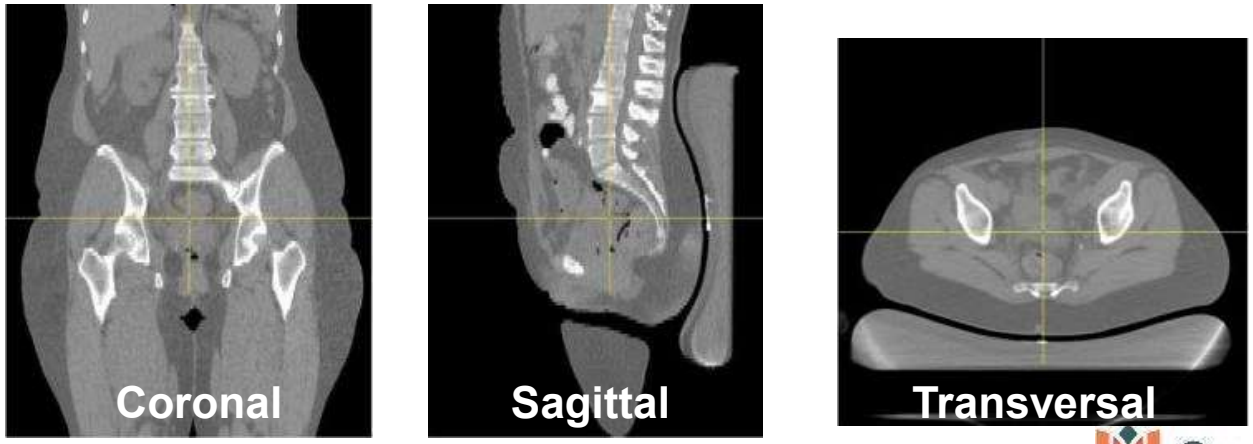
## Hyperthermia treatment planning

- Process/ workflow
  - Create dielectric patient model
  - CT data set
    - Clinical treatment position
      - Water bolus (ALBA) or hammock (BSD)

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## Hyperthermia treatment planning

- Process/ workflow
  - Create dielectric patient model
  - CT data set
    - Clinical treatment position
  - Manual tumour delineation (radiation oncologist)
    - Focus of heating for optimization/ evaluation

## Hyperthermia treatment planning

- Process/ workflow
  - Create dielectric patient model
  - CT data set
    - Clinical treatment position
  - Manual tumour delineation (radiation oncologist)
    - Focus of heating for optimization/ evaluation
  - Normal tissue segmentation



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## Hyperthermia treatment planning

- Process/ workflow
  - Normal tissue segmentation
    - Large number of tissue types and organs
    - Manual delineation ? (time consuming)
    - How detailed ?

## Hyperthermia treatment planning

- Process/ workflow
  - Normal tissue segmentation
    - Large number of tissue types and organs
    - Manual delineation ? (time consuming)
    - How detailed ?
    - Dielectric contrast is important*
      - Discriminate muscle-like, fatty tissues, bone, lung, air
      - Advantage: this can be done automatically

Kok et al. *Int. J. Hyperthermia*; 2017; 33(6): 593-607 *VilasBoas-Ribeiro et al. *Cancers*; 2020; 12, 2646

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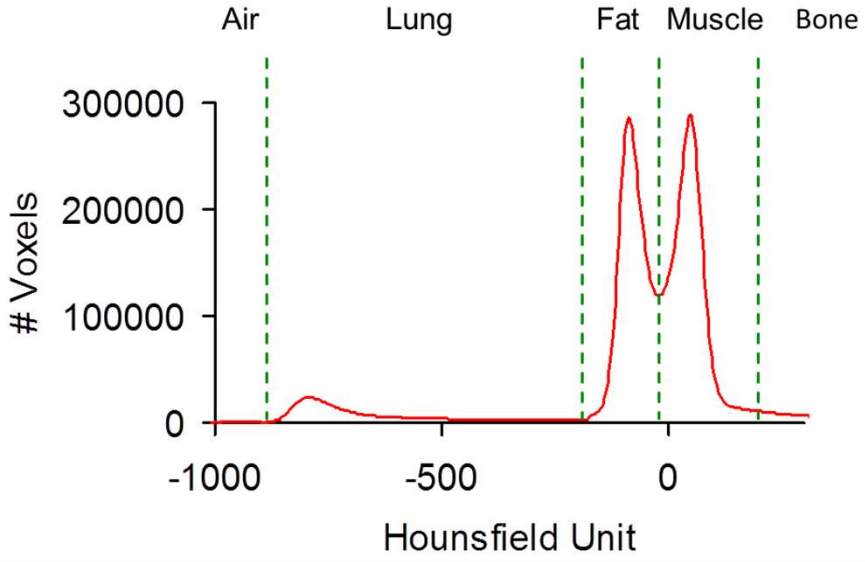
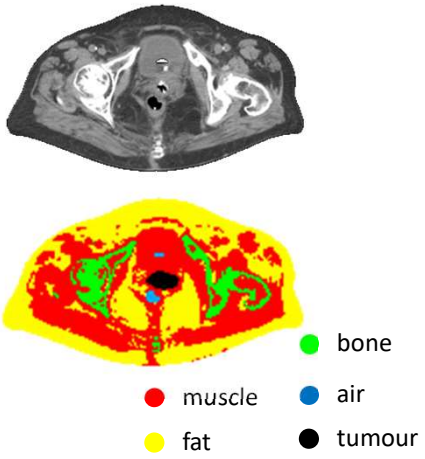
# Hyperthermia treatment planning

- Process/ workflow
  - Normal tissue segmentation in clinical practice
    - Based on CT Hounsfield units

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## Hyperthermia treatment planning

- Process/ workflow
  - Create dielectric patient model
  - CT data set
    - Clinical treatment position
  - Manual tumour delineation (radiation oncologist)
    - Focus of heating for optimization/ evaluation
  - Normal tissue segmentation
  - Position patient in heating device model



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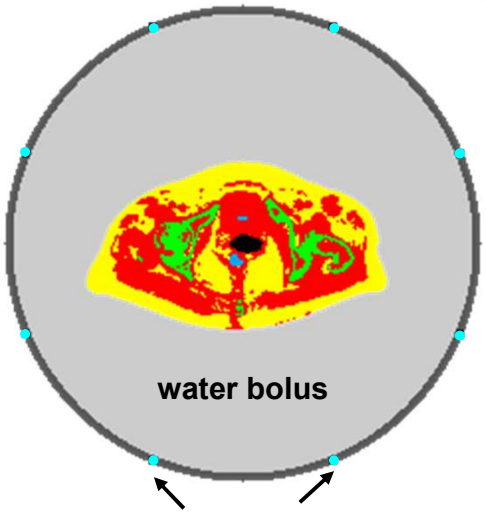
# Hyperthermia treatment planning

- Example: cervical cancer patient

BSD Sigma-60

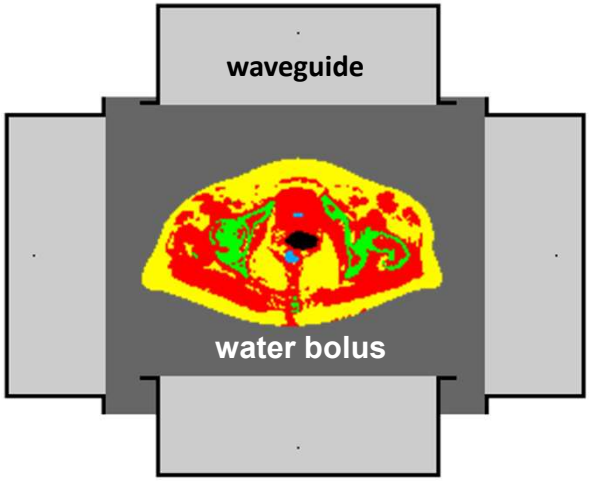
4 paired dipoles




muscle
fat
bone
air
tumour

ALBA-4D

4 waveguides

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## Hyperthermia treatment planning

- Assign dielectric and thermal tissue properties.
  - Electrical conductivity σ (S $m^{-1}$)
  - Relative permittivity ε (-)

*Frequency dependent*

  - Density $\rho$ (kg $m^{-3}$)
  - Thermal conductivity $k$ ( W $m^{-1}$ °$C^{-1}$)
  - Specific heat capacity $c$ (J $kg^{-1}$ °$C^{-1}$)
  - Blood perfusion $W_b$ (kg $m^{-3}$ $s^{-1}$)



Kok et al. *Int. J. Hyperthermia*; 2017; 33(6): 593-607

## Hyperthermia treatment planning

- Planning process
  - Create dielectric patient model
  - CT data set
    - Clinical treatment position
  - Manual tumour delineation (radiation oncologist)
    - Focus of heating for optimization/ evaluation
  - Normal tissue segmentation
  - Position patient in heating device
  - Calculate E-Fields, power and temperature

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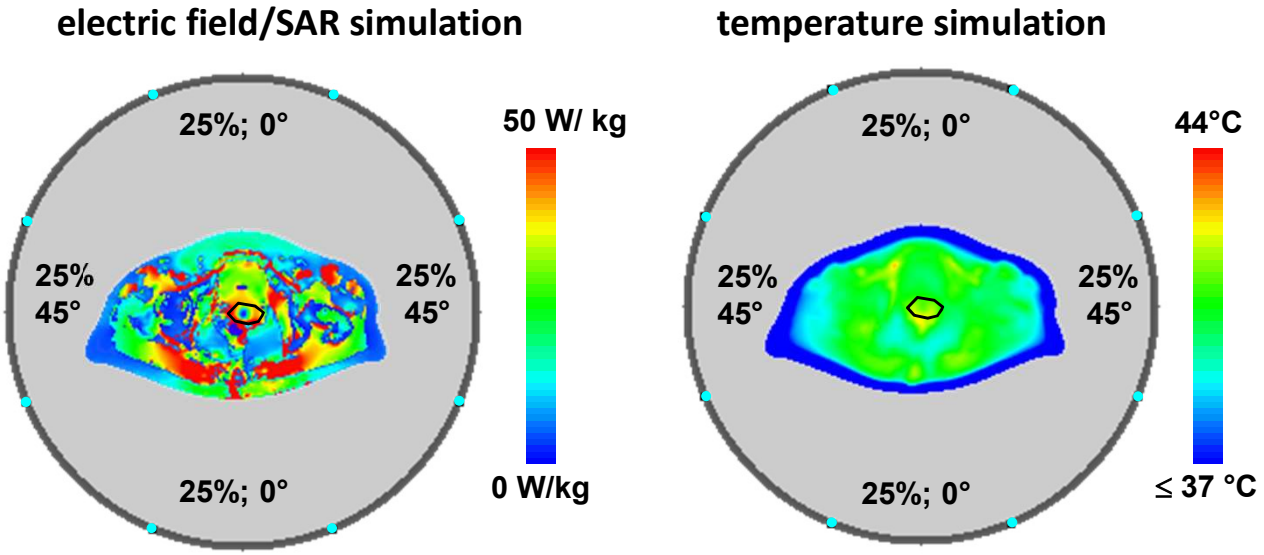
# Hyperthermia treatment planning

- Planning simulations; mimic clinical settings




$$\text{SAR} = \frac{\sigma}{2\rho}\left\|\vec{E}\right\|^2$$

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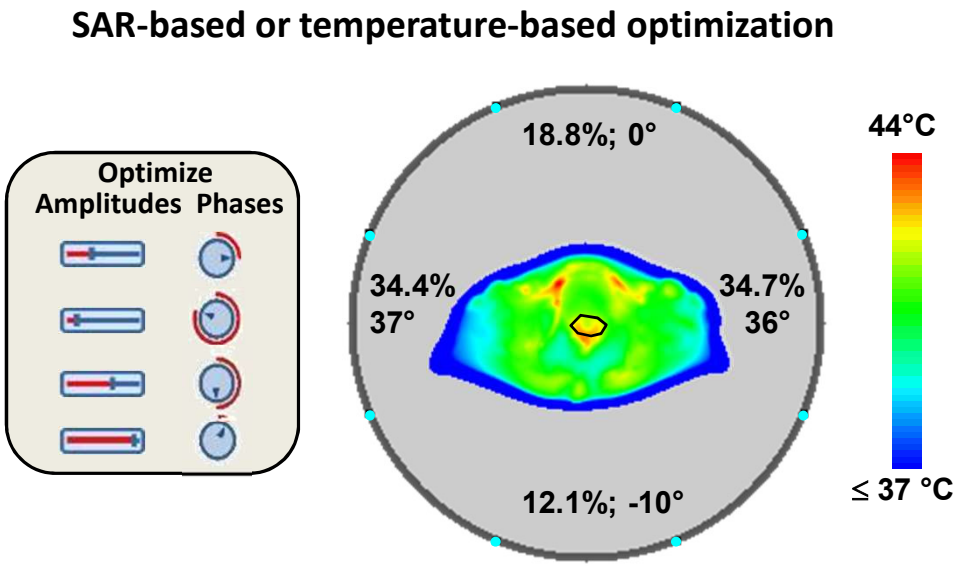
# Hyperthermia treatment planning

- Planning simulations; optimization



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## Hyperthermia treatment planning

- Calculation methods
  - Electric field: solve Maxwell's Equations

$$\nabla \cdot \mathbf{E} = \frac{\rho_v}{\varepsilon} \qquad \text{(Gauss' Law)}$$

$$\nabla \cdot \mathbf{H} = 0 \qquad \text{(Gauss' Law for Magnetism)}$$

$$\nabla \times \mathbf{E} = -\mu \frac{\partial \mathbf{H}}{\partial t} \qquad \text{(Faraday's Law)}$$

$$\nabla \times \mathbf{H} = \mathbf{J} + \varepsilon \frac{\partial \mathbf{E}}{\partial t} \qquad \text{(Ampere's Law)}$$

## Hyperthermia treatment planning

- Calculation methods
  - Electric field: solve Maxwell's Equations
    - Finite difference time domain (FDTD)
    - Finite element method (FEM)

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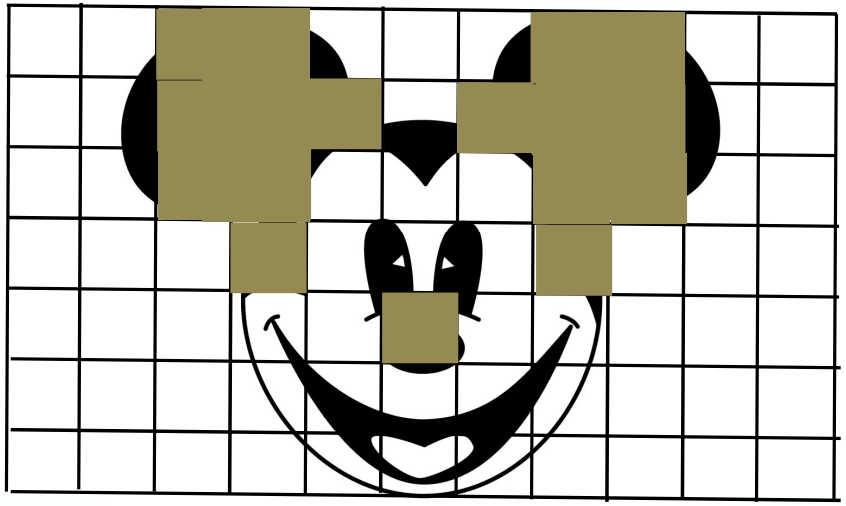
- Calculation methods
  - Electric field: solve Maxwell's Equations
    - Finite difference time domain (FDTD)
      - Voxel-based method



Taflove A. Computational Electrodynamics. 1995

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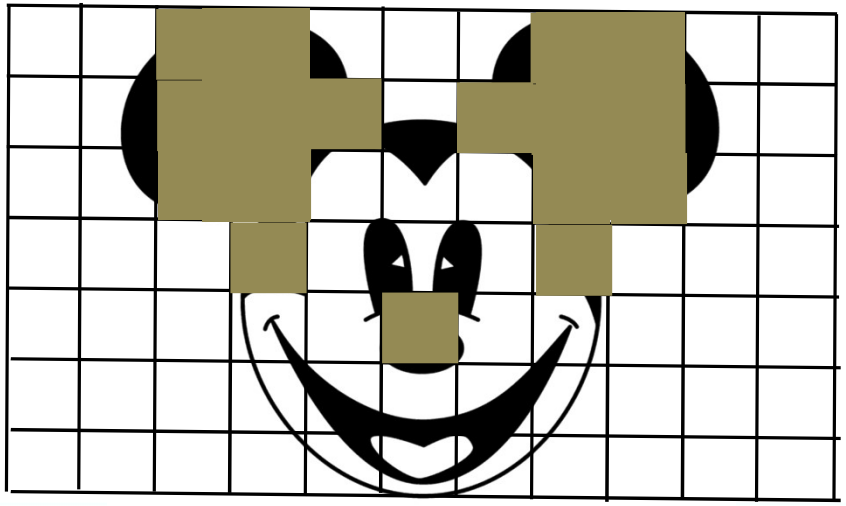
## Hyperthermia treatment planning

- Calculation methods
  - Electric field: solve Maxwell's Equations
    - Finite difference time domain (FDTD)
      - Voxel-based method
      - Easy grid generation directly from imaging



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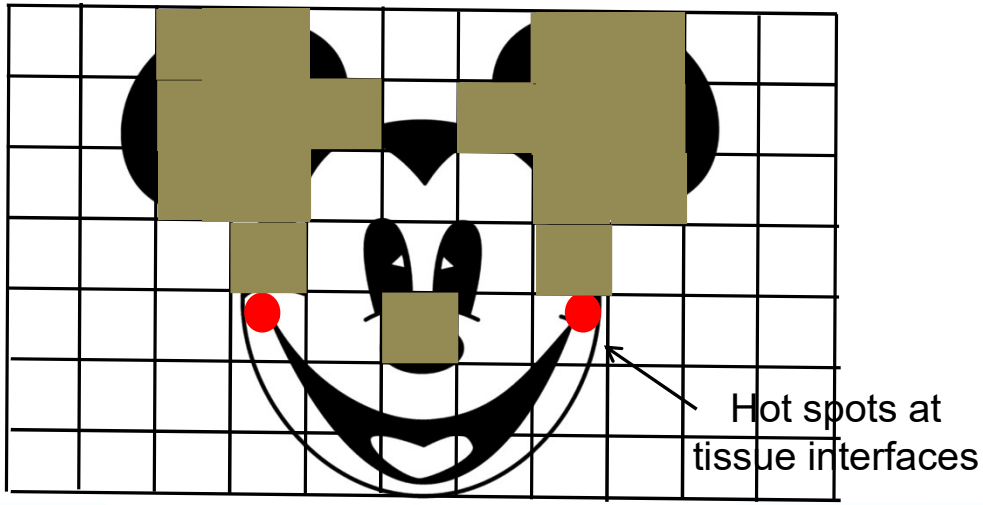


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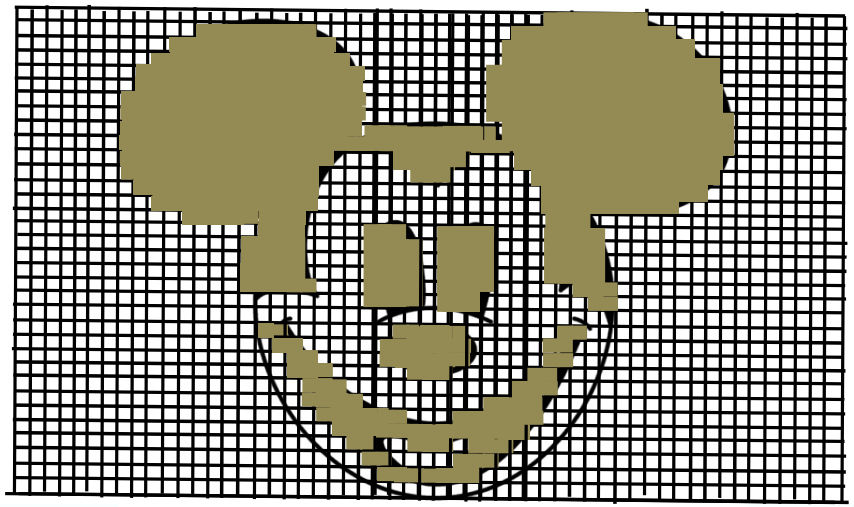

Adequate resolution important to represent tissue interfaces

variable resolution depending on anatomical detail

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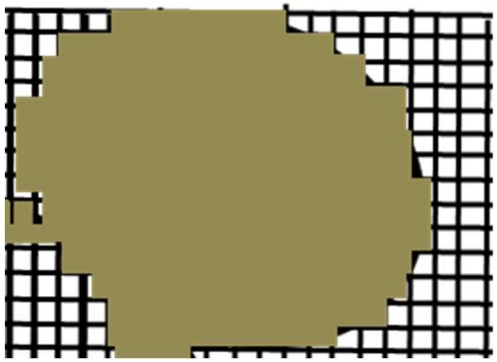

Stair-casing errors

Samaras *et al.* Phys. Med. Biol; 2006, 51: N221–N229

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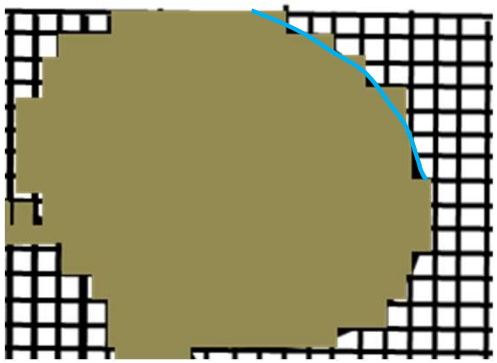

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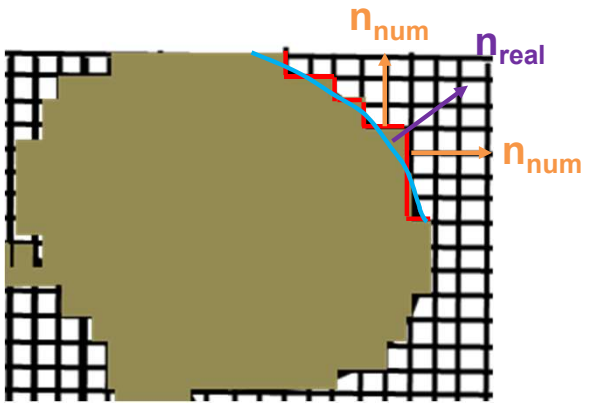


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- Calculation methods
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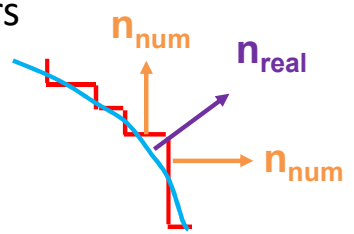
    - Finite difference time domain (FDTD)
      - Voxel-based method
      - Easy grid generation directly from imaging
      - Stair-casing errors

Post-processing correction possible
- Interpolation at points between calculated values
- Correction based on geometry of interfaces and parameters of the surrounding medium

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Nadobny *et al.* IEEE Trans Microw Theory Tech. 1998;46:1759–66.

# Hyperthermia treatment planning

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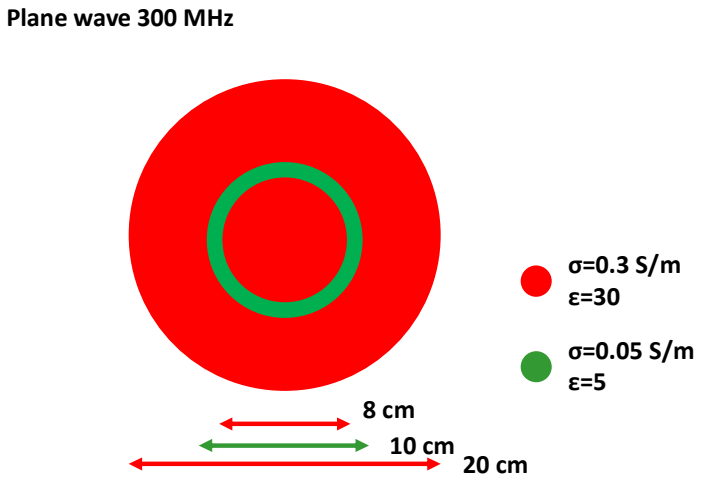
      - Geometry-based correction of stair-casing errors

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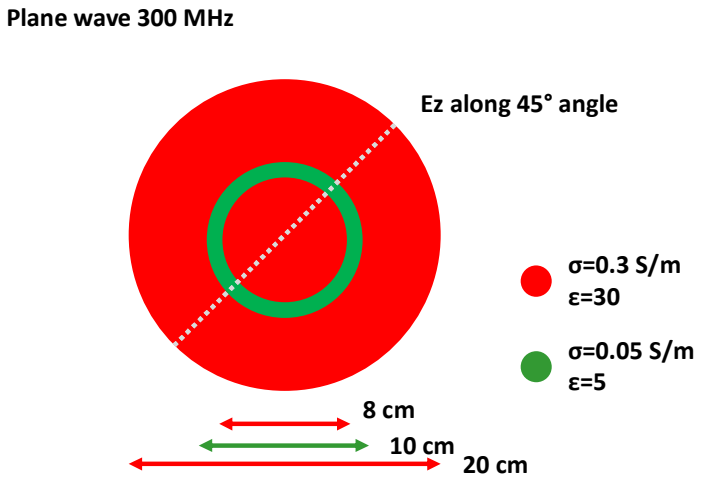


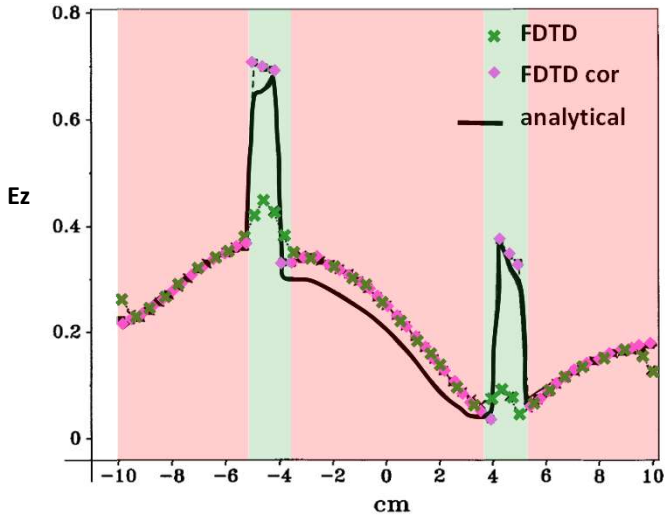


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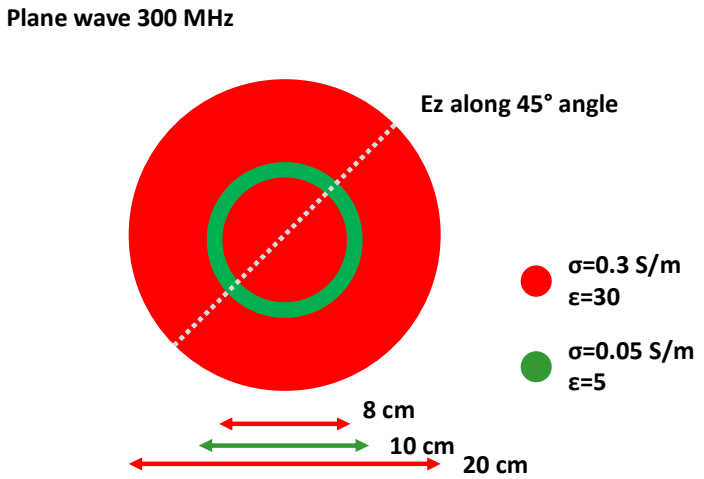
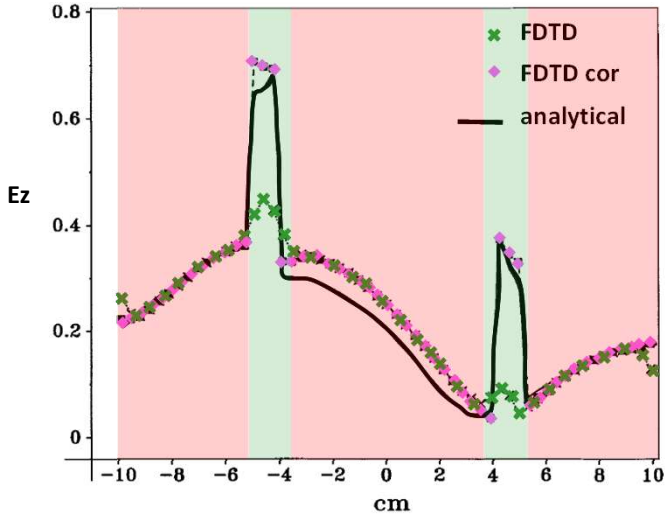
Application on patient models requires contouring

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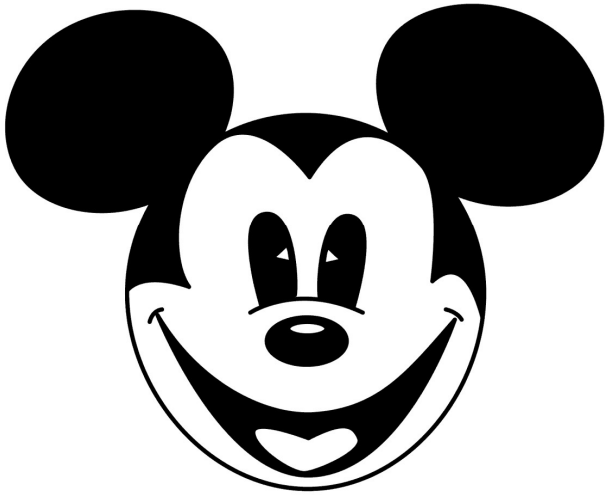
## Hyperthermia treatment planning

- Calculation methods
  - Electric field: solve Maxwell's Equations
    - Finite element method (FEM)

## Hyperthermia treatment planning

- Calculation methods
  - Electric field: solve Maxwell's Equations
    - Finite element method (FEM)
    - Subdivision into "finite elements" (triangles)



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## Hyperthermia treatment planning

- Calculation methods
  - Electric field: solve Maxwell's Equations
    - Finite element method (FEM)
    - Subdivision into "finite elements" (triangles)
    - Accurate representation of complex geometry and interfaces
    - Mesh generation less straighforward

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## Hyperthermia treatment planning

- Calculation methods
  - Temperature: Pennes' bioheat equation

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

Pennes J Appl Physiol. 1948;1(2):93-122

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

$\rho$ : tissue density (kg/m$^3$),

$c$ : specific heat (J/kg°C) ,

$c_b$ : specific heat blood (J/kg°C) ,

$W_b$ : volumetric perfusion (kg/m$^3$ s),

$T_{art}$: body core temperature (°C)

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$\nabla\cdot\left(k\nabla T\right)$ models thermal conductivity (heat displacement)

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$\nabla\cdot\left(k\nabla T\right)$ models thermal conductivity (heat displacement)

$-c_b W_b (T - T_{art})$ models blood perfusion (heat removal)

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| | |
|---|---|
| $\nabla\cdot(k\nabla T)$ | models thermal conductivity (heat displacement) |
| $-c_b W_b (T - T_{art})$ | models blood perfusion (heat removal) |
| $P$ | power added by heating device (W/m$^3$) |

Pennes J Appl Physiol. 1948;1(2):93-122

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## Hyperthermia treatment planning

- Calculation methods
  - Temperature: Pennes' bioheat equation

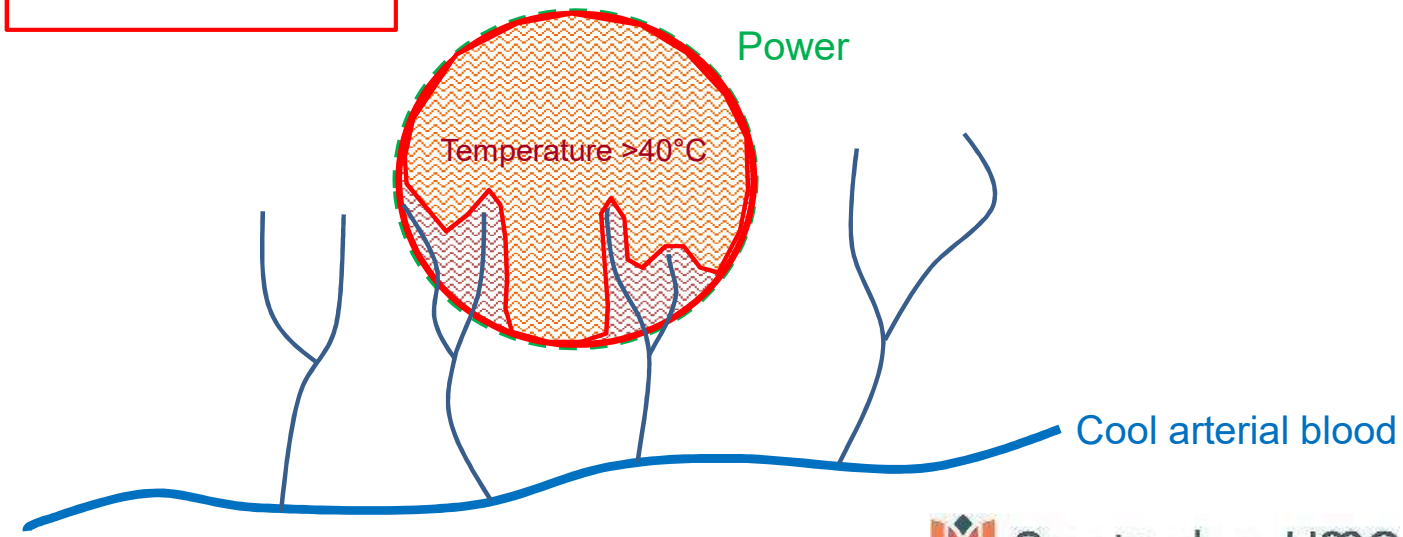
$$c\rho\frac{\partial T}{\partial t} = \nabla\cdot(k\nabla T) - c_b W_b (T - T_{art}) + P$$

Blood perfusion accounted for by heat sink

## Hyperthermia treatment planning

- Calculation methods
  - Temperature: Pennes' bioheat equation

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

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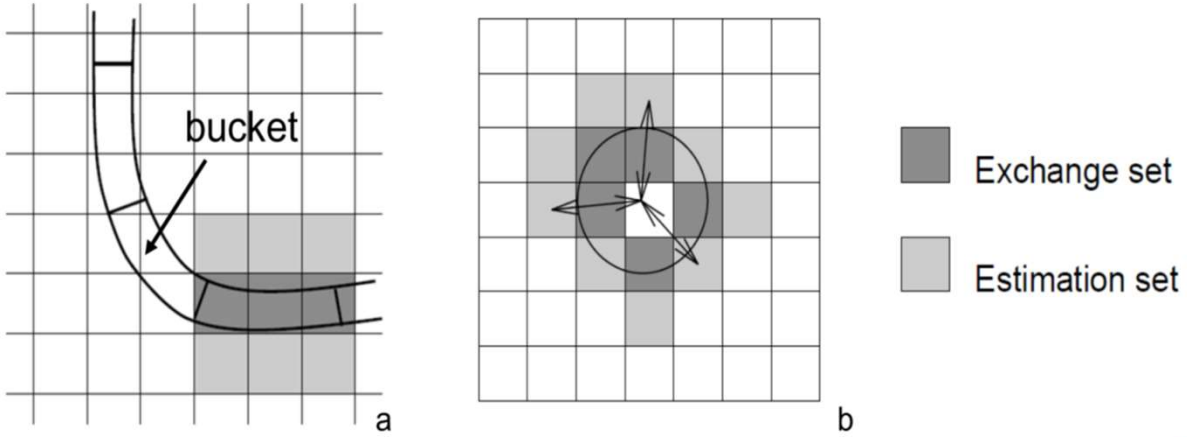
## Hyperthermia treatment planning

- Calculation methods
  - Temperature: Discrete vasculature
    - Model vasculature as 3D curves




Kotte et al. Phys. Med. Biol. 1996; 41: 865 – 884

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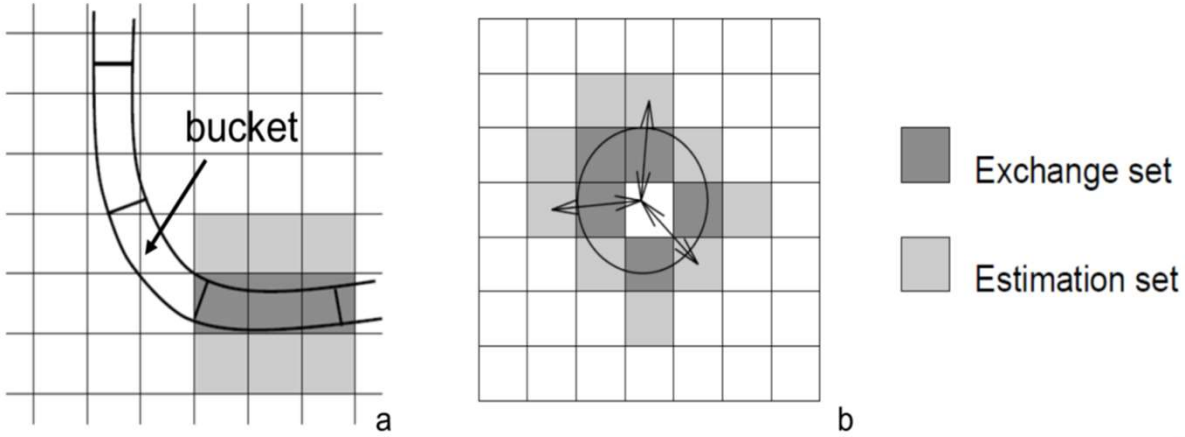
## Hyperthermia treatment planning

- Calculation methods
  - Temperature: Discrete vasculature
    - Model vasculature as 3D curves
    - Separate from tissue grid
      - vessels with ø < voxel size can be included




Kotte et al. Phys. Med. Biol. 1996; 41: 865 – 884

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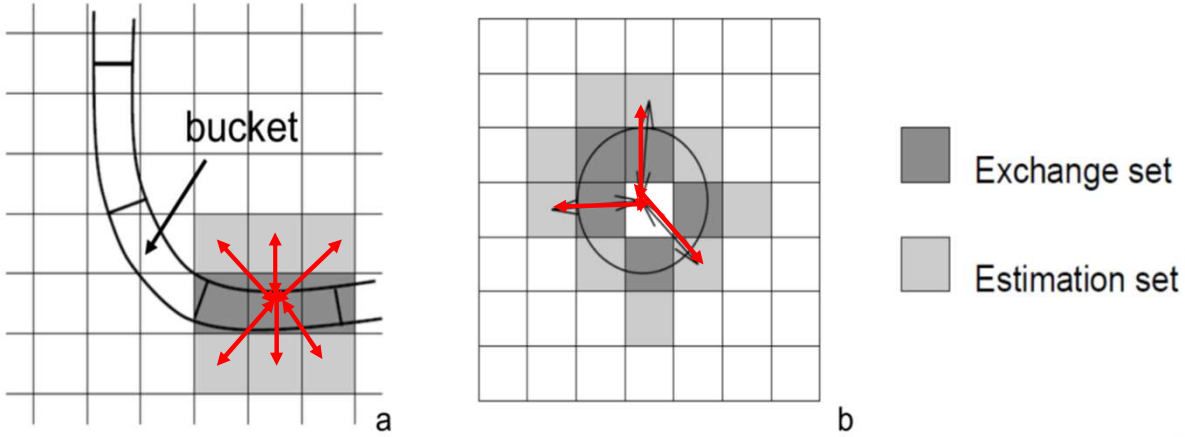
## Hyperthermia treatment planning

- Calculation methods
  - Temperature: Discrete vasculature
    - Model vasculature as 3D curves
    - Separate from tissue grid
    - Heat exchange between vessel and tissue

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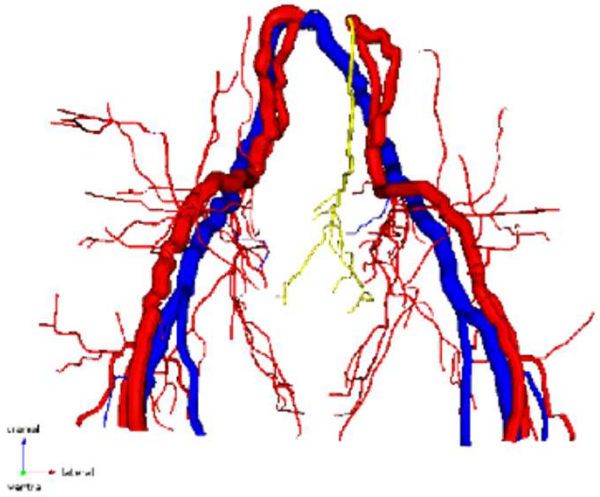
## Hyperthermia treatment planning

- Calculation methods
  - Temperature: Discrete vasculature



**Example: pelvic vasculature reconstructed from angiography**

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

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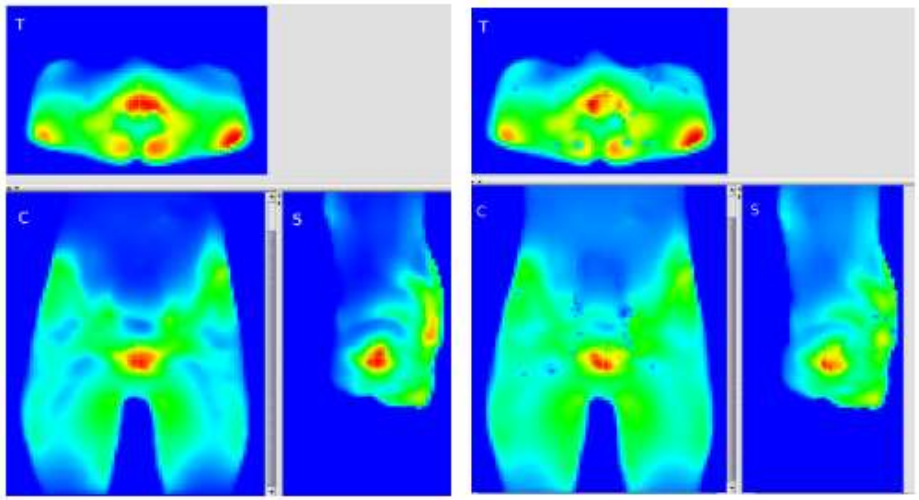
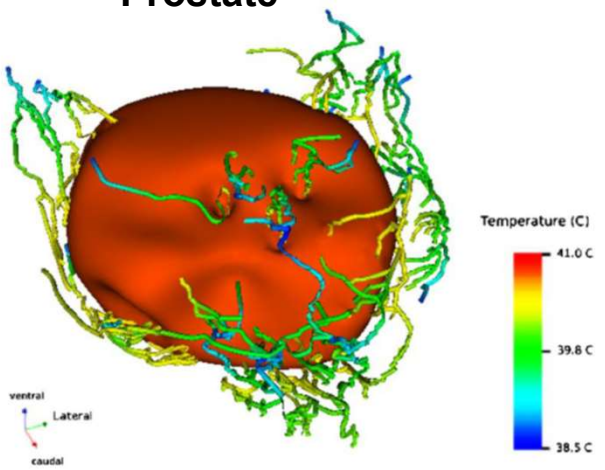
## Hyperthermia treatment planning

- Calculation methods
  - Temperature: Discrete vasculature

**Pennes** **Discrete vasculature**




**Prostate**




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

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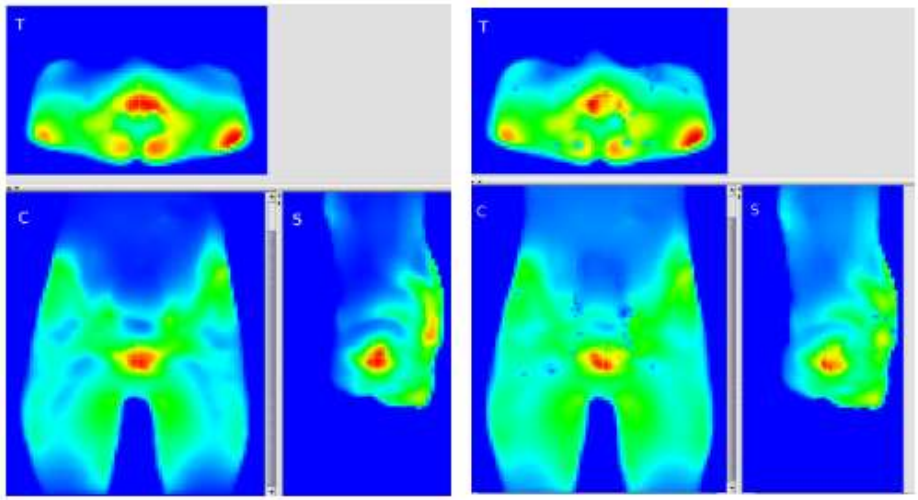
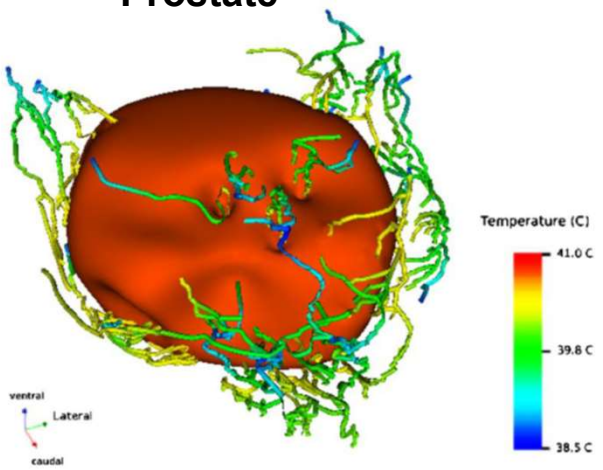
## Hyperthermia treatment planning

- Calculation methods
  - Temperature: Discrete vasculature
    - Differences up to 2°C
    - Very relevant to predict hot spots

**Pennes** **Discrete vasculature**




**Prostate**




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

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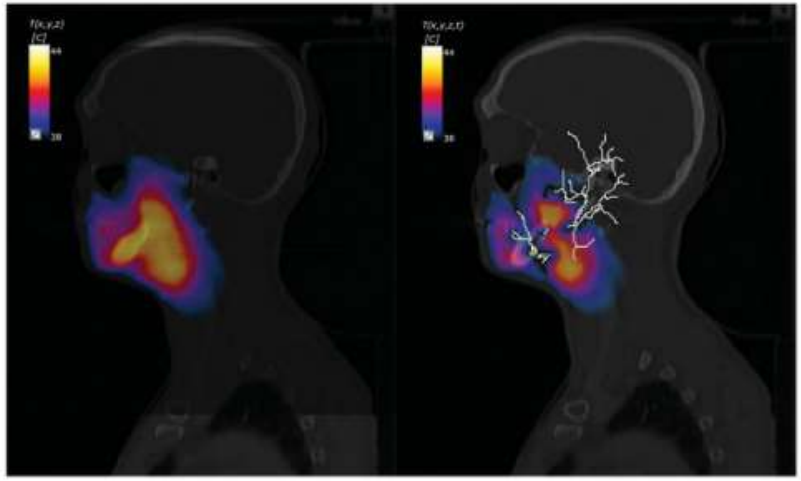
## Hyperthermia treatment planning

- Calculation methods
  - Temperature: Discrete vasculature
    - Differences up to 2°C
    - Very relevant to predict hot spots

**Pennes** **Discrete vasculature**

**Head&Neck**



Sumser et al. Int J. Hyperthermia 2019, 36(1): 800–810

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## Hyperthermia treatment planning

- Calculation methods
  - Optimization: Determine phase-amplitude settings to maximize tumor heating
    - SAR based
    - Temperature based

## Hyperthermia treatment planning

- Calculation methods
  - Optimization: Determine phase-amplitude settings to maximize tumor heating
    - SAR based
    - Several SAR indicators
      - Target SAR
      - SAR ratio ($SAR_{target}/SAR_{total}$)
      - Hot spot target ratio ($SAR_{Vx}/SAR_{target}$)
      - ….
      - ….

Canters et al. Int J. Hyperthermia 2009; 25(7): 593–608

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## Hyperthermia treatment planning

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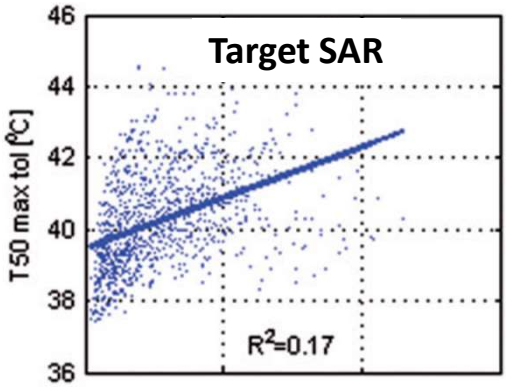
      - ….
      - ….

**Correlation with target temperatures ?**

## Hyperthermia treatment planning

- Calculation methods
  - Optimization: Determine phase-amplitude settings to maximize tumor heating
    - SAR based




    - Several SAR indicators
      - Target SAR
      - SAR ratio ($SAR_{target}/SAR_{total}$)
      - Hot spot target ratio ($SAR_{Vx}/SAR_{target}$)
      - ….
      - ….

Canters et al. Int J. Hyperthermia 2009; 25(7): 593–608

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## Hyperthermia treatment planning

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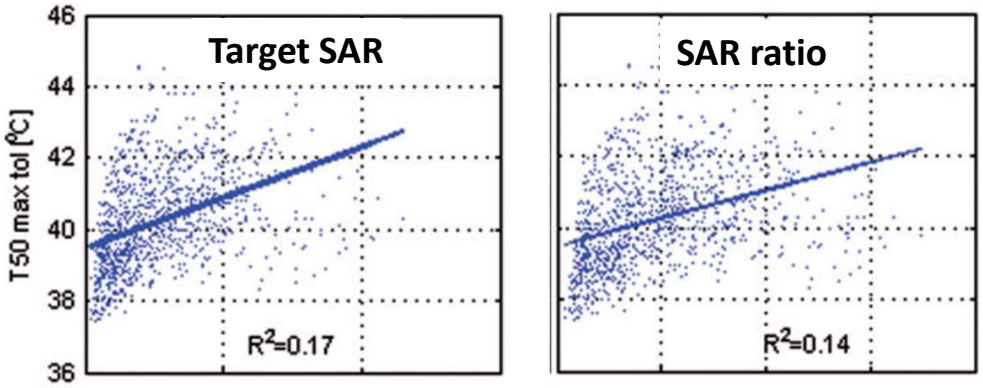


Canters et al. Int J. Hyperthermia 2009; 25(7): 593–608

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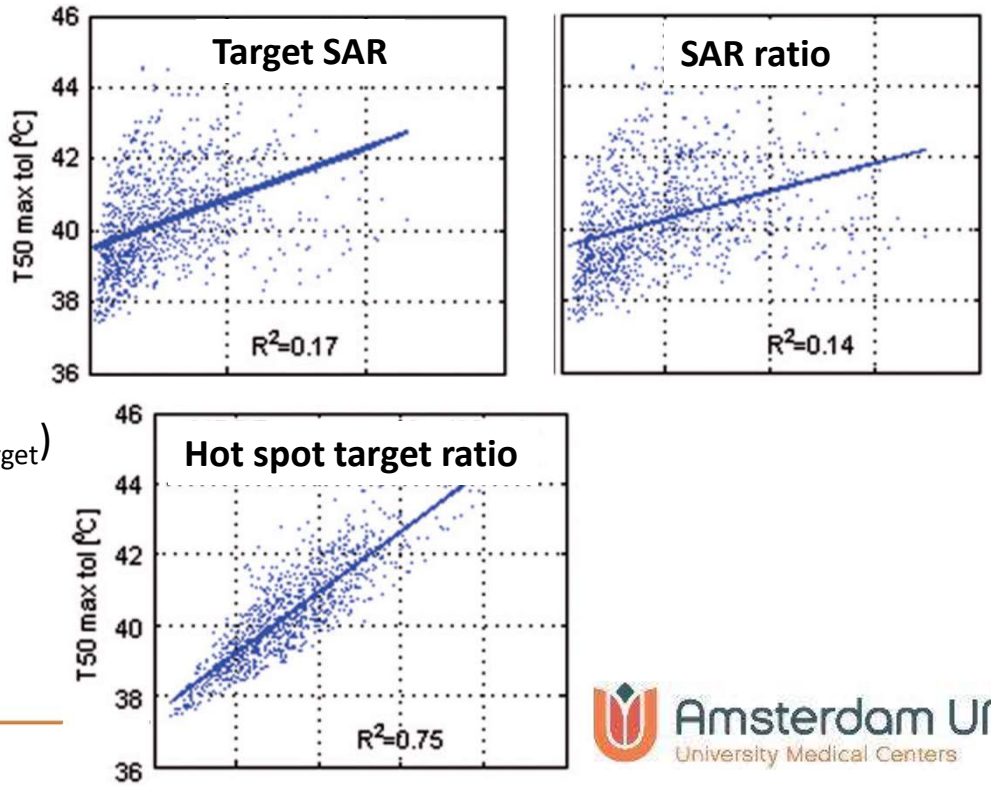


Canters et al. Int J. Hyperthermia 2009; 25(7): 593–608

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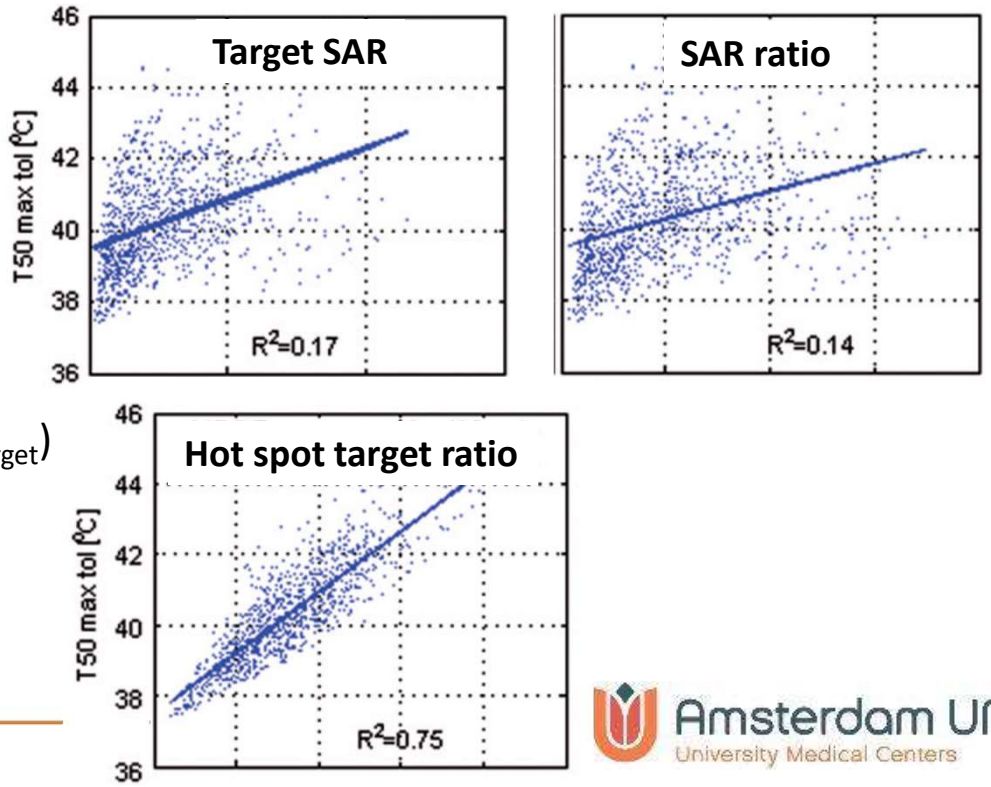
## Hyperthermia treatment planning

- Calculation methods
  - Optimization: Determine phase-amplitude settings to maximize tumor heating
    - SAR based
    - Several SAR indicators
      - Target SAR
      - SAR ratio ($SAR_{target}/SAR_{total}$)
      - Hot spot target ratio ($SAR_{Vx}/SAR_{target}$)
      - ….
      - ….

$SAR_{Vx}$ also correlates with clinical hot spots




Canters et al. Phys Med Biol. 2011;56(2):439–451

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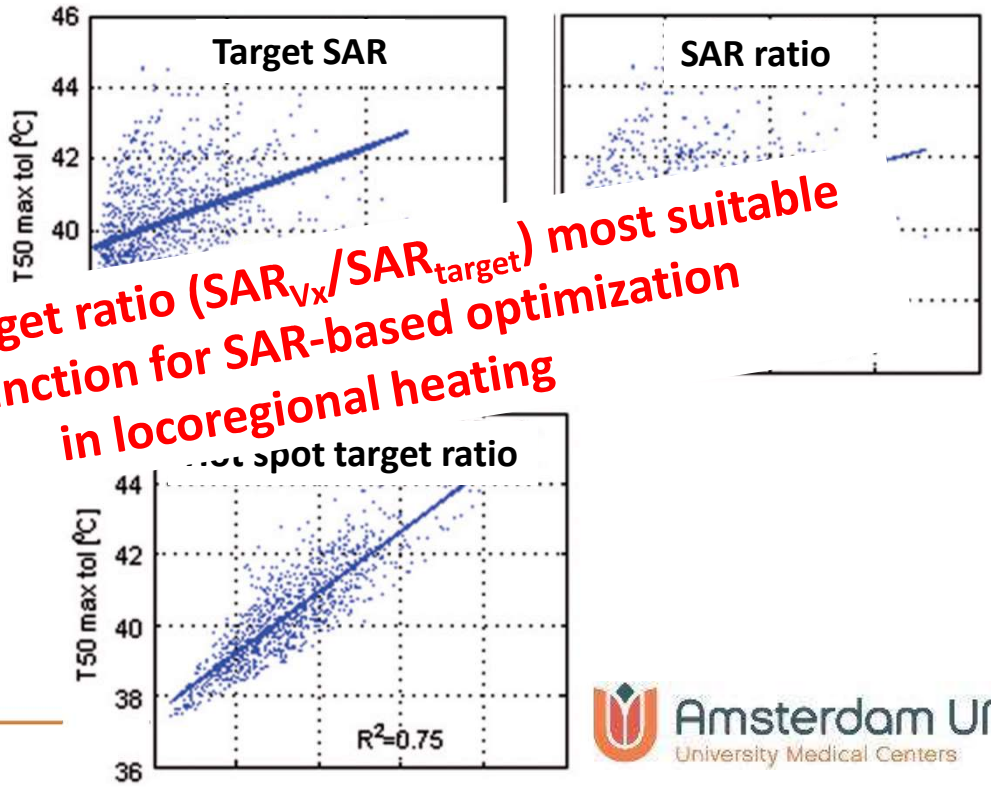
## Hyperthermia treatment planning

- Calculation methods
  - Optimization: Determine phase-amplitude settings to maximize tumor heating
    - SAR based
    - Several SAR indicators
      - Target SAR
      - SAR
      - Hot
      - ....
      - ....

$SAR_{Vx}$ also correlates with clinical hot spots




**Hot spot target ratio ($SAR_{Vx}/SAR_{target}$) most suitable goal function for SAR-based optimization in locoregional heating**

Canters et al. Int J. Hyperthermia 2009; 25(7): 593–608

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## Hyperthermia treatment planning

- Calculation methods
  - Optimization: Determine phase-amplitude settings to maximize tumor heating
    - SAR based
      - Easy to implement
      - SAR hot spots can be relatively superficial
        - » Bolus cooling not accounted for
      - Temperature achieved at specific SAR level depends on tissue type

## Hyperthermia treatment planning

- Calculation methods
  - Optimization: Determine phase-amplitude settings to maximize tumor heating
    - SAR based
    - Temperature based
      - Accounts for thermal effects (bolus cooling, blood perfusion)

## Hyperthermia treatment planning

- Calculation methods
  - Optimization: Determine phase-amplitude settings to maximize tumor heating
    - SAR based
    - Temperature based
      - Accounts for thermal effects (bolus cooling, blood perfusion)
      - Maximize tumor heating (e.g. T90)
      - Subject to normal tissue constraints (e.g. 44-45°C, or lower in case of critical tissues)

## Hyperthermia treatment planning

- Calculation methods
  - Optimization: Determine phase-amplitude settings to maximize tumor heating
    - SAR based
    - Temperature based
      - Accounts for thermal effects (bolus cooling, blood perfusion)
      - Maximize tumor heating (e.g. T90)
      - Subject to normal tissue constraints (e.g. 44-45°C, or lower in case of critical tissues)
      - Fast calcultions by temperature superpositioning
        - » $T(x,y,z) = v^H \underline{T}\, v$,
          - $\underline{T}$ : pre-calculated temperature matrix, v: amplitudes-phases

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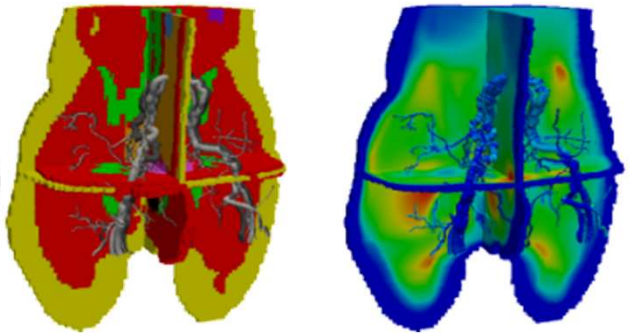
Das et al. Med phys 1999. 26, 319–328 Kok et al Phys Med Biol 2005. 50, 3127–3141

## Hyperthermia treatment planning

- Calculation methods
  - Optimization: Determine phase-amplitude settings to maximize tumor heating
    - SAR based
    - Temperature based
      - Accounts for thermal effects (bolus cooling, blood perfusion)



      - Maximize tumor heating (e.g. T90)
      - Subject to normal tissue constraints (e.g. 44-45°C, or lower in case of critical tissues)
      - Fast calcultions by temperature superpositioning
        - » $T(x,y,z) = v^H \underline{T}\, v$,

***also possible including vasculature***

- $\underline{T}$ : pre-calculated temperature matrix, v: amplitudes-phases

Kok et al. *Med Phys*; 2013 Oct;40(10)

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## Hyperthermia treatment planning

- Software packages general modelling
  - Sim4Life
  - CST studio
  - COMSOL multiphysics
  - …



## Hyperthermia treatment planning

- Software packages general modelling
  - Sim4Life
  - CST studio
  - COMSOL multiphysics
  - …

- Planning software
  - HyperPlan (BSD systems)
  - PLAN2heat (Alba systems, …)

## Hyperthermia treatment planning

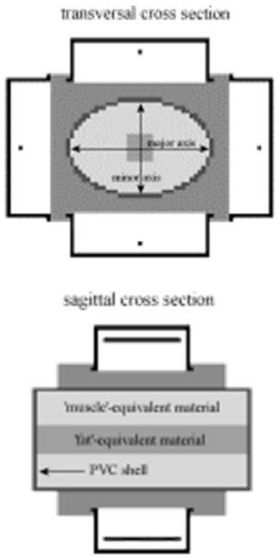
- Hyperthermia treatment planning
  - Reliability of simulations

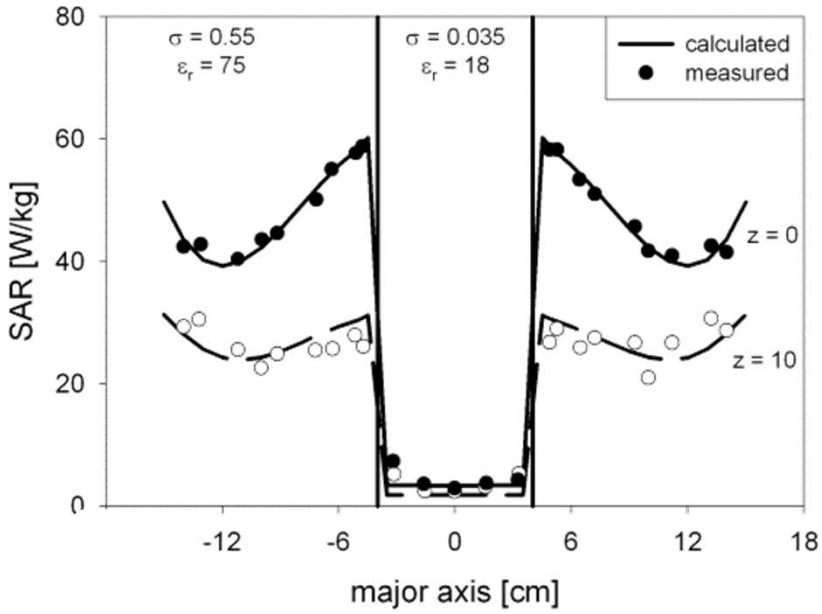
# Hyperthermia treatment planning

- Reliability of simulations
  - Phantom-based validation

**Locoregional heating**

**AMC-4/ ALBA-4D**




Van Haaren *et al*. ICHO 2004; Kok, PhD thesis 2007

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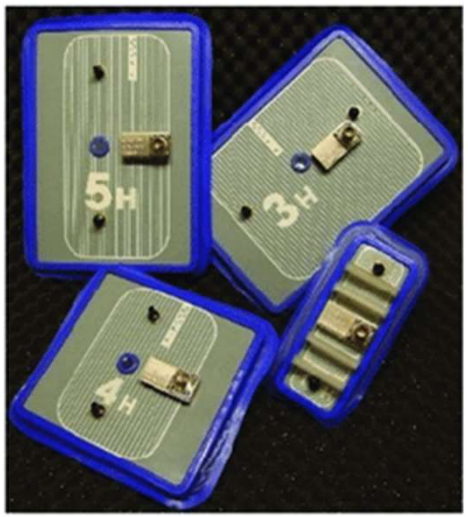
# Hyperthermia treatment planning

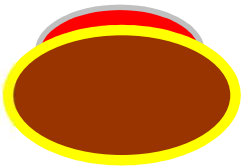
- Reliability of simulations
  - Phantom-based validation

**Superficial heating**

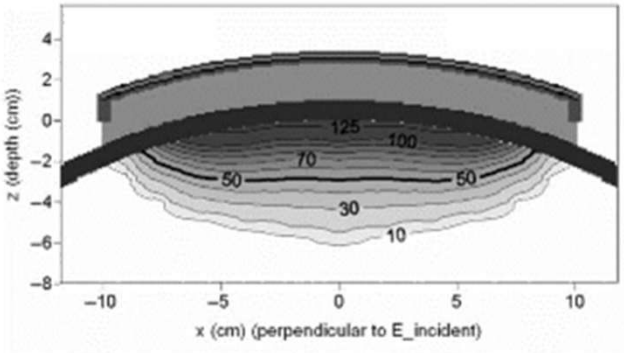
**Contact flexible microstrip applicators (CFMAs)**



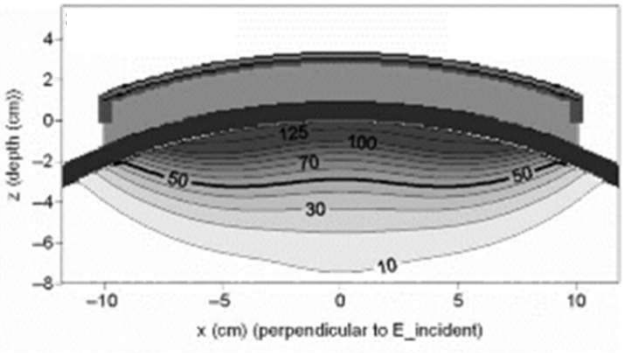

Superficial antenna on phantom



**Measured**




**Simulated**




Kok et al. *Int J. Hyperthermia* 2010; 26(2), 171–184

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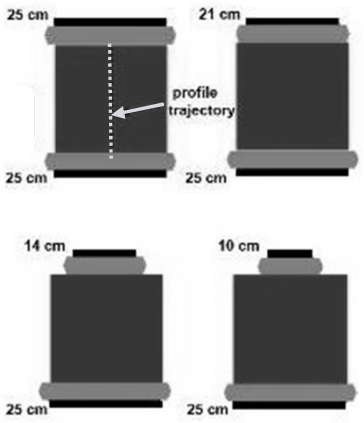
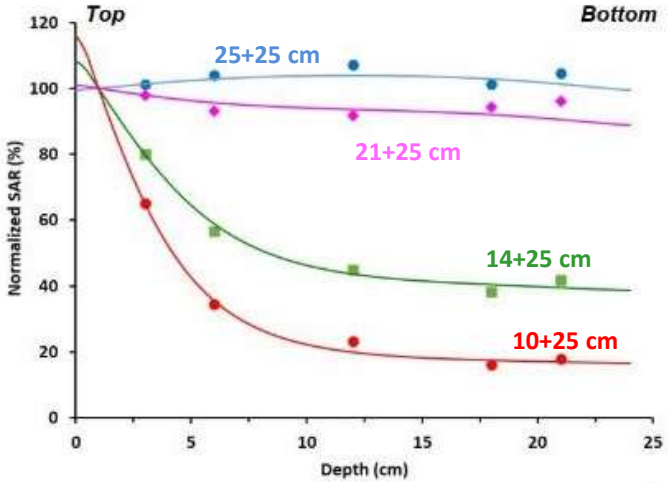
# Hyperthermia treatment planning

- Reliability of simulations
  - Phantom-based validation

**Capacitive heating**

**Thermotron RF-8**




Kok et al. *Int J. Hyperthermia* 2022; 39(1):952-966

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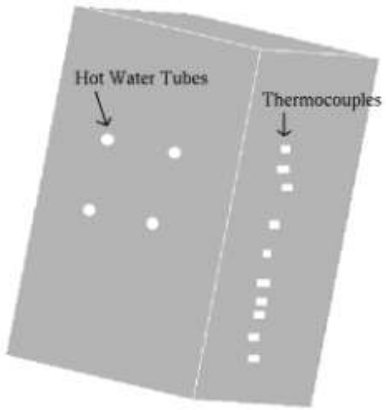
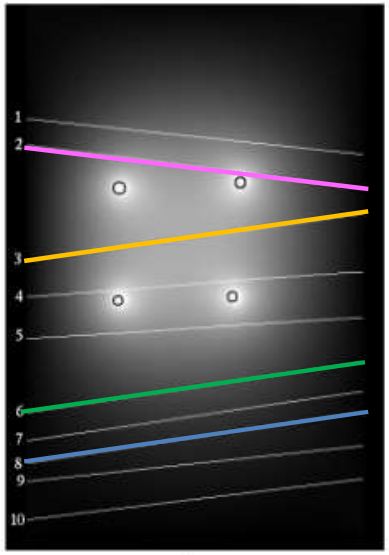
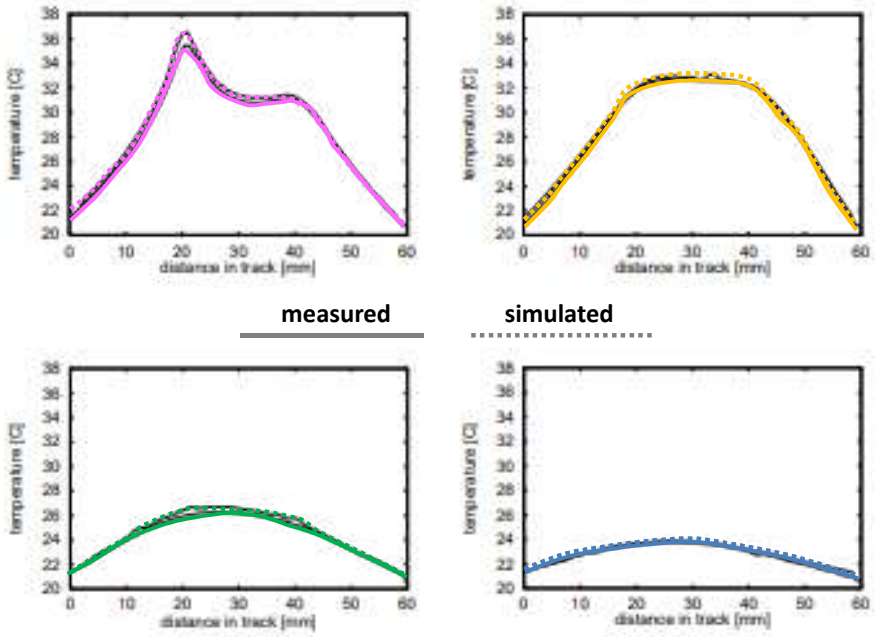
# Hyperthermia treatment planning

- Reliability of simulations
  - Phantom-based validation
  - Thermal modelling

**Phantom with water flow tubes ('blood vessels')**




Raaijmakers et al. *Phys Med Biol* 2000. 45(3): 765-780

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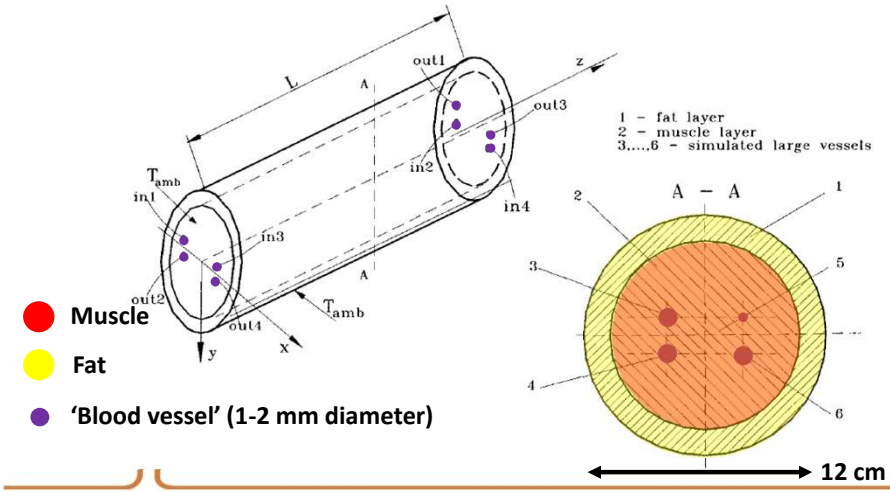
# Hyperthermia treatment planning

- Reliability of simulations
  - Phantom-based validation
  - Thermal modelling

**Phantom with water flow tubes ('blood vessels'), heated with mini annular phased array**




- **Muscle**
- **Fat**
- **'Blood vessel' (1-2 mm diameter)**

Craciunsecu et al. *IEEE TBME* 2000. 47(4): 435-443

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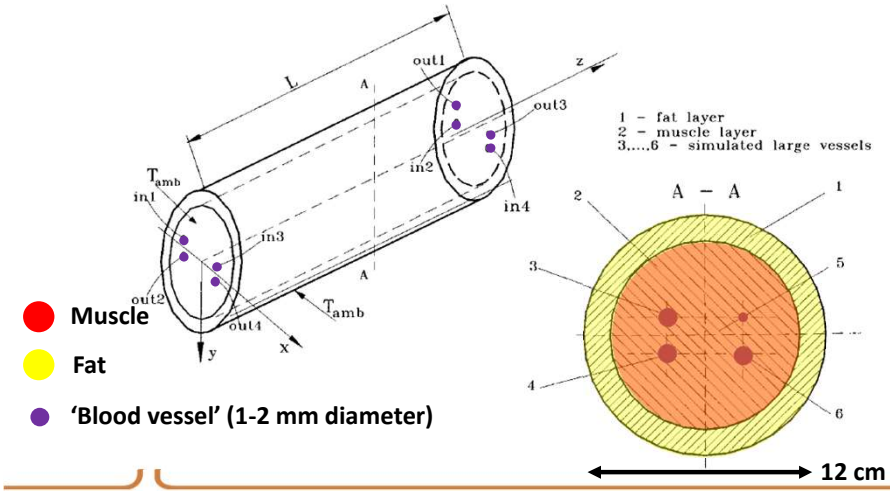
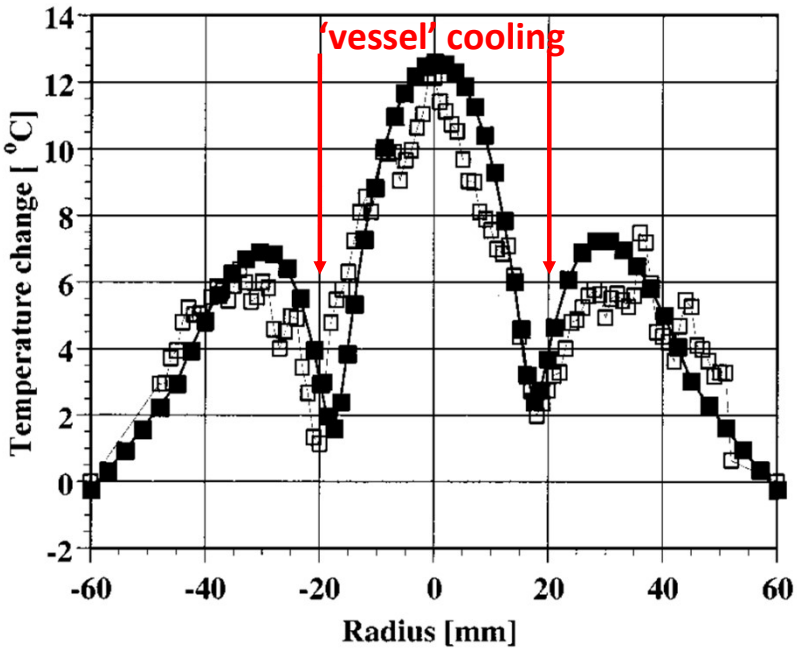
# Hyperthermia treatment planning

- Reliability of simulations
  - Phantom-based validation
  - Thermal modelling

**Phantom with water flow tubes ('blood vessels'), heated with mini annular phased array**




Craciunsecu et al. *IEEE TBME* 2000. 47(4): 435-443

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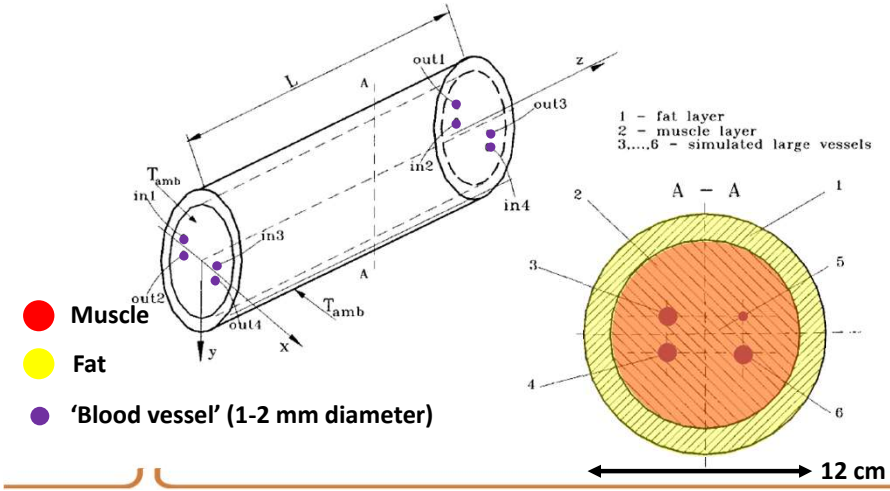
# Hyperthermia treatment planning

- Reliability of simulations — ***Known properties -> reliable predictions***
  - Phantom-based validation
  - Thermal modelling

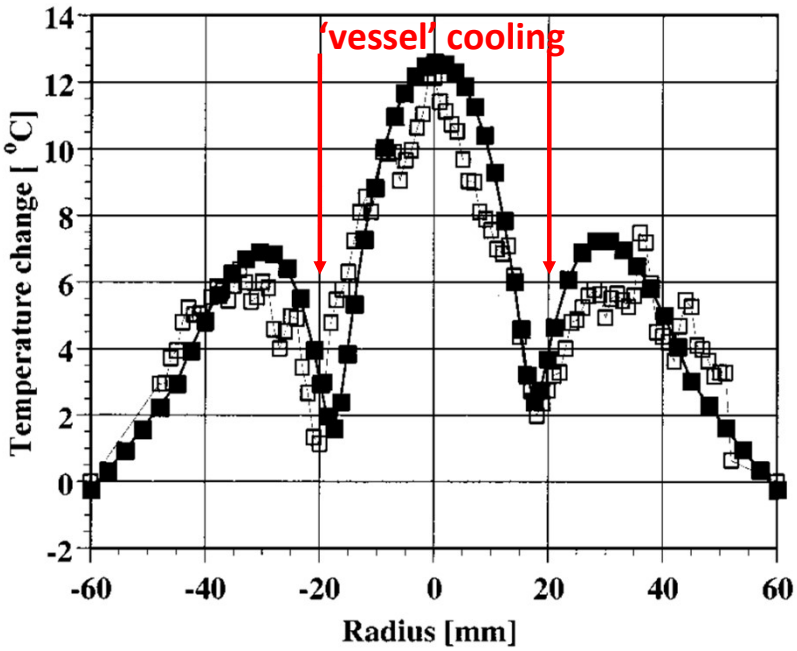
**Phantom with water flow tubes ('blood vessels'), heated with mini annular phased array**




Muscle

Fat

'Blood vessel' (1-2 mm diameter)




■ simulated □ measured (MR)

Craciunsecu et al. *IEEE TBME* 2000. 47(4): 435-443

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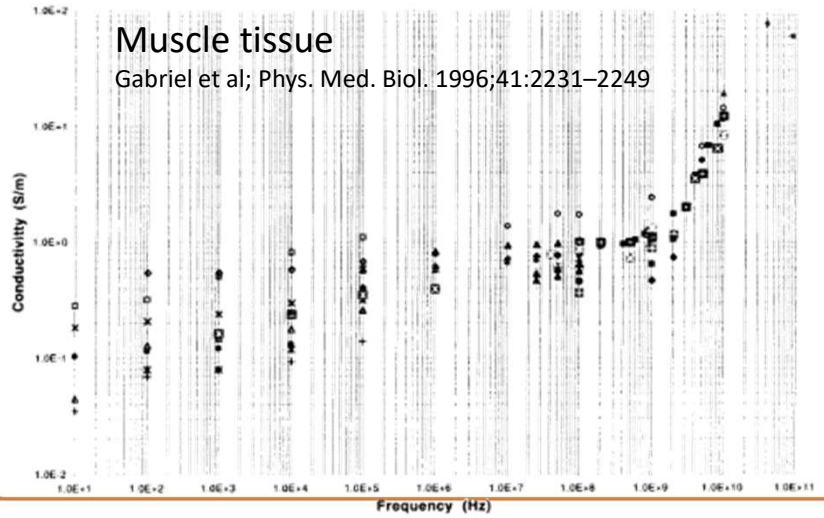
## Hyperthermia treatment planning

- Reliability of simulations
  - Patients -> unknown tissue properties
  - Literature dielectric values
    - Large spread

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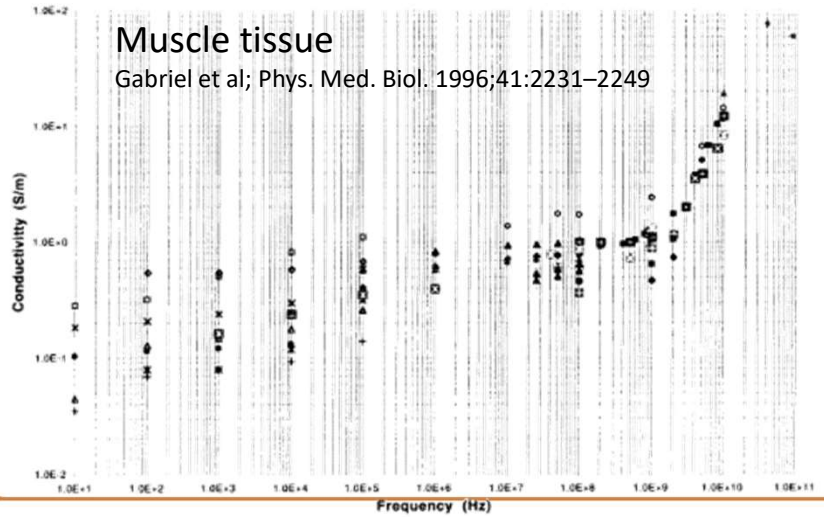
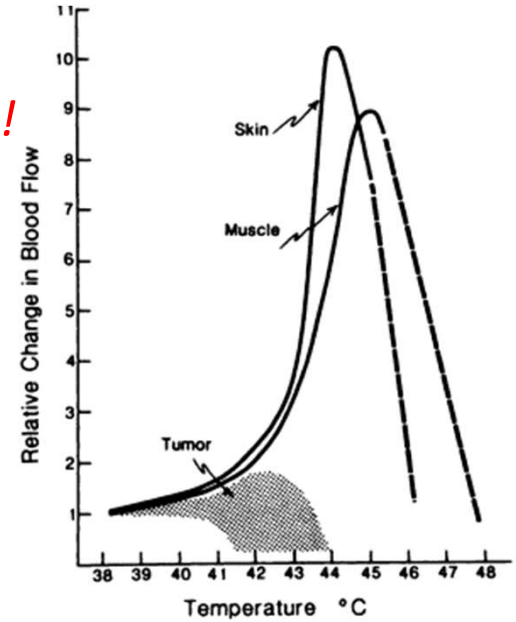
# Hyperthermia treatment planning

- Reliability of simulations
  - Patients -> unknown tissue properties
  - Literature dielectric values
    - Large spread

*Patient-dependent !*




Perfusion increases with temperature




Song. *Cancer research (SUPPL.)* 1984. 44, 4721S-4730S,

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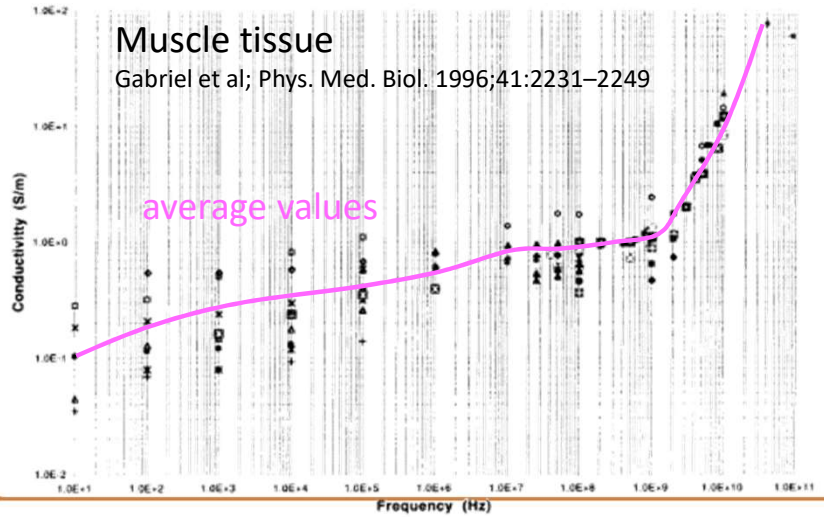
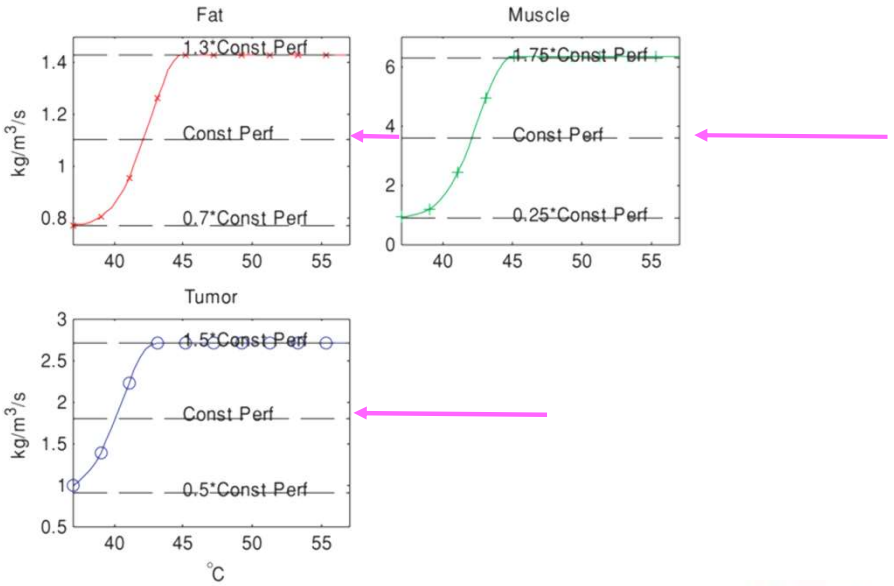
# Hyperthermia treatment planning

- Reliability of simulations
  - Patients -> unknown tissue properties
  - Literature dielectric values
    - Large spread
    - Uncertainty in SAR/temperature




Cheng et al; *Phys. Med. Biol*. 2009; 54(7): 1979–1995

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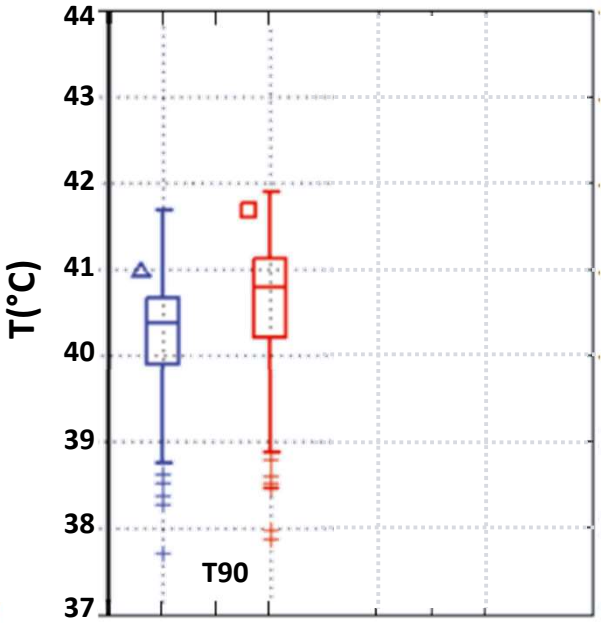
## Hyperthermia treatment planning

- Reliability of simulations
  - Patients -> unknown tissue properties
  - Literature dielectric values; perfusion increases with temperature
    - Large spread
    - Uncertainty in SAR/temperature

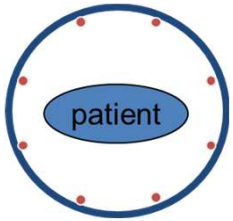
How will these uncertainties affect the reliability ?

# Hyperthermia treatment planning

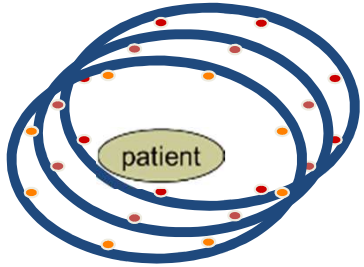
- Reliability of simulations
  - Monte Carlo analysis 20 cervical cancer patients
    - Dielectric and thermal parameters




**BSD Sigma-60**
(4 paired dipoles)




**BSD Sigma-eye**
24 paired dipoles




Canters et al. *Strahlenther Onkol 2013 · 189:74–80*

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# Hyperthermia treatment planning

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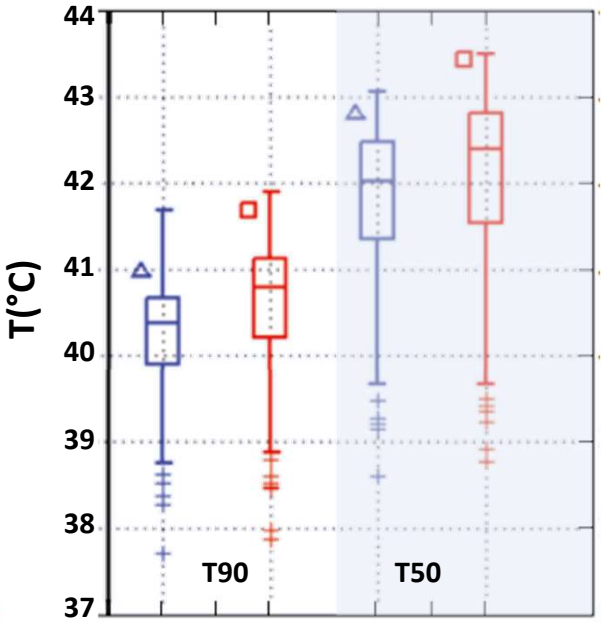


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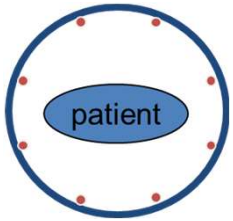


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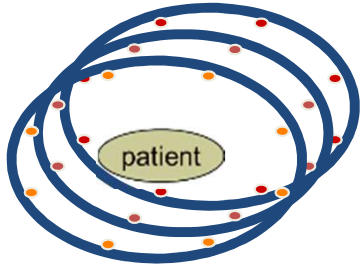


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# Hyperthermia treatment planning

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  - Monte Carlo analysis 20 cervical cancer patients
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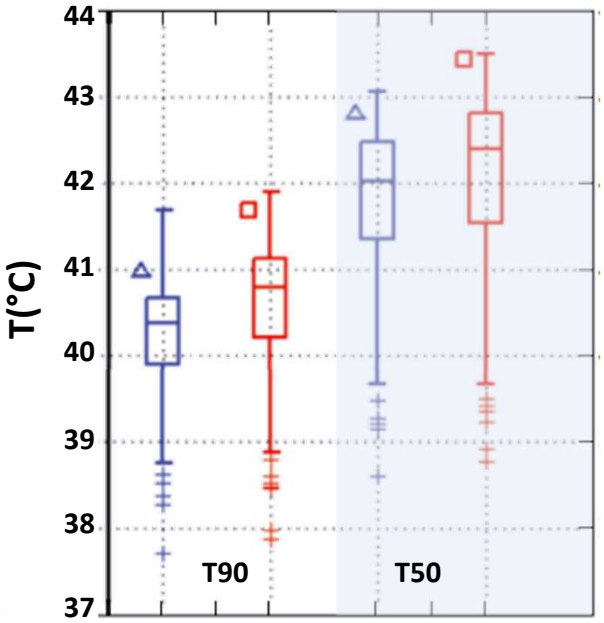
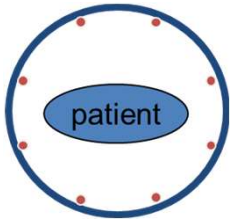



Variation can be up to several °C

**BSD Sigma-60**
(4 paired dipoles)

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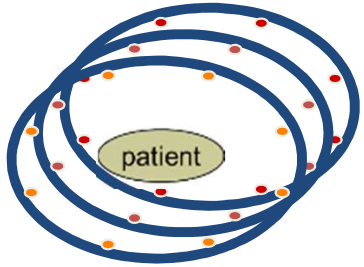


Canters et al. *Strahlenther Onkol 2013 · 189:74–80*

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## Hyperthermia treatment planning

- Reliability of simulations
  - Correlation between measured and simulated SAR values
    - Retrospective study:
      15 bladder cancer patients (78 sessions)

Kok *et al*. *Int. J. Rad. Onc. Biol. Phys.* 2014 vol. 90, pp. 438-445

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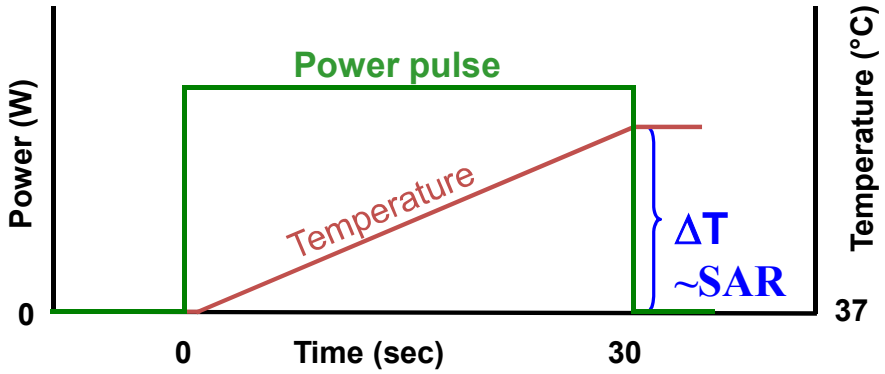
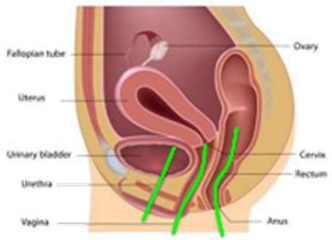
## Hyperthermia treatment planning

- Reliability of simulations
  - Correlation between measured and simulated SAR values
  - ”ΔT pulses” at the start with 3 different settings
    - 30 sec pulse: conduction and perfusion negligible →SAR



Thermometry probes

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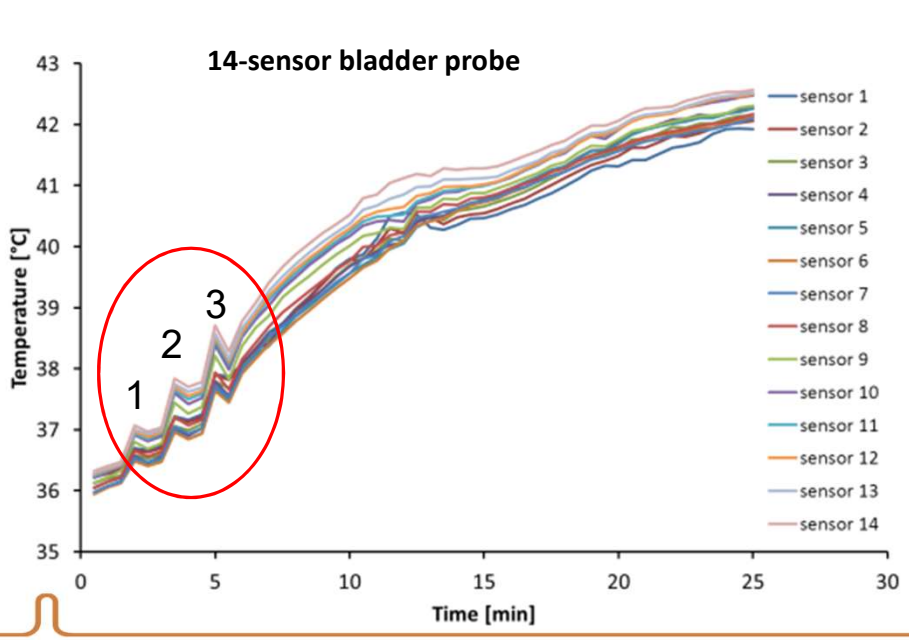
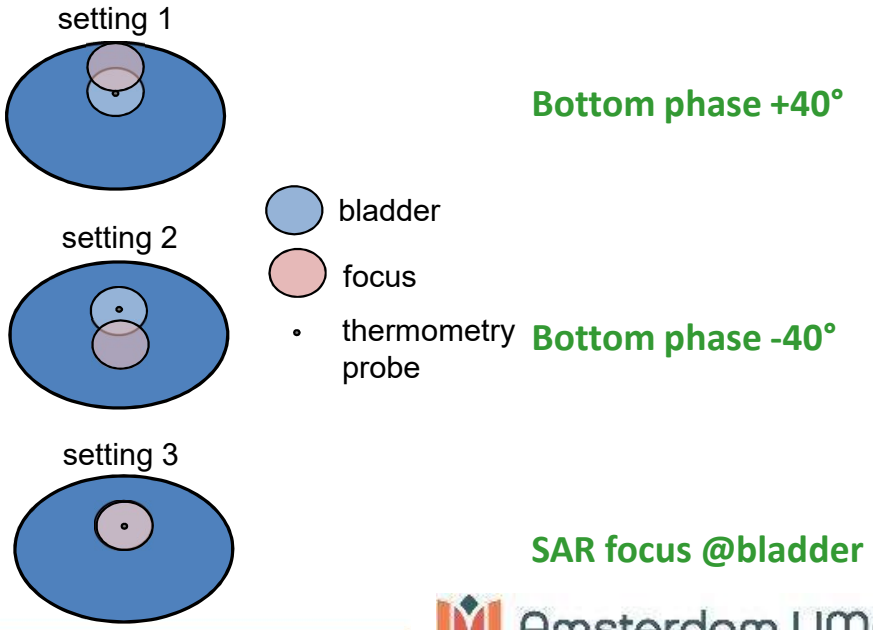
# Hyperthermia treatment planning

- Reliability of simulations
  - Correlation between measured and simulated SAR values
  - ”ΔT pulses” at the start with 3 different settings

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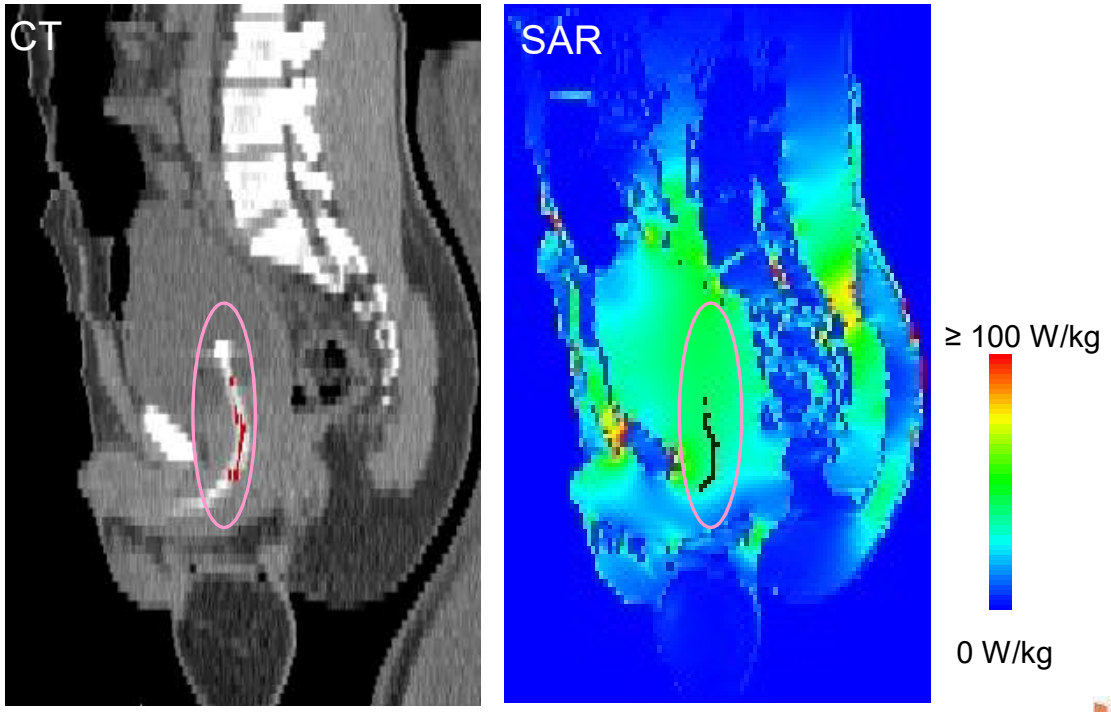
## Hyperthermia treatment planning

- Reliability of simulations
  - ”$\Delta$T pulses” at the start with 3 different settings

*Compare **simulated** and **measured** SAR along the thermometry tracks*

# Hyperthermia treatment planning

*Compare **simulated** and **measured** SAR along the thermometry tracks*

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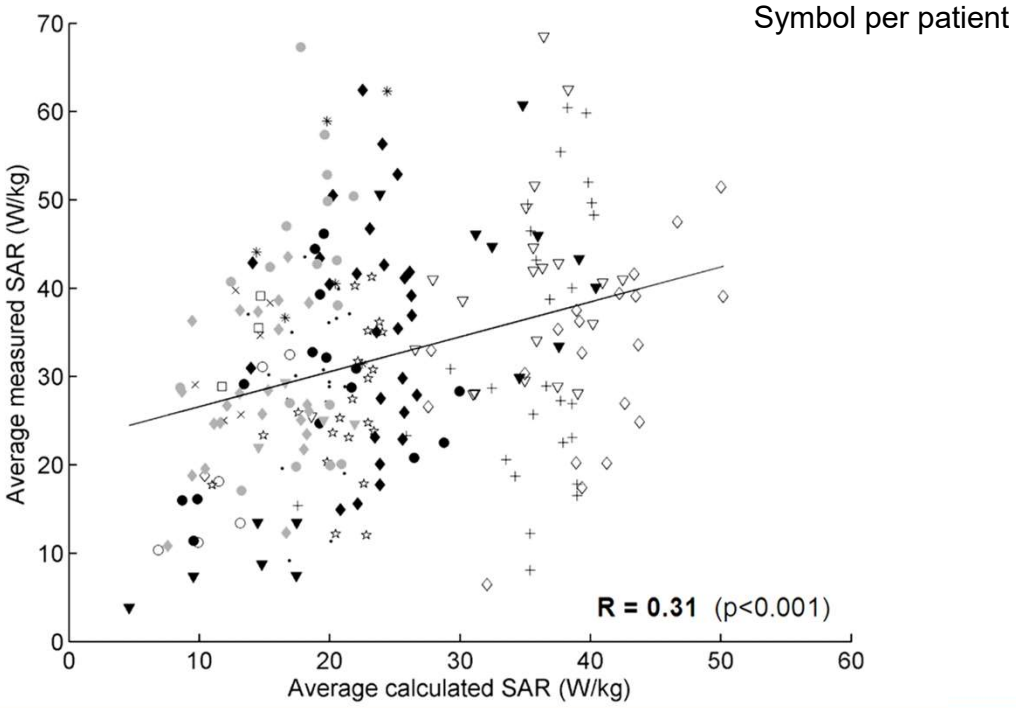
# Hyperthermia treatment planning

- Reliability of simulations
  - Absolute SAR values

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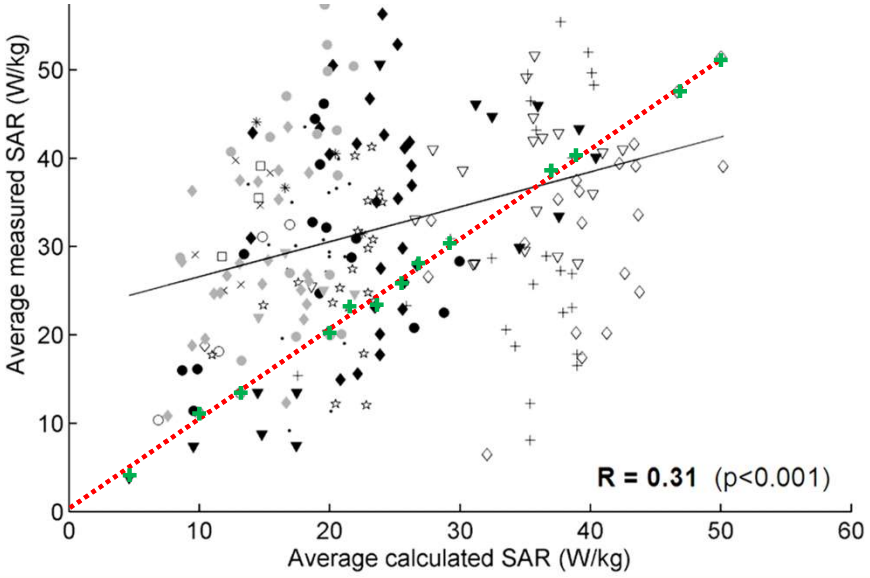
## Hyperthermia treatment planning

- Reliability of simulations
  - Absolute SAR values: no/poor correlation

***For only a few cases measurements and simulations coincide (by chance)***

***Also poor correlation -> Planning is not quantitatively reliable !***

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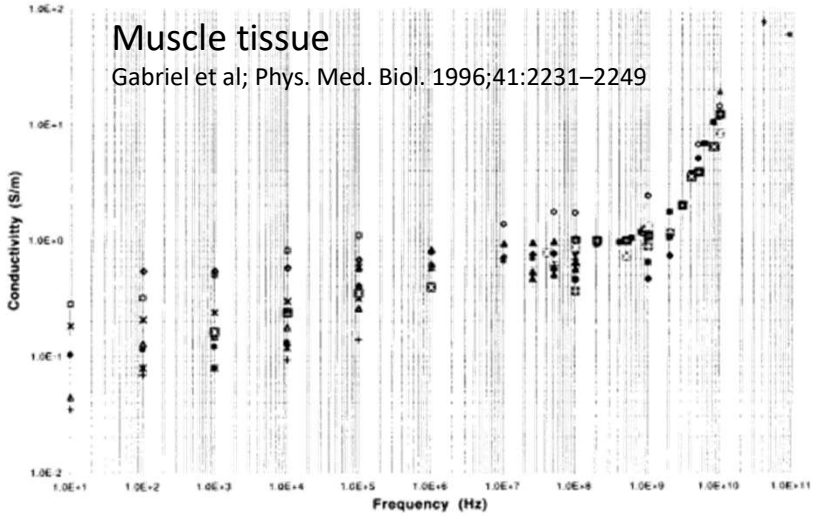
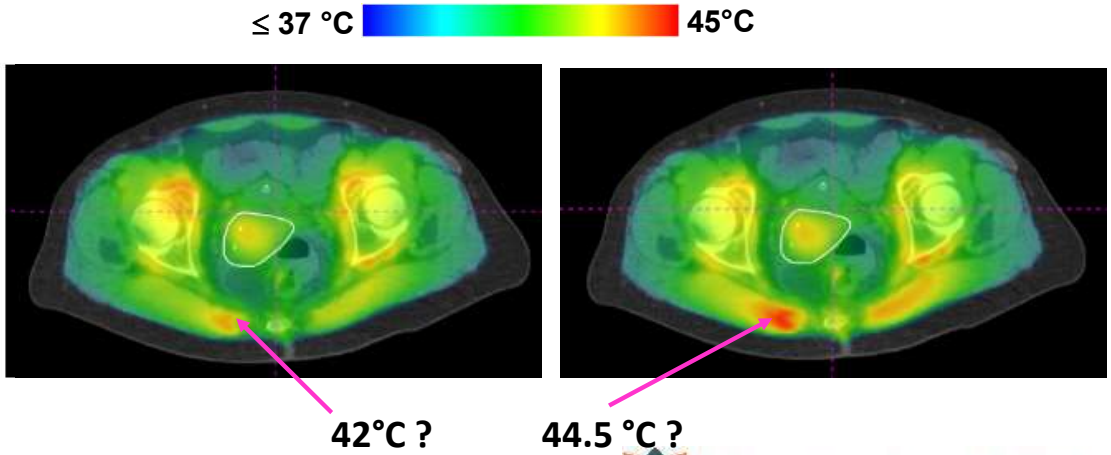
## Hyperthermia treatment planning

- Treatment planning not quantitatively reliable
  - Due to uncertainties in tissue properties
    - Different tissue properties yield different absolute predictions




→ **Uncertainty in simulation result**

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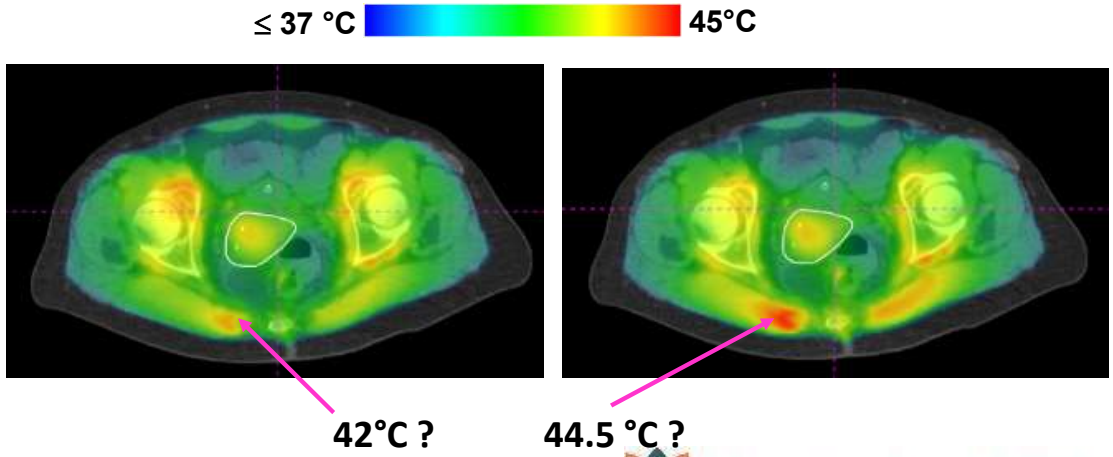
## Hyperthermia treatment planning

- Treatment planning not quantitatively reliable
  - Due to uncertainties in tissue properties
    - Different tissue properties yield different absolute predictions

→ **Uncertainty in simulation result**

  - Potential hot spot locations are predictable
    - Anatomy-related: tissue interfaces
  - ‘Amplitude’ unknown



***So this means planning is useless in clinical hyperthermia ???***

***NO !***

## Hyperthermia treatment planning

- Reliability
  - Consider changes after adjusting phase-amplitude settings

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# Hyperthermia treatment planning

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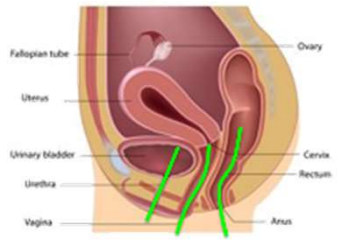
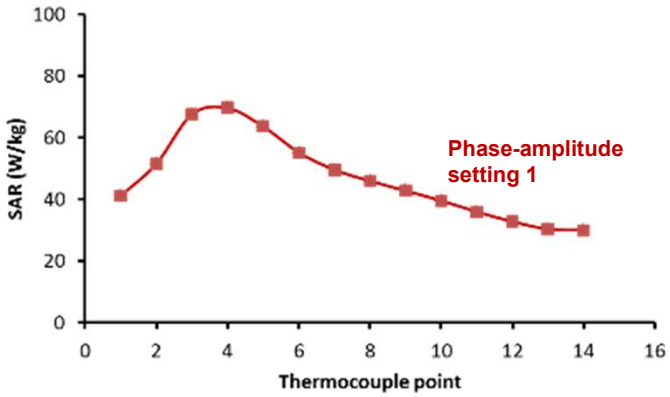
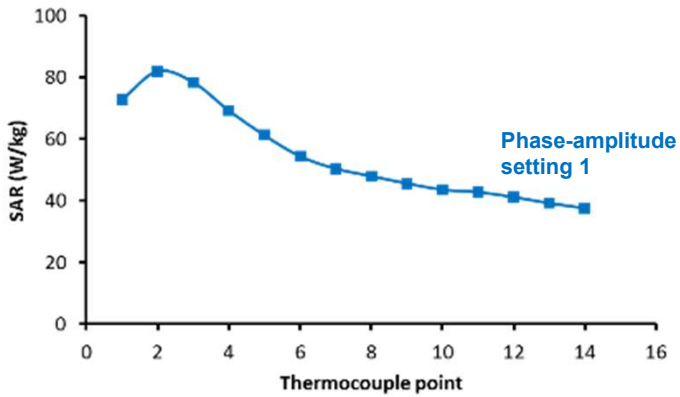



**probe trajectory**

**Measured**




**Simulated**

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# Hyperthermia treatment planning

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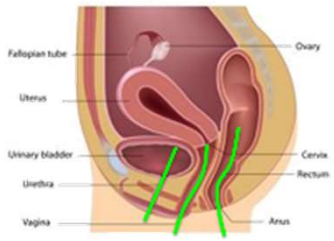


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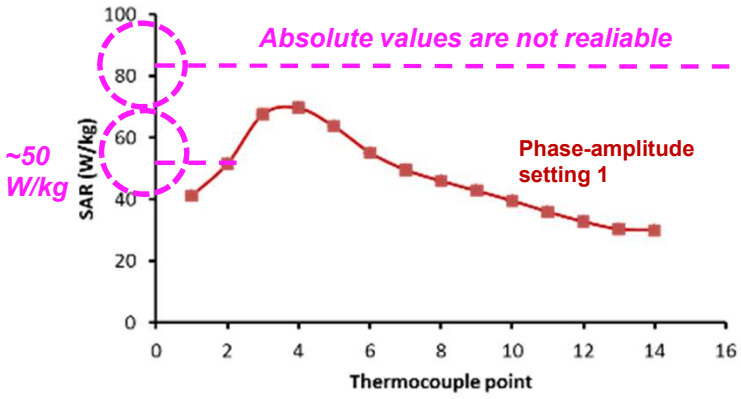


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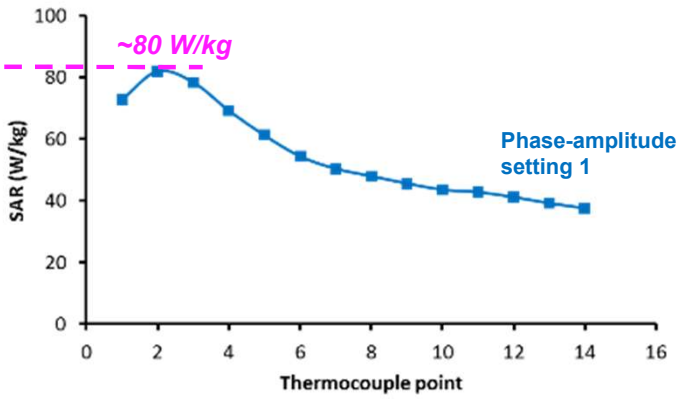


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# Hyperthermia treatment planning

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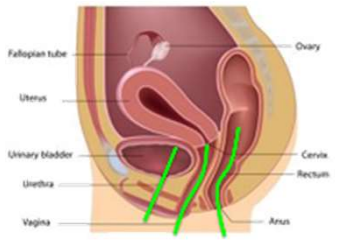


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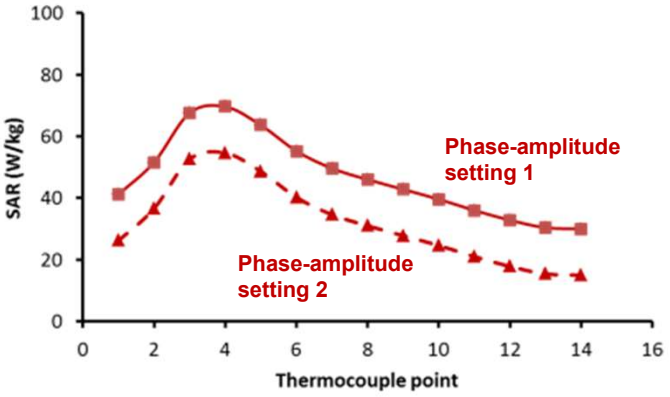


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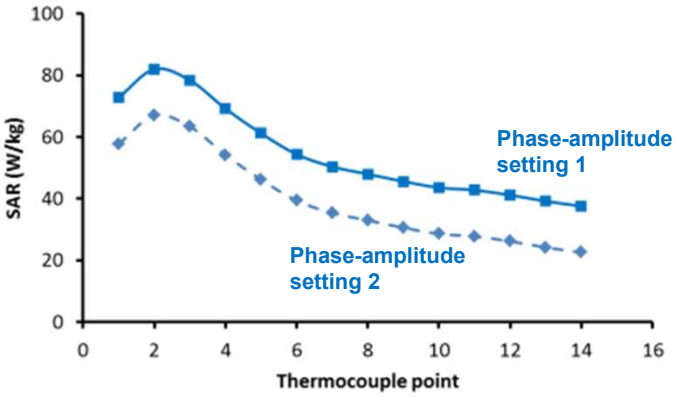


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# Hyperthermia treatment planning

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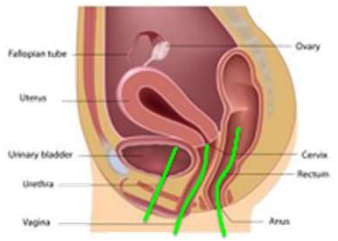


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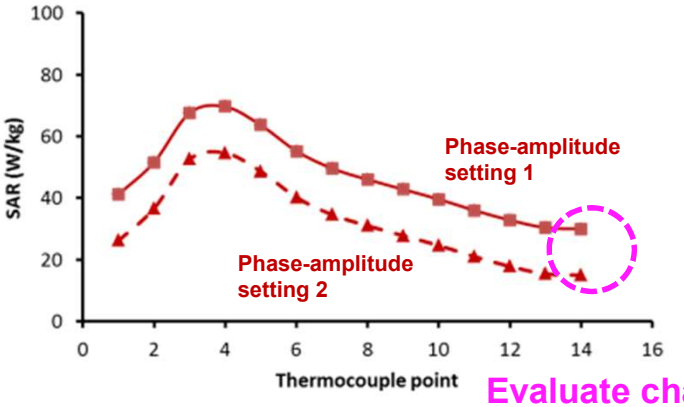


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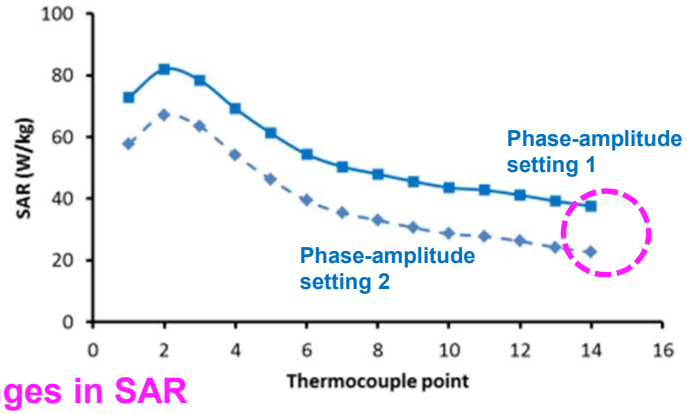


**Evaluate changes in SAR**

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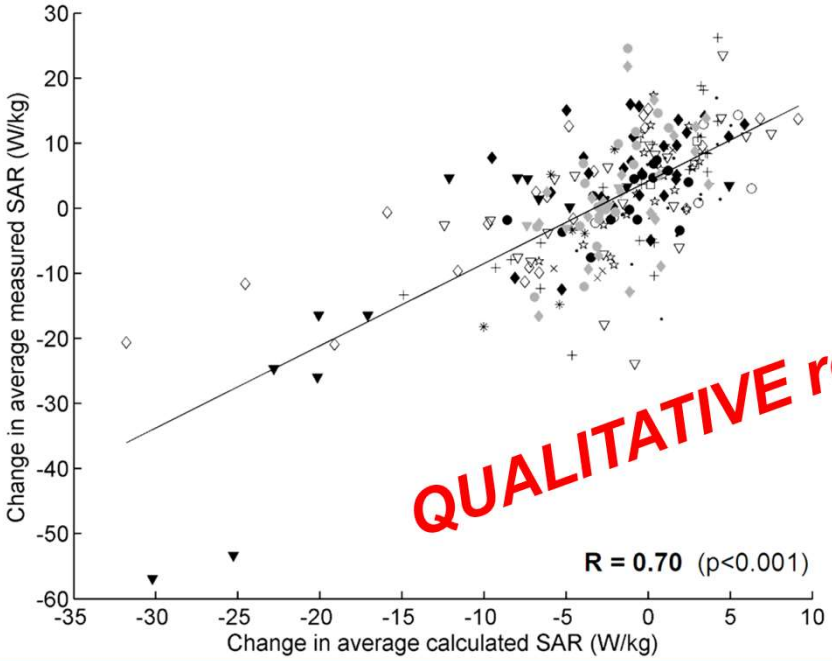
## Hyperthermia treatment planning

- Reliability
  - Consider changes after adjusting phase-amplitude settings -> correlation

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## Hyperthermia treatment planning

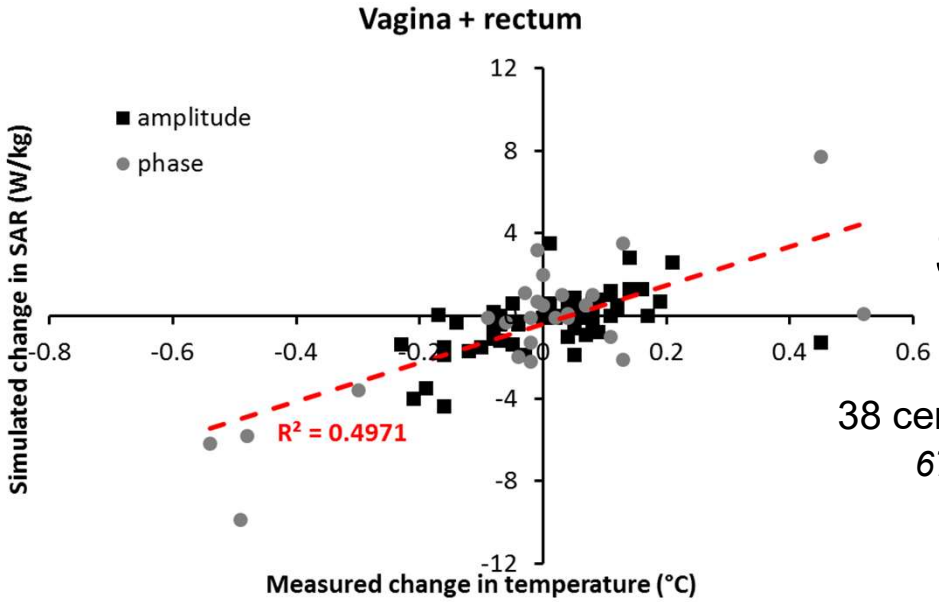
- Reliability
  - Simulated and measured changes in SAR correlate at the start of treatment

## Hyperthermia treatment planning

- Reliability
  - Simulated and measured changes in SAR correlate at the start of treatment
  - But during treatment ?
    with enhanced perfusion and its uncertainty ?

## Hyperthermia treatment planning

- Reliability
  - Correlation between predicted and measured changes in SAR/temperature during treatment




SAR

38 cervix/ bladder patients
*67 steering events*

Kok *et al Int J Hyperthermia. 2019; 35(1):330-339*

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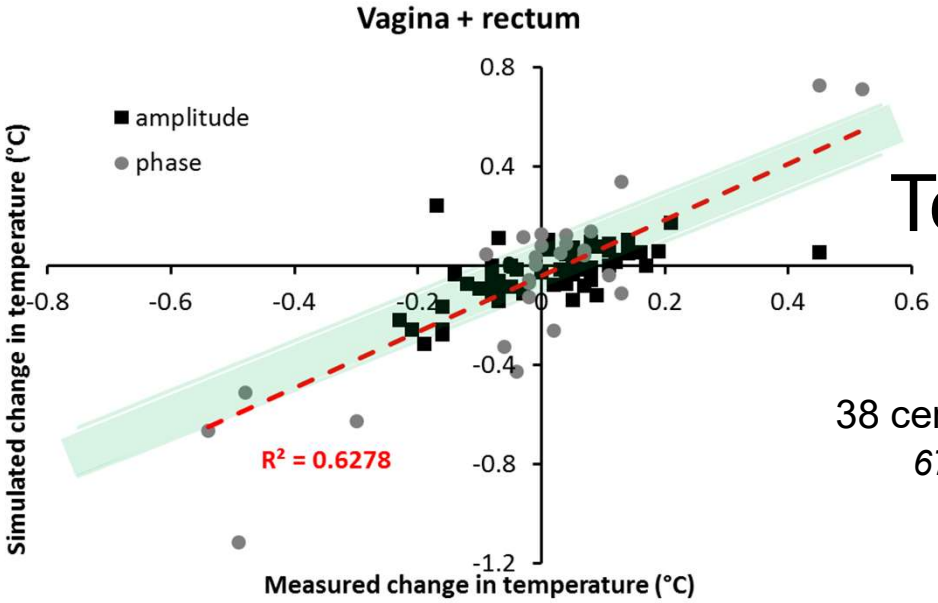
## Hyperthermia treatment planning

- Reliability
  - Correlation between predicted and measured changes in SAR/temperature during treatment




Temperature

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Kok *et al Int J Hyperthermia. 2019; 35(1):330-339*

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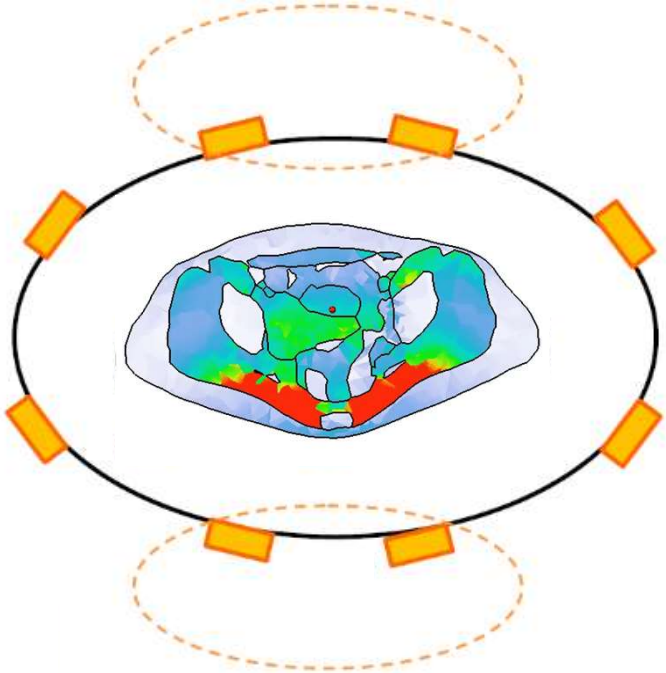
## Hyperthermia treatment planning

- Reliability
  - Not quantitatively reliable
  - *Qualitative* reliability:
    - Comparison of different treatment strategies
    - Assistance in phase-amplitude steering

*BSD Sigma-60*



*Planning can qualitatively predict effects of steering*

**AP SAR steering by Phase**

Difference top-bottom:

-120 ~ +120

Courtesy: G.C. van Rhoon

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## Hyperthermia treatment planning

- Reliability
  - Not quantitatively reliable
  - *Qualitative* reliability:
    - Comparison of different treatment strategies
    - Assistance in phase-amplitude steering

***Allows use of treatment planning for clinical application and in a clinical workflow***

# Hyperthermia treatment planning

## *Applications*

## Hyperthermia treatment planning

- Hyperthermia treatment planning
  - Wide variety of applications

1. Device design
2. Clinical applicator selection
3. (Pre-)treatment evaluation
4. On-line assistance in treatment guidance
5. Full treatment guidance

## Hyperthermia treatment planning

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  - Wide variety of applications

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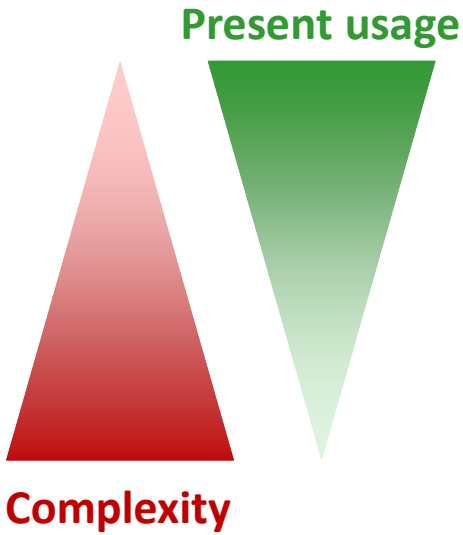

## Hyperthermia treatment planning

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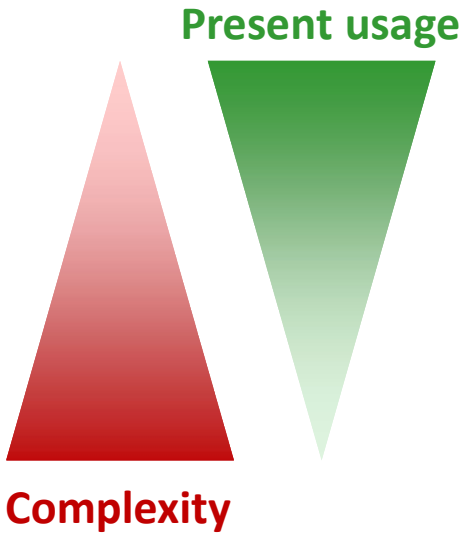

## Device design

- *Purpose:* develop new applicator system
  - Model different antenna designs for the same geometries
    - Only variable is the applicator design, everything else is constant

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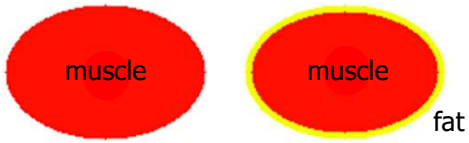
    - Uncertainties in tissue properties not a major issue
  - Compare heating characteristics to optimize the design

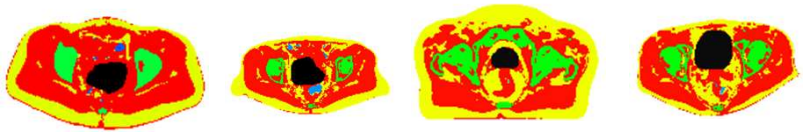
## Device design

- *Purpose:* develop new applicator system
  - Model different antenna designs for the same geometries
    - Only variable is the applicator design, everything else is constant
    - Uncertainties in tissue properties not a major issue
  - Compare heating characteristics to optimize the design
  - First evaluate basic heating characteristics: homogeneous + simple inhomogeneous structure
    - Focus size, steering properties,…



# Device design

- *Purpose:* develop new applicator system
  - Model different antenna designs for the same geometries
    - Only variable is the applicator design, everything else is constant
    - Uncertainties in tissue properties not a major issue
  - Compare heating characteristics to optimize the design
  - Various human anatomies: clinical heating properties
    - Target heating, hot spots incidence,…



Models can be used from:
- clinical patient data sets
- standard data sets (e.g. virtual human data set)

https://itis.swiss/virtual-population/

## Device design

Evaluation metrics

- SAR:
  - Average target SAR

# Device design

## Evaluation metrics

- SAR:
  - Average target SAR
    - Useful to evaluate power absorption in the target (heating quality) in case of a fixed power level.
      - Correlates with T50 for locoregional heating*

*Canters et al. *Int J Hyperthermia*. 2009;25(7):593–608

## Device design

Evaluation metrics

- SAR:
  - $HTQ = \frac{<SA\ \ hotspot>}{<SA\ \ target>}$
    - ratio between target and normal tissue heating to compare different strategies and identify the strategy with the lowest risk of hot spots

*Canters et al. Phys Med Biol. 2011;56(2):439–451

# Device design

## Evaluation metrics

- SAR:
  - $HTQ = \frac{<SAR_{hotspot}>}{<SAR_{target}>}$
    - ratio between target and normal tissue heating to compare different strategies and identify the strategy with the lowest risk of hot spots
    - $SAR_{hotspot:}$ e.g the 0.1% or 1% exposed to the highest SAR
      - Correlates with clinical hot spot complaints*

*Canters et al. Phys Med Biol. 2011;56(2):439–451

## Device design

Evaluation metrics

- SAR:
  - Average target SAR
  - HTQ
  - Target coverage TCx
    - Target volume covered by x% of the max. overall SAR

# Device design

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- SAR:
  - Average target SAR
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  - Target coverage TCx
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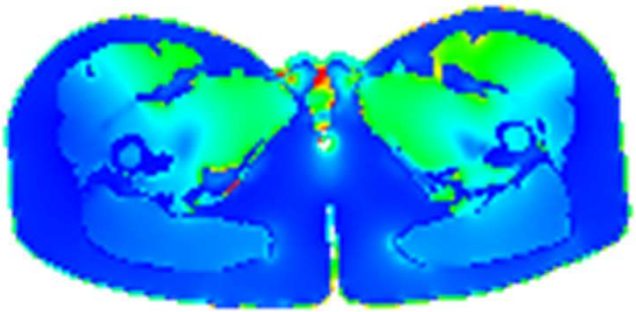
    - $TC_{25}$ is a prognostic factor in superficial hyperthermia*
      - Typically $TC_{25} > 75\%$ ensures adequate treatment

*Myerson et al. *Int J Radiat Oncol Biol Phys*. 1990;18(5):1123–1129

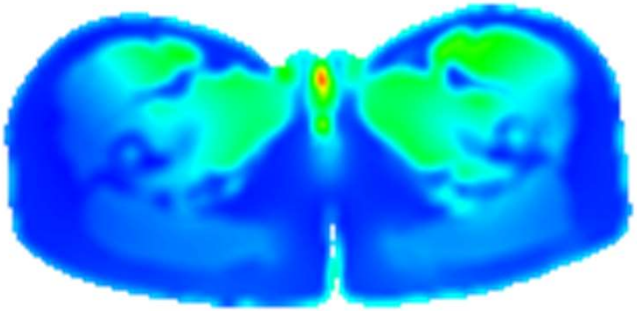
# Device design

## Evaluation metrics

- SAR:
  - Local high SAR peaks can affect conclusions
    - → use 1cc average SAR for evaluation



**voxel-based SAR**



**1 cc averaged SAR**

# Device design

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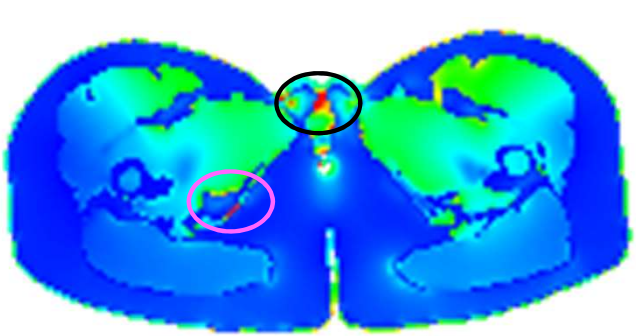
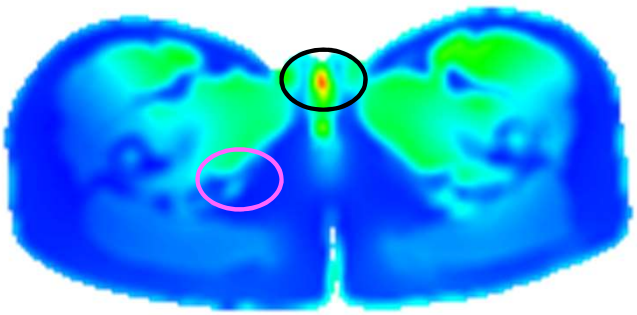


voxel-based SAR



1 cc averaged SAR

Very small peaks will not lead to thermal hot spots. Averaged out in 1cc

**Larger regions remain**

## Device design

Evaluation metrics

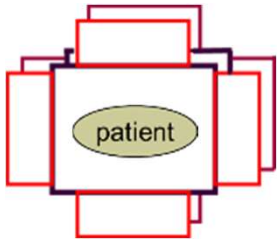
- Temperature:
  - T10, T50 and T90
    - Txx = temperature achieved in xx% of tumor volume
  - Bolus cooling influences superficial hot spots

## Device design

- Clinical systems designed with help of simulations:

***AMC-8 system*** (pelvic hyperthermia)

– 8 waveguides
– 2 rings
– 70 MHz





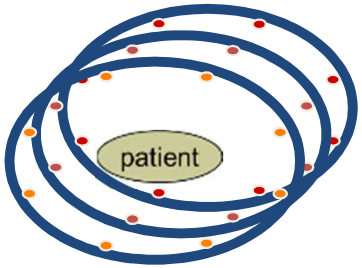

Crezee et al *Int. J. Hyperthermia*. 2009;25(7):581-92.

## Device design

- Clinical systems designed with help of simulations:

***BSD Sigma-Eye system*** (pelvic hyperthermia)

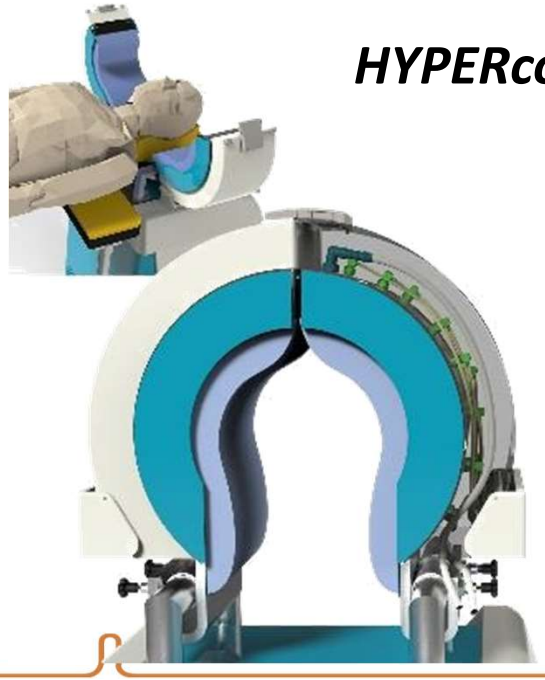
– 24 (paired) dipoles
– 3 rings
– 100 MHz




Wust et al, *Int. J. Hyperthermia, 2009; 25(7): 517–528*.

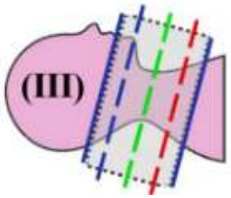
## Device design

- Clinical systems designed with help of simulations:



***HYPERcollar*** (Head & Neck hyperthermia)

- 12 patch antennas
- 3 rings
- 434 MHz





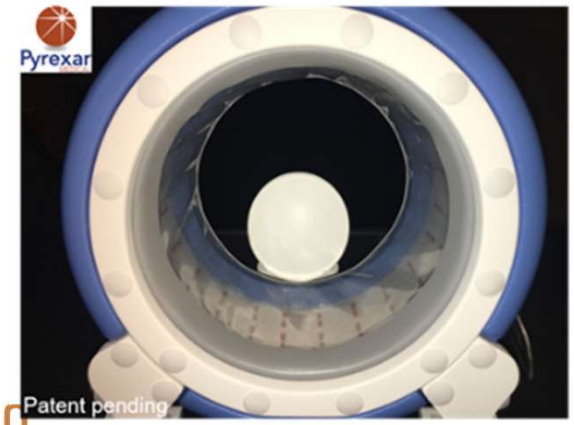

Togni et al *Phys Med Biol* 2013: 58(17):5997-6009.

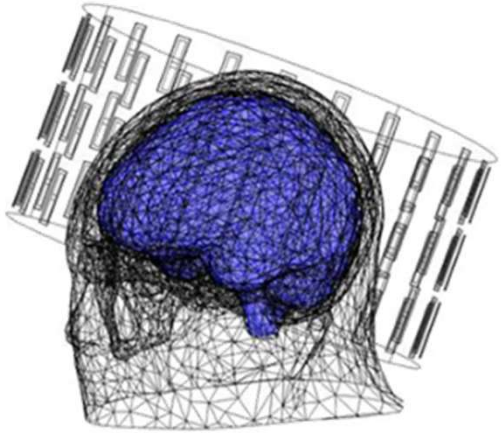
## Device design

- Dedicated systems for challenging sites under development:

***Crown applicator*** (Brain hyperthermia)

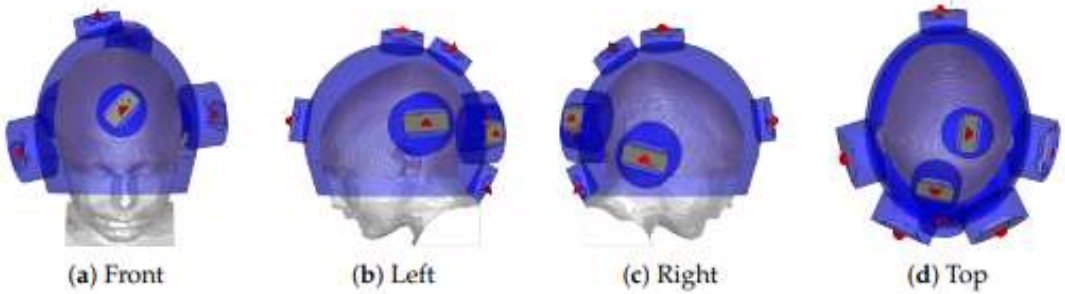
72 channel 915 MHz system (Pyrexar medical)

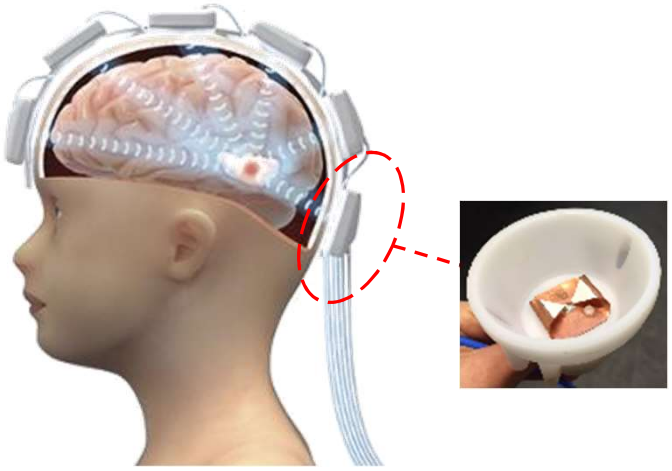


## Device design

- Dedicated systems for challenging sites under development:
  - Multifrequency multichannel UWB array
    - Pediatric brain tumors
    - 8 self grounded bow tie antennas
      - 4x 300-600 MHz
      - 4x 400-800 MHz



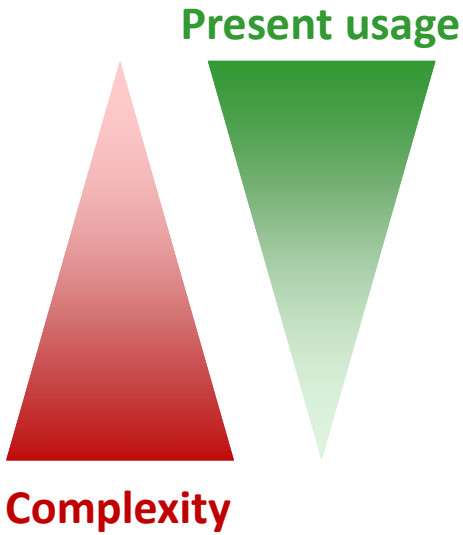
Takook et al, Int J Hyperthermia. 2017;33:387-400

Aram et al, Cancers 2021. 13: 3277

## Hyperthermia treatment planning

- Hyperthermia treatment planning
  - Wide variety of applications

1. Device design
2. Clinical applicator selection
3. (Pre-)treatment evaluation
4. On-line assistance in treatment guidance
5. Full treatment guidance



## Applicator selection

- *Purpose:* determine the best treatment strategy with the equipment available.

# Applicator selection

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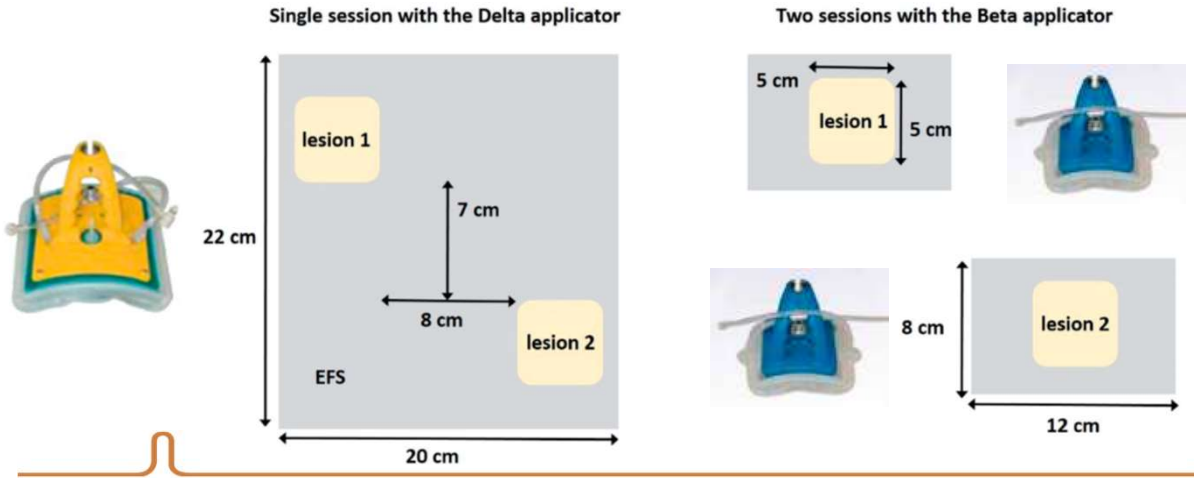
***Clinical problem:*** *Patient with 2 melanoma lesions on the back*
*Treated with ALBA4000-ON*




*Use one large antenna or seperate session per lesion ?*

Kok *et al Int J Hyperthermia. 2021; 38(1): 532–551*

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## Applicator selection

- Use one large antenna or seperate session per lesion ?
  - Calculate 1cc SAR for both options
  - Target coverage TCx
    - Target volume covered by x% of the max. overall SAR
    - $TC_{25}$ is a prognostic factor in superficial hyperthermia*
      - Typically $TC_{25}$ > 75% ensures adequate treatment

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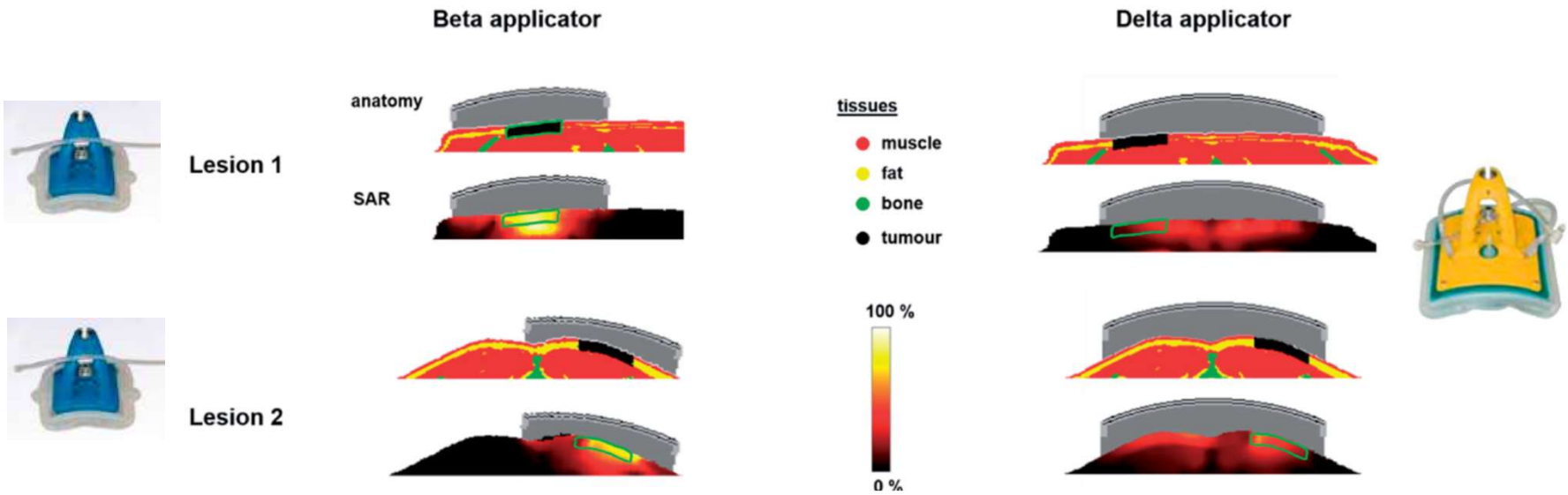


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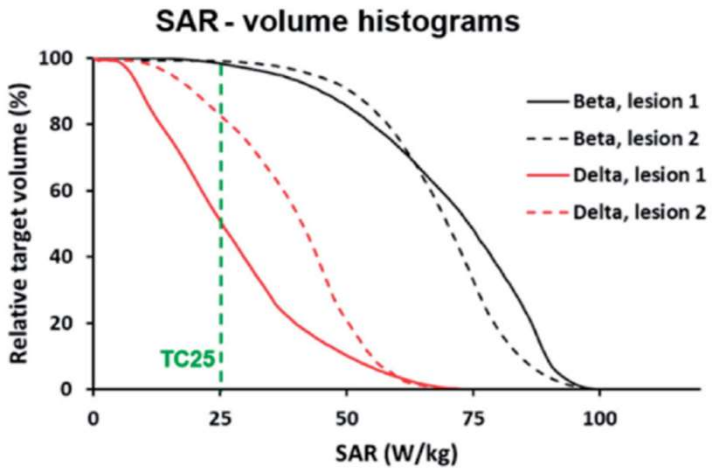


TC25

| | Beta | Delta |
|---|---|---|
| Lesion 1 | 98% | 51% |
| Lesion 2 | 99% | 83% |

Kok *et al Int J Hyperthermia. 2021; 38(1): 532–551*

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# Applicator selection

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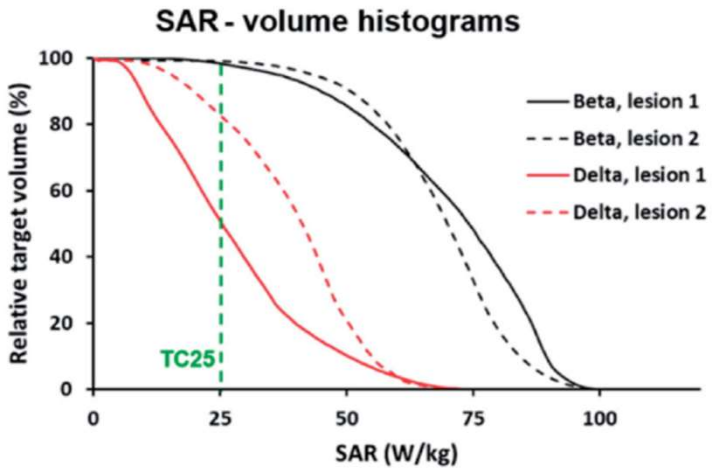


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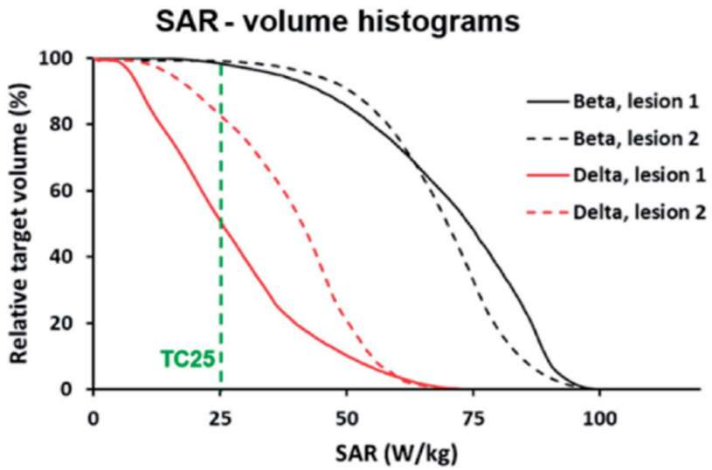
# Applicator selection

- Use one large antenna or seperate session per lesion ?

*Conclusion based on planning evaluation: 2 separate sessions with Beta*

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# Applicator selection

- *Purpose:* determine the best treatment strategy with the equipment available.

***Celsius TCS device***

***Clinical problem:*** *Bladder cancer patient treated with Celsius TCS capacitive device in supine position*

*Which electrode combination would be most effective:*

- *25 cm + 25 cm*
- *15 cm + 25 cm (focusing toward 15 cm top electrode)*

## Applicator selection

- Which electrode combination is most effective ?
  - Calculate 1cc SAR for both options (same power)
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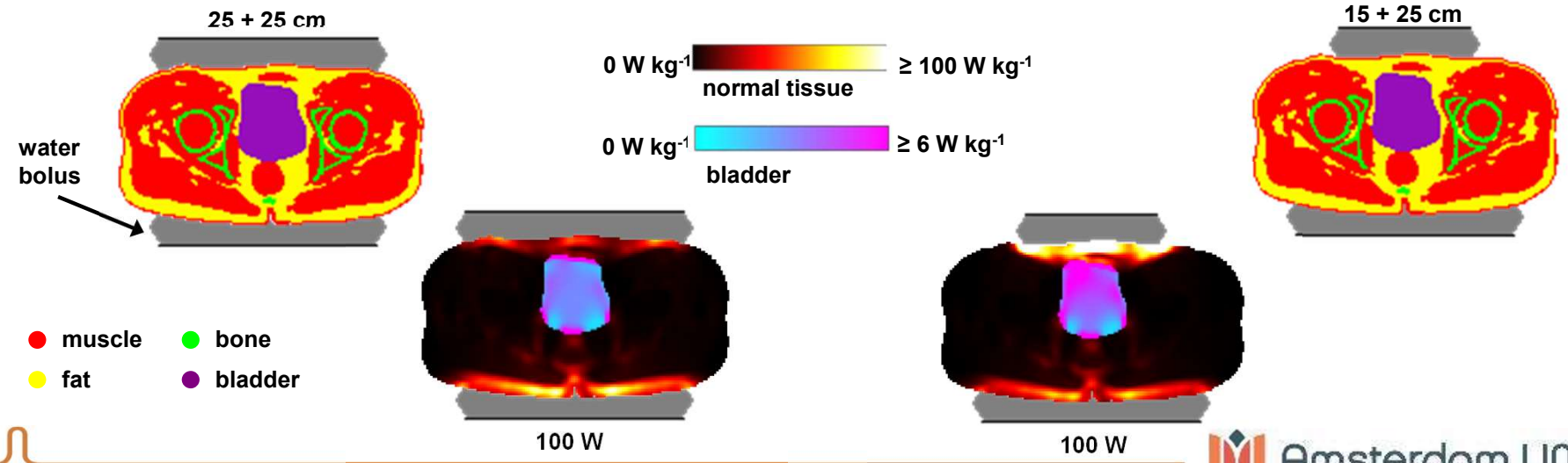

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| Electrode diameters top + bottom | $\langle SAR_{hotspot} \rangle$ (W/kg) | $\langle SAR_{target} \rangle$ (W/kg) | HTQ |
|---|---|---|---|
| 25 + 25 cm | 85.2 | 3.6 | 23.7 |
| 15 + 25 cm | 153.9 | 6 | 25.6 |

Kok *et al Int J Hyperthermia. 2021; 38(1): 532–551*

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**Rather comparable HTQ**
**(sligthly more favorable for 25+25 cm)**

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**Better target SAR/ focusing**

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**Higher risk of hot spots?** **Better target SAR/ focusing**



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# Applicator selection

- Which electrode combination is most effective ?
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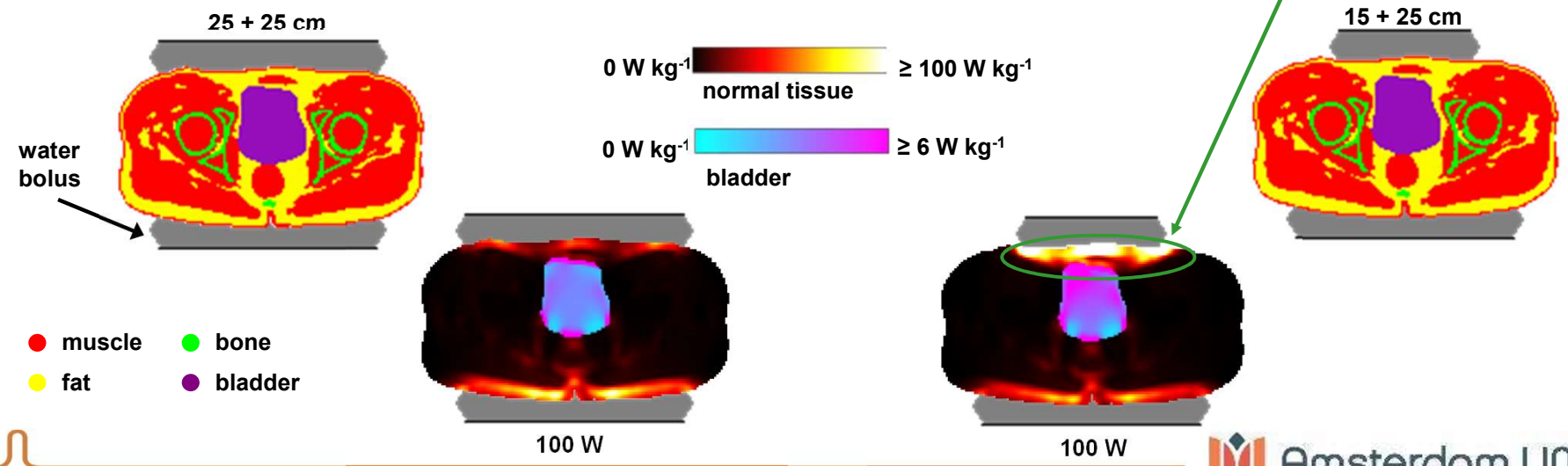
Hot spots are superficial
-> Bolus cooling is important

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## Applicator selection

- Which electrode combination is most effective ?
  - Calculate 1cc SAR for both options (same power)
  - Evaluate hot-spot-target ratio
  - Evaluate temperature
    - Clinical range of bolus water temperatures (10-18°C)
    - Scale power till treatment limiting temperatures (44-45°C)

Kok *et al Int J Hyperthermia. 2021; 38(1): 532–551*

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| Electrode diameters top + bottom | T90 (°C) | T50 (°C) | T10 (°C) |
|---|---|---|---|
| Water bolus 18 °C | | | |
| 25 + 25 cm | 38.6 | 38.9 | 39.6 |
| 15 + 25 cm | 38.3 | 38.7 | 39.6 |
| Water bolus 10 °C | | | |
| 25 + 25 cm | 38.8 | 39.1 | 39.7 |
| 15 + 25 cm | 38.4 | 38.9 | 39.9 |

**Slightly higher T90 with 25+25 cm**

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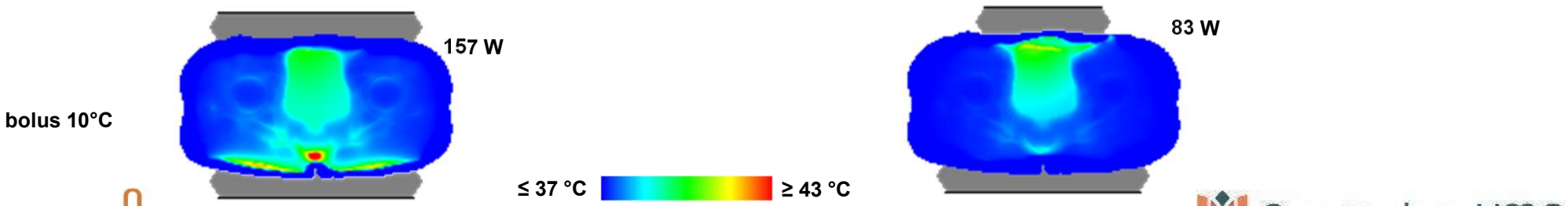


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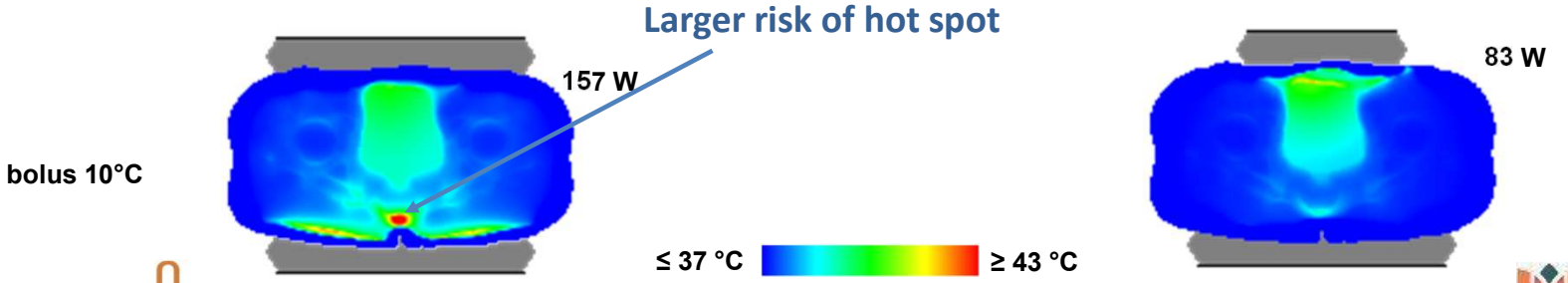


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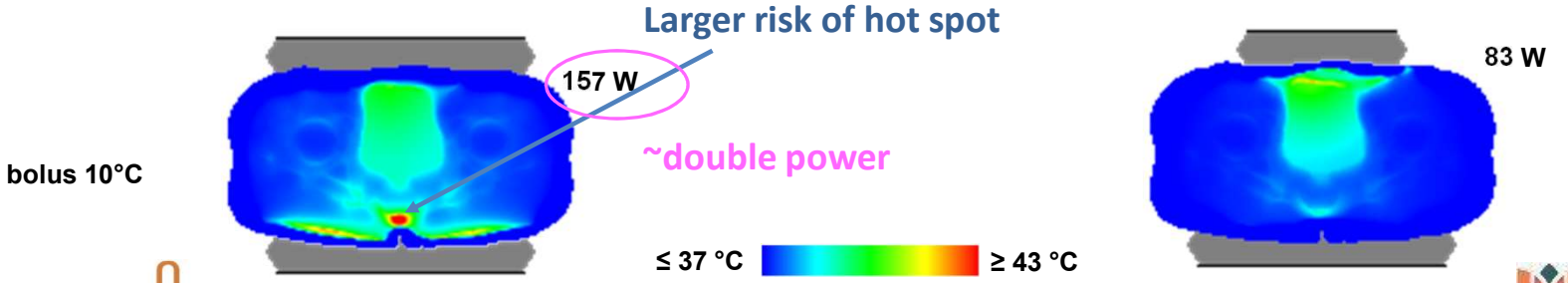


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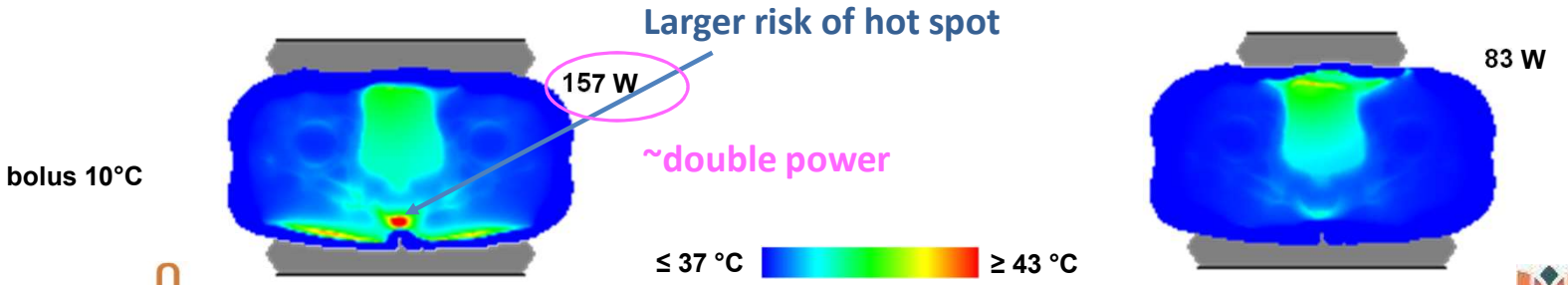
**Clinical experience:**

Power < 150-200 W
beyond 150W the risk of hot spots is substantially increased

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*Conclusion based on planning evaluation: choose 15 + 25 cm*



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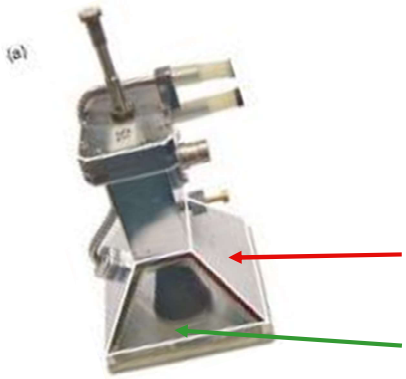
# Applicator selection

- *Purpose:* determine the best treatment strategy with the equipment available.

***Orientation Lucite cone applicator***



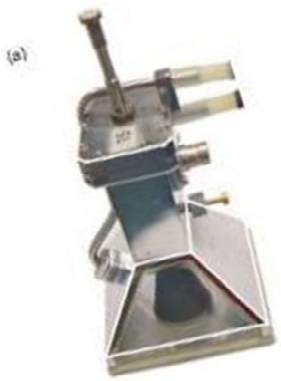

***Clinical problem:*** *Head and neck cancer patient treated with Lucite cone applicator*

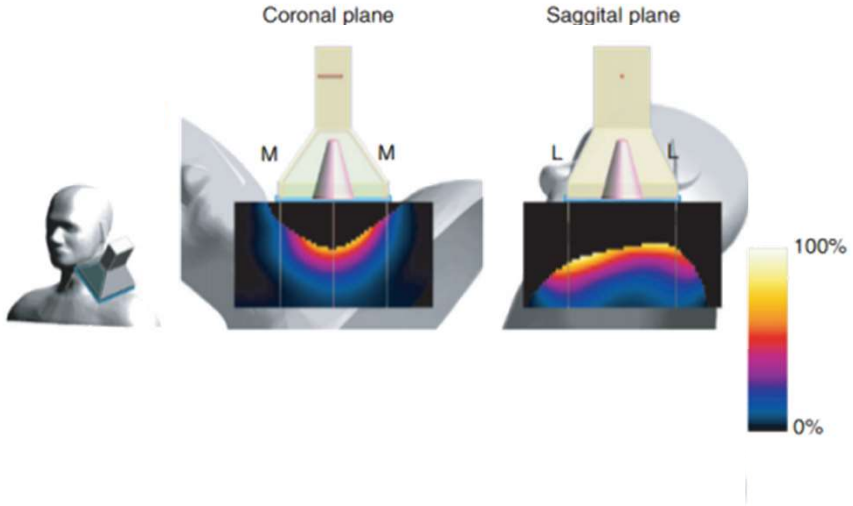
*Best positioning with metal edge facing neck and shoulder…. or lucite window ?*

# Applicator selection

- *Positioning with metal edge or lucite window facing neck/ shoulder?*

***Orientation Lucite cone applicator***





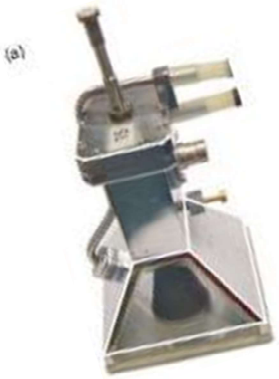

**<u>Metal edge facing neck and shoulder:</u>**
*SAR maximum outside the central plane of the applicator*

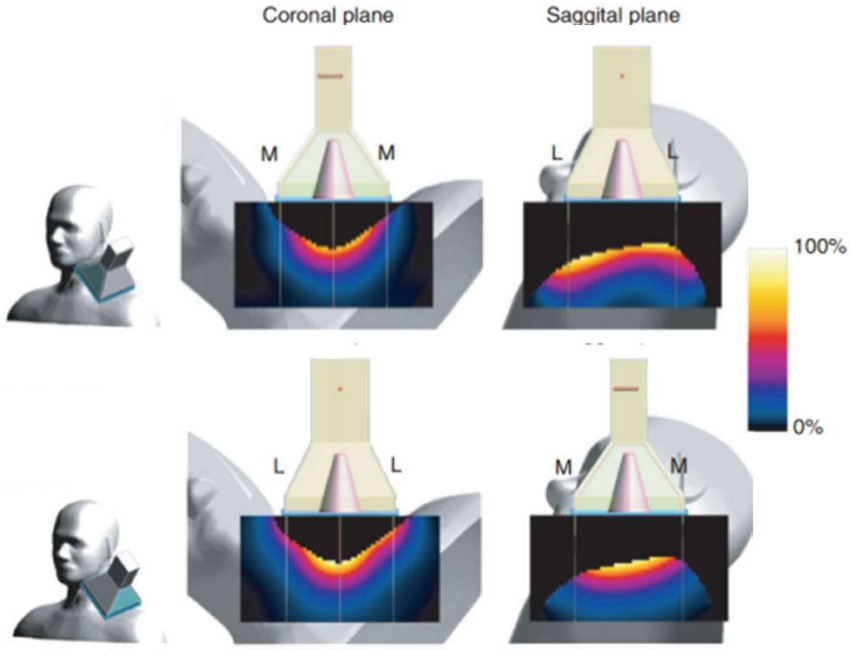
De Bruijne et al. *Int. J. Hyperthermia. 2007; 23(5): 417–429*

# Applicator selection

- *Positioning with metal edge or lucite window facing neck/ shoulder?*

***Orientation Lucite cone applicator***






**Metal edge facing neck and shoulder:**
*SAR maximum outside the central plane of the applicator*

**Lucite window facing neck and shoulder:**
*SAR focus centrally below the applicator at the site of the tumour (better focusing)*

De Bruijne et al. *Int. J. Hyperthermia. 2007; 23(5): 417–429*

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# Applicator selection

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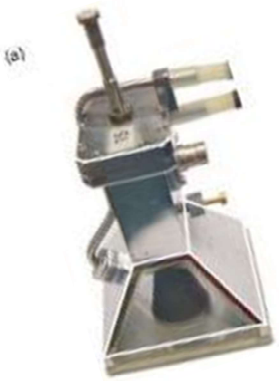
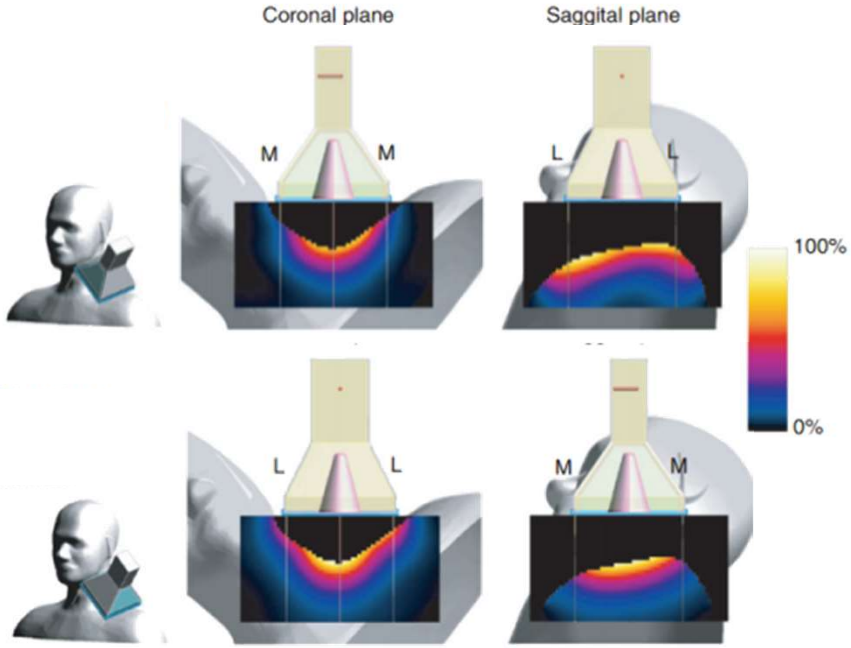
***Orientation Lucite cone applicator***






**Metal edge facing neck and shoulder:**
*SAR maximum outside the central plane of the applicator*

***Possible metrics to evaluate: TC25 and HTQ***

**Lucite window facing neck and shoulder:**
*SAR focus centrally below the applicator at the site of the tumour (better focusing)*

De Bruijne et al. *Int. J. Hyperthermia. 2007; 23(5): 417–429*

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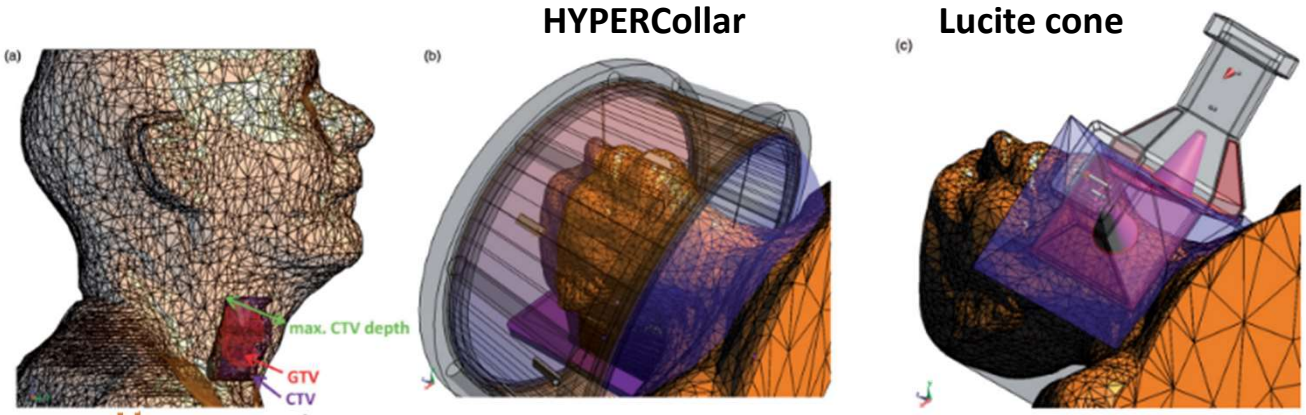
# Applicator selection

- *Purpose:* determine the best treatment strategy with the equipment available.

***Clinical problem:*** *Head and neck cancer patient best treated with HYPERcollar or Lucite cone applicator ?*




Drizdal et al. *Int. J. Hyperthermia. 2018; 34(6): 704-713*

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# Applicator selection

- *Head and neck cancer patient best treated with HYPERcollar or Lucite cone applicator?*

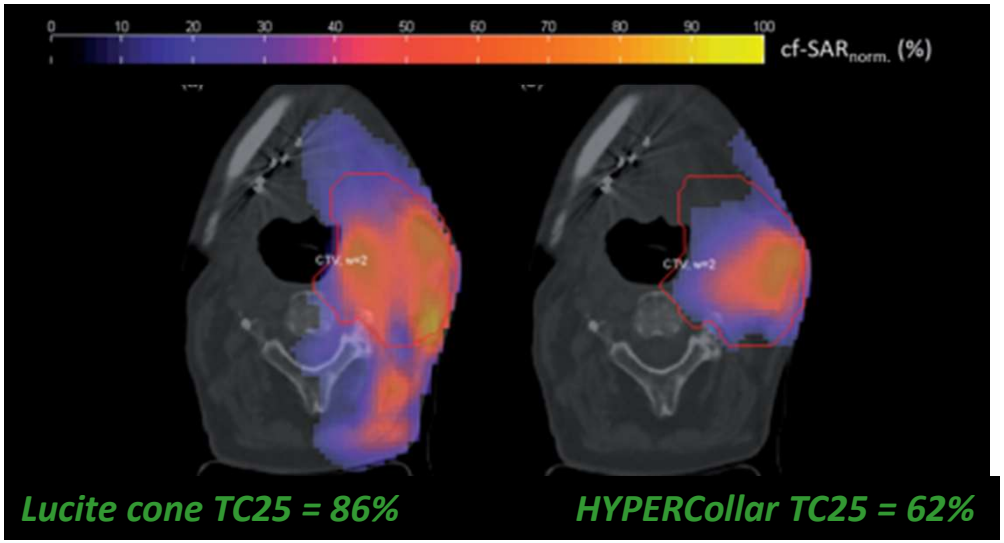
  - Target coverage TCx
    - Target volume covered by x% of the max. overall SAR
    - $TC_{25}$ is a prognostic factor in superficial hyperthermia*
      - Typically $TC_{25}$ > 75%  ensures adequate treatment

*Myerson et al. *Int J Radiat Oncol Biol Phys*. 1990;18(5):1123–1129

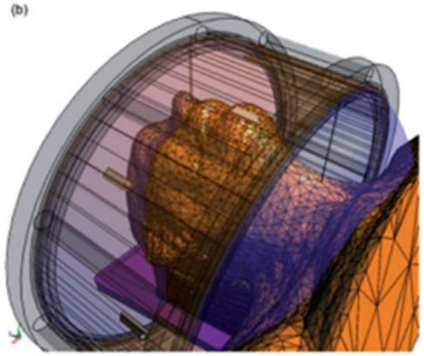
# Applicator selection

- *Head and neck cancer patient best treated with HYPERcollar or Lucite cone applicator?*
  - Target coverage TC25

Lucite cone




HYPERCollar



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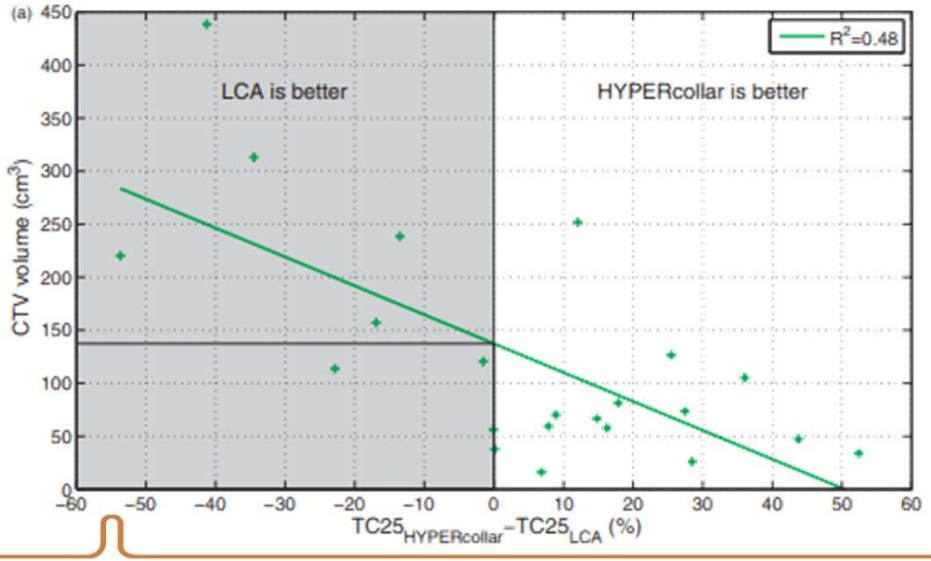
Drizdal et al. *Int. J. Hyperthermia. 2018; 34(6): 704-713*

# Applicator selection

- *Head and neck cancer patient best treated with HYPERcollar or Lucite cone applicator?*
  - Target coverage TC25 for 24 patients

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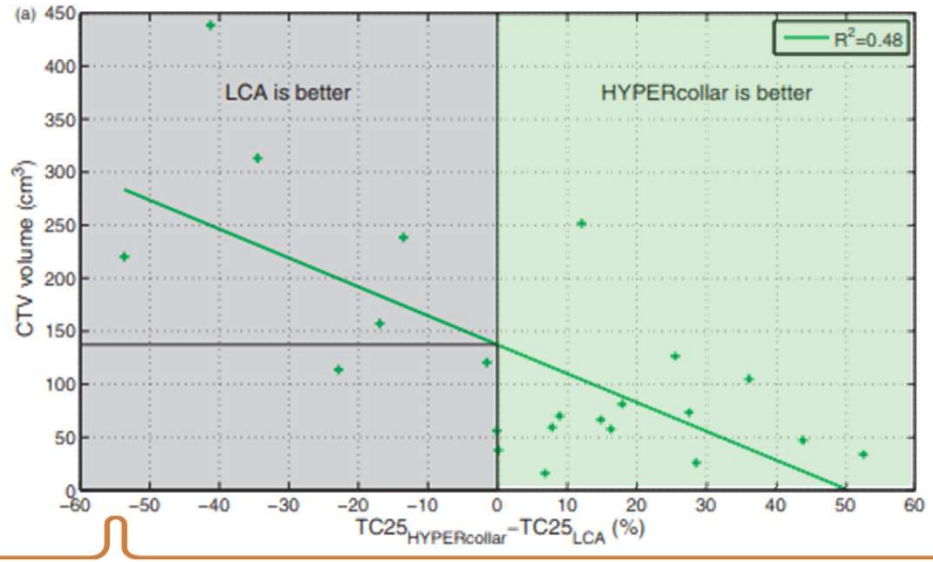


HYPERcollar: better SAR coverage when target region is fully enclosed by the applicator frame.

Drizdal et al. *Int. J. Hyperthermia. 2018; 34(6): 704-713*

# Applicator selection

- *Head and neck cancer patient best treated with HYPERcollar or Lucite cone applicator?*
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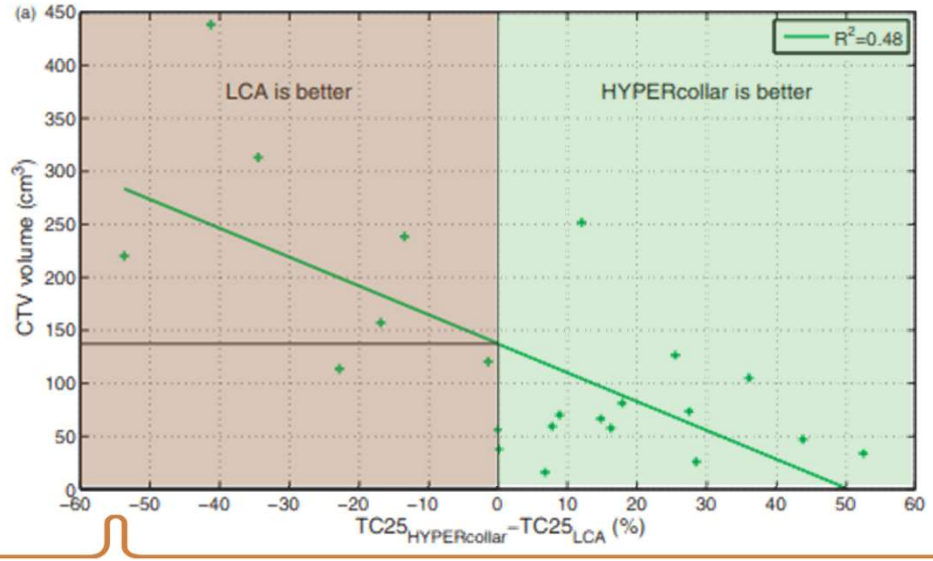


HYPERcollar: better SAR coverage when target region is fully enclosed by the applicator frame.

Lucite cone: better SAR coverage when target extends outside the HYPERcollar frame.

<u>Adequate coverage</u>
- Target fully under the LCA aperture
- Not deeper than 5 cm from the patient surface

Drizdal et al. *Int. J. Hyperthermia. 2018; 34(6): 704-713*

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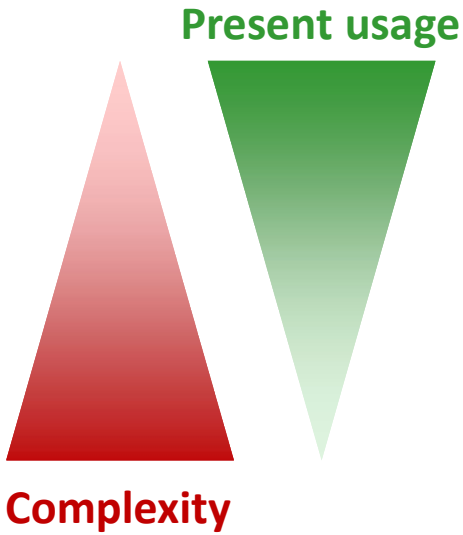
## Hyperthermia treatment planning

- Hyperthermia treatment planning
  - Wide variety of applications

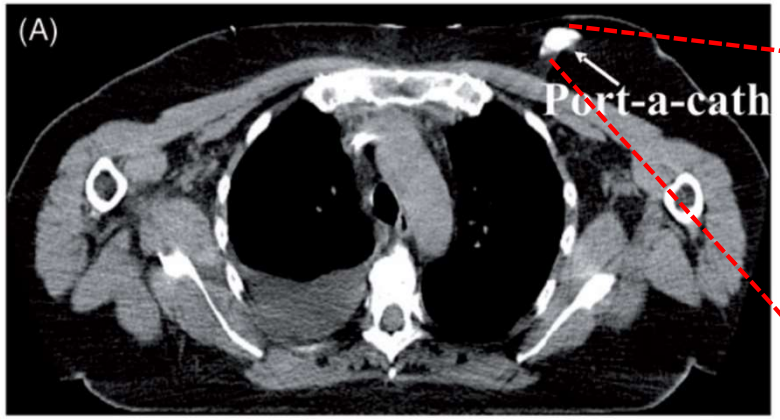
1. Device design
2. Clinical applicator selection
3. (Pre-)treatment evaluation
4. On-line assistance in treatment guidance
5. Full treatment guidance



## (Pre-)treatment evaluation

- *Purpose:* Evaluate heating quality and/or feasibility.

***Clinical problem:*** *Can breast cancer patients with a port-a-cath be treated with superficial hyperthermia ?*





Trujillo-Romero et al. *Int. J. Hyperthermia. 2015; 31(1): 15–22*

## (Pre-)treatment evaluation

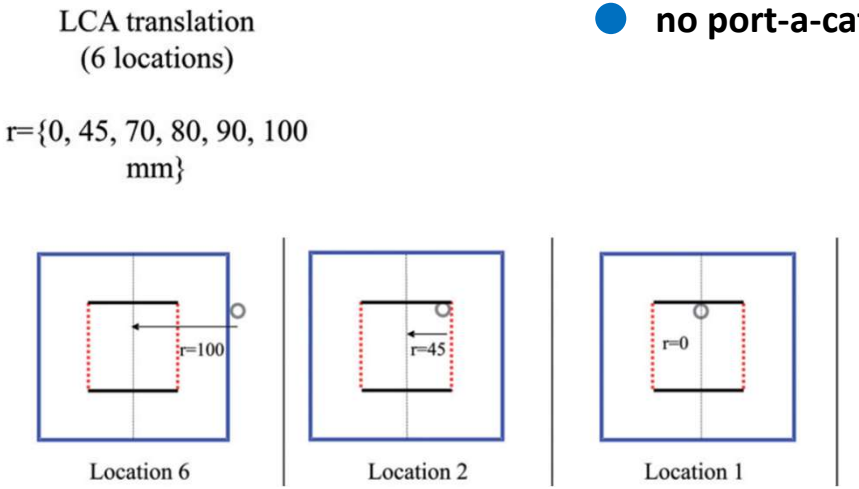
- *Can breast cancer patients with a port-a-cath be treated with superficial hyperthermia ?*
  - Patient model with lucite cone applicator

## (Pre-)treatment evaluation

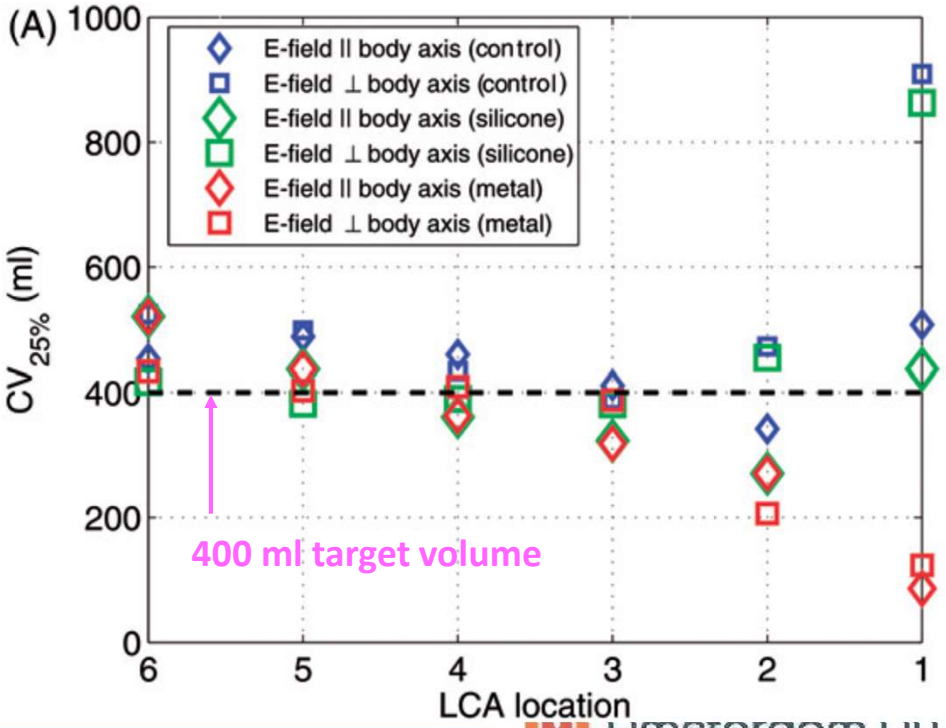
- *Can breast cancer patients with a port-a-cath be treated with superficial hyperthermia ?*
  - Patient model with lucite cone applicator
    - Metal/silicone port-a-cath
    - Evaluate different applicator positions/orientations
    - TC25 target coverage
    - Compare with situation without port-a-cath

# (Pre-)treatment evaluation

- *Can breast cancer patients with a port-a-cath be treated with superficial hyperthermia ?*




- **metal**
- **silicone**
- **no port-a-cath**




Trujillo-Romero et al. *Int. J. Hyperthermia. 2015; 31(1): 15–22*

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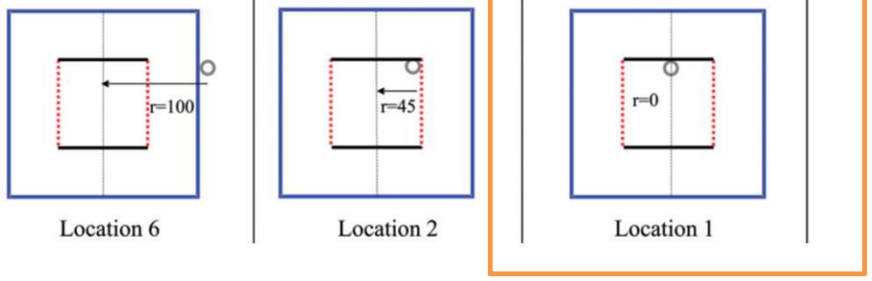
# (Pre-)treatment evaluation

- *Can breast cancer patients with a port-a-cath be treated with superficial hyperthermia ?*

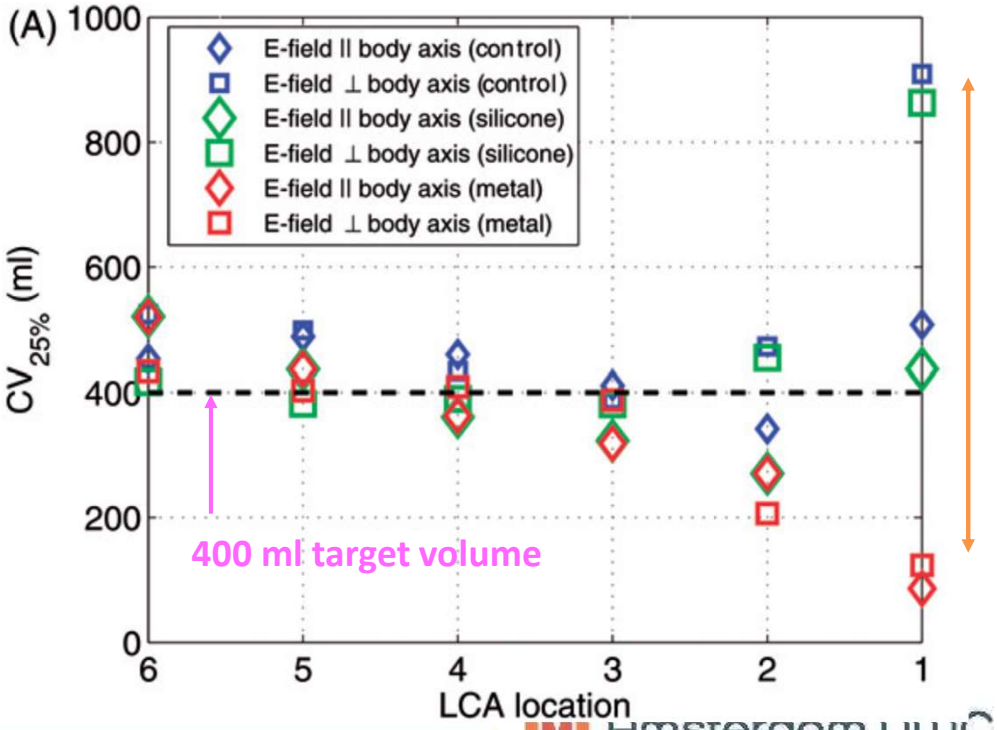
metal
silicone
no port-a-cath

LCA translation
(6 locations)

r={0, 45, 70, 80, 90, 100 mm}




Worst case ~88% reduction in coverage for a metal port-a-cath

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# (Pre-)treatment evaluation

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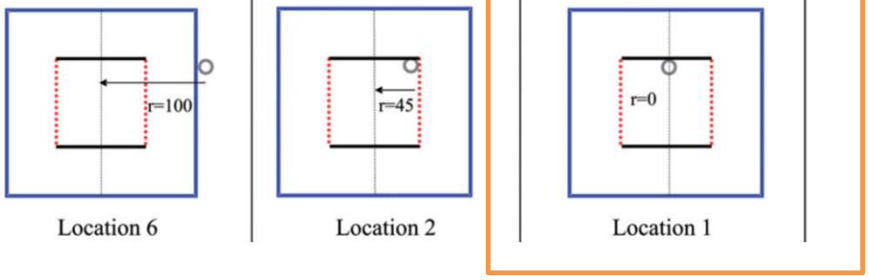
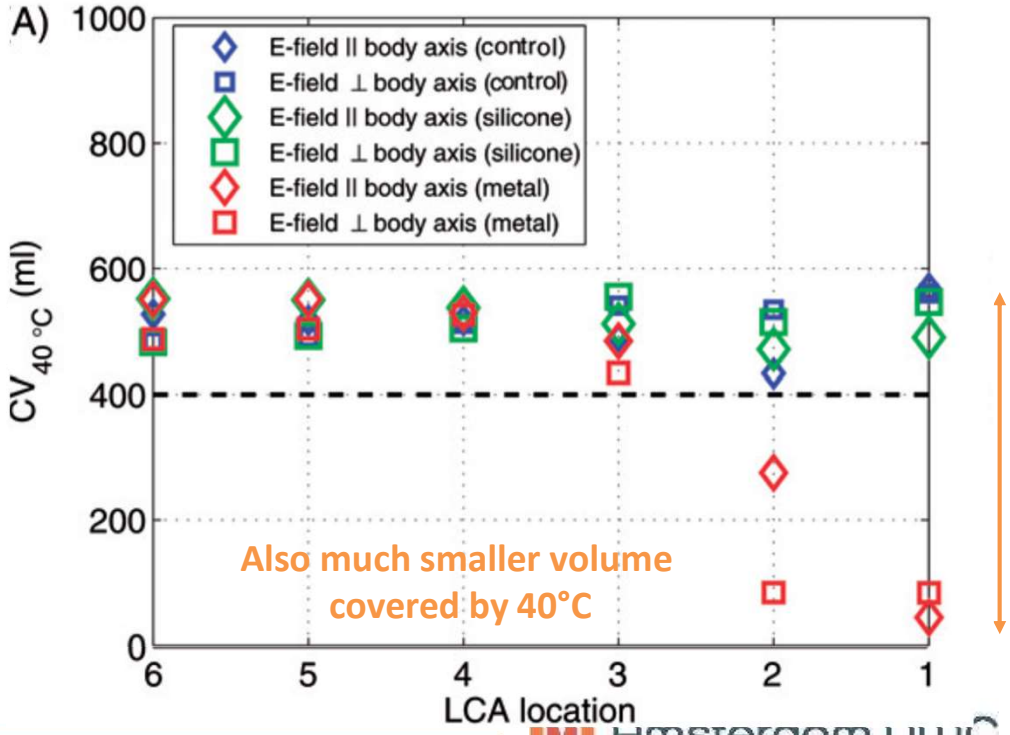



Worst case ~88% reduction in coverage for a metal port-a-cath




Also much smaller volume covered by 40°C

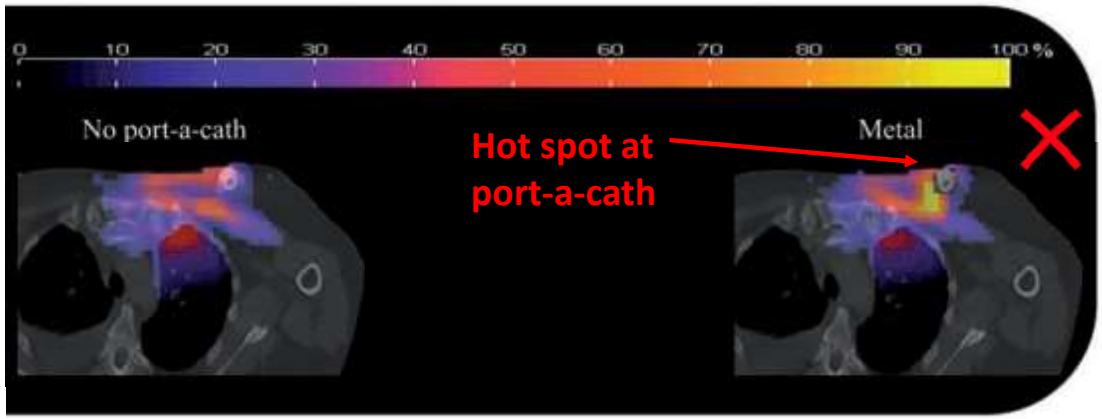
Trujillo-Romero et al. *Int. J. Hyperthermia. 2015; 31(1): 15–22*

# (Pre-)treatment evaluation

- *Can breast cancer patients with a port-a-cath be treated with superficial hyperthermia ?*
  - Example

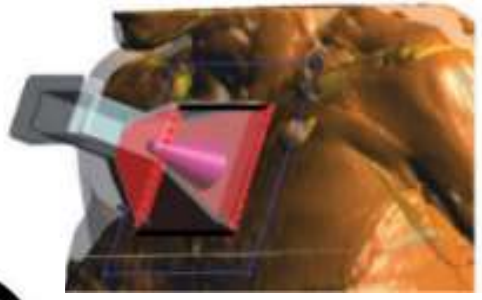
**port-a-cath**

*metal* *silicone*



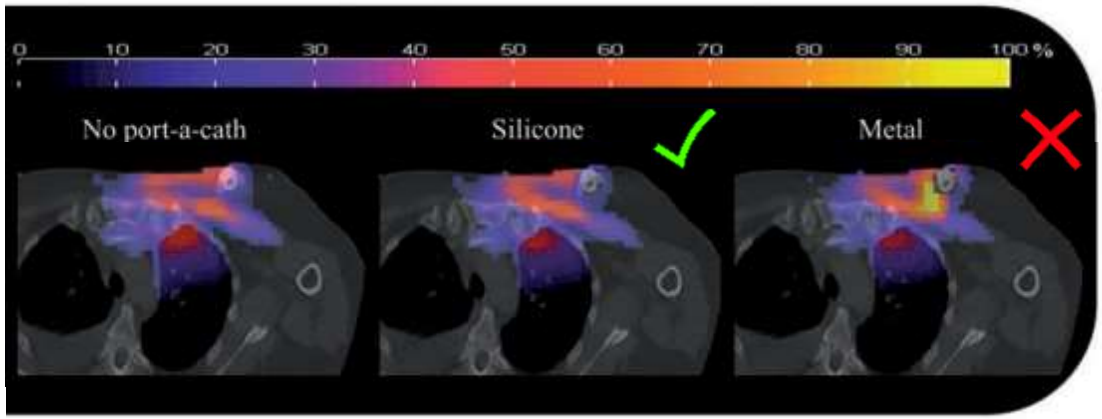
# (Pre-)treatment evaluation

- *Can breast cancer patients with a port-a-cath be treated with superficial hyperthermia ?*
  - Example



**port-a-cath**

*metal* *silicone*



# (Pre-)treatment evaluation

- *Can breast cancer patients with a port-a-cath be treated with superficial hyperthermia ?*

*<u>Conclusion based on planning evaluation:</u>*

- *Port-a-cath affects target coverage*

# (Pre-)treatment evaluation

- *Can breast cancer patients with a port-a-cath be treated with superficial hyperthermia ?*

*<u>Conclusion based on planning evaluation:</u>*

- *Port-a-cath affects target coverage*
- *Especially a metal port-a-cath can be treatment limiting*
- *Effect depends on the location with respect to the applicator.*

## (Pre-)treatment evaluation

- *Purpose:* Evaluate heating quality and/or feasibility.

***Clinical problem:*** *A recurrent breast cancer patient has a silicone breast implant.*

## (Pre-)treatment evaluation

- *Purpose:* Evaluate heating quality and/or feasibility.

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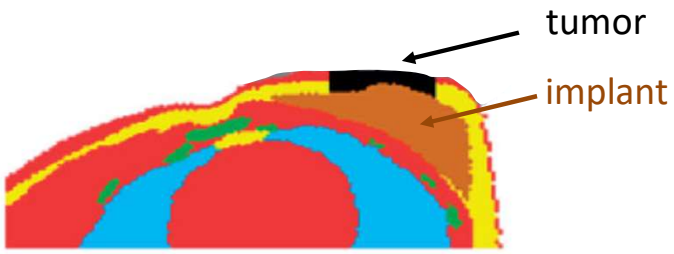
Implant directly behind the tumor;
tumor starting at the skin and reaching up to 1.5 cm depth



# (Pre-)treatment evaluation

- *Purpose:* Evaluate heating quality and/or feasibility.

***Clinical problem:*** *A recurrent breast cancer patient has a silicone breast implant.*

Implant directly behind the tumor;
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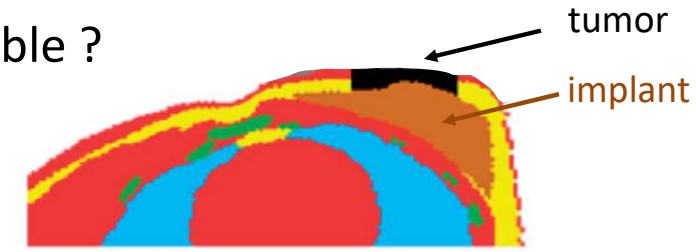
Is superficial hyperthermia (with the ALBA4000-ON) feasible ?



## (Pre-)treatment evaluation

- *Is superficial hyperthermia feasible with a silicone breast implant ?*

- Risk of hot spots at the tissue-implant interface
  - Inhomogeneous dielectric properties
  - Implant not perfused; low thermal conductivity

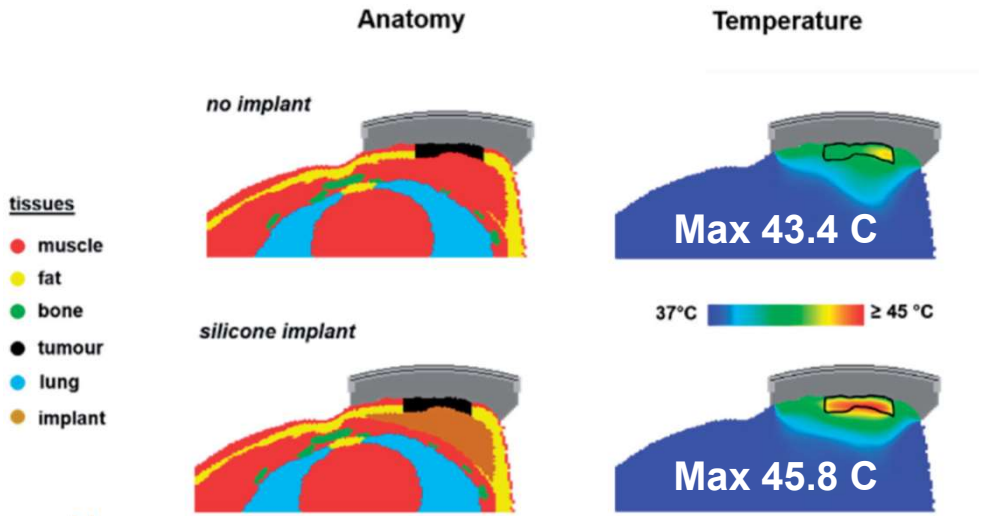
## (Pre-)treatment evaluation

- *Is superficial hyperthermia feasible with a silicone breast implant ?*

- Risk of hot spots at the tissue-implant interface
  - Inhomogeneous dielectric properties
  - Implant not perfused; low thermal conductivity
- Calculate temperature for standard clinical power level
- Compare with reference situation without implant

# (Pre-)treatment evaluation

- *Is superficial hyperthermia feasible with a silicone breast implant ?*

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# (Pre-)treatment evaluation

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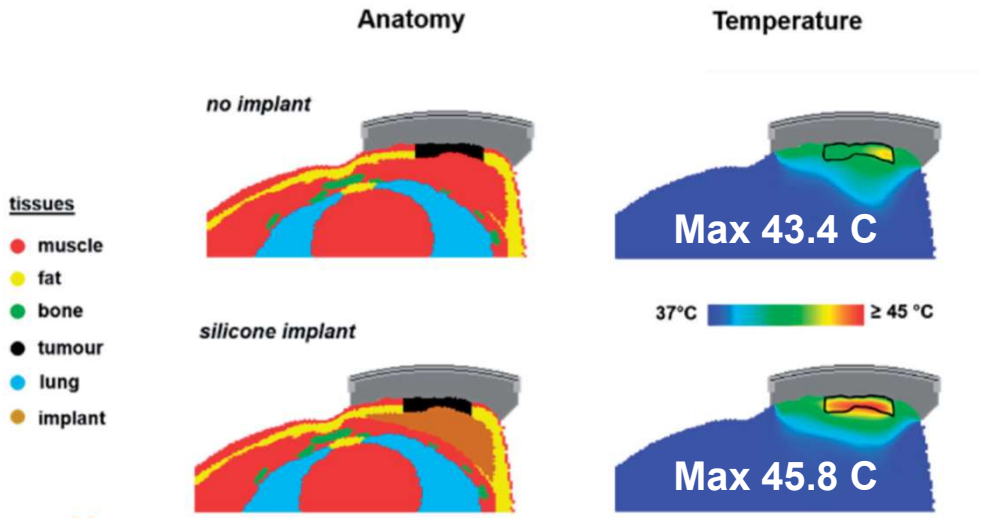


**Clinical data indicate T < 43.5°C to avoid toxicity**

Is treatment feasible ?

Scale both situations to max 43.5°C and evaluate distributions

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# (Pre-)treatment evaluation

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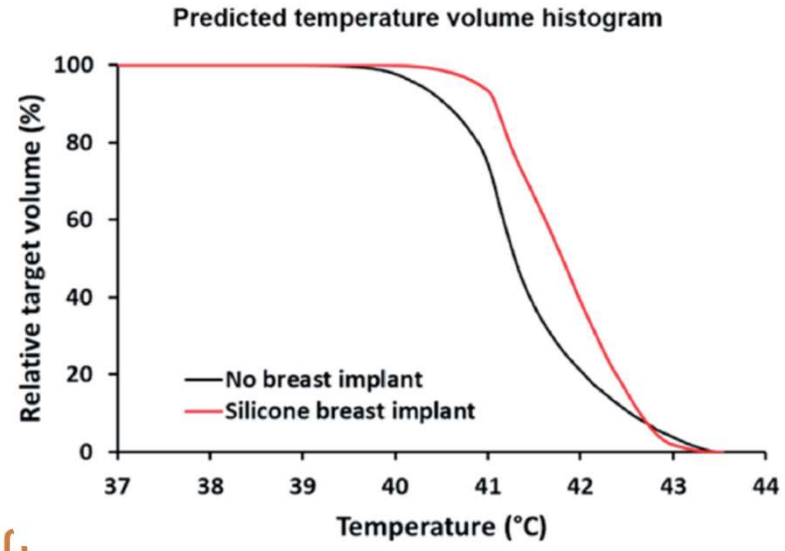


**YES, feasible**

*Additional invasive thermometry at the tissue-implant interface is warranted for direct feedback during treatment to avoid thermal toxicity*

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## Hyperthermia treatment planning

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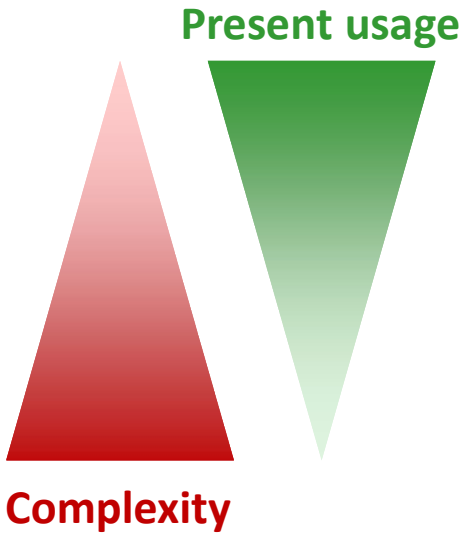

## On-line assistance in treatment guidance

- *Purpose:* phase-amplitude steering assisted by on-line planning predictions.

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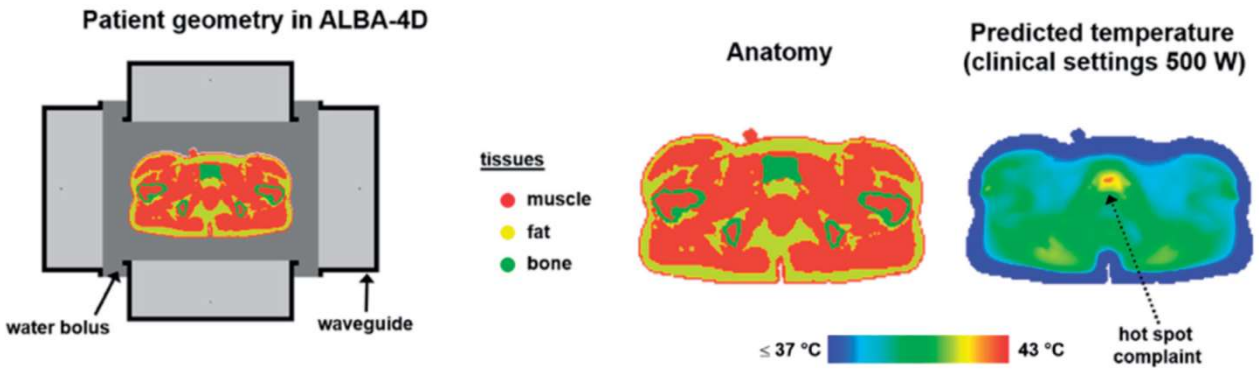
***Clinical problem:*** *Rectum cancer patient; ALBA-4D, 500W*
*- Hot spot pubic bone*
*- Inexperienced operator reduced total power with 100W*

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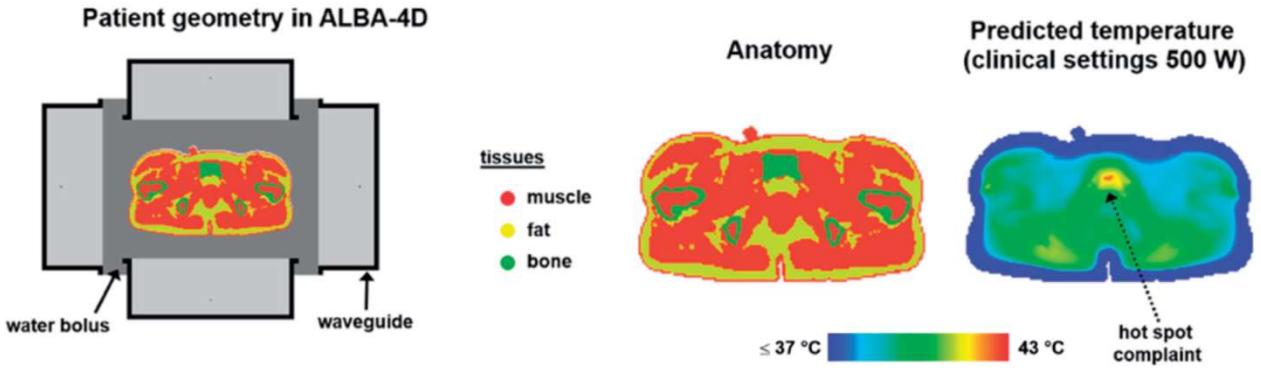


***0.8°C reduction in measured T90; can we do better ?***

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## On-line assistance in treatment guidance

- *Find more effective phase-amplitude settings*.
  - 0.8°C reduction in measured T90.
  - 0.5°C reduction in predicted T90

***Predicted***

| | Power ratios T:B:L:R | Phases T:B:L:R (°) | T90 (°C) | Hot spot (°C) | Overall max (°C) |
|---|---|---|---|---|---|
| Clinical | | | | | |
| 500 W | 1:1:1:1 | 75:0:70:60 | 39.6 | 42.5 | 44.8 |
| 400 W | 1:1:1:1 | 75:0:70:60 | 39.1 | 41.4 | 43.2 |

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## On-line assistance in treatment guidance

- *Find more effective phase-amplitude settings*.
  - 0.8°C reduction in measured T90.
  - 0.5°C reduction in predicted T90
  - We need to find settings that:

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**Reduce predicted hot spot temperature with ~1°C**

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## On-line assistance in treatment guidance

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**Realize predicted T90 > 39.1°C**

**Reduce predicted hot spot temperature with ~1°C**

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## On-line assistance in treatment guidance

- *Find more effective phase-amplitude settings*.
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| 400 W | 1:1:1:1 | 75:0:70:60 | 39.1 | 41.4 | 43.2 |

Keep predicted overall max < 44.8°C

Realize predicted T90 > 39.1°C

Reduce predicted hot spot temperature with ~1°C

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## On-line assistance in treatment guidance

- *Find more effective phase-amplitude settings*.
  - Hot spot at pubic bone close to top waveguide
  - Gradually reduce top power; keep total power constant

| | Power ratios T:B:L:R | Phases T:B:L:R (°) | T90 (°C) | Hot spot (°C) | Overall max (°C) |
|---|---|---|---|---|---|
| Clinical | | | | | |
| 500 W | 1:1:1:1 | 75:0:70:60 | 39.6 | 42.5 | 44.8 |
| 400 W | 1:1:1:1 | 75:0:70:60 | 39.1 | 41.4 | 43.2 |
| alternatives | | | | | |
| 500 W | 0.9:1:1:1 | 75:0:70:60 | 39.6 | 42.4 | 44.9 |
| | 0.75:1:1:1 | 75:0:70:60 | 39.6 | 42.3 | 45.0 |
| | 0.5:1:1:1 | 75:0:70:60 | 39.7 | 42.0 | 45.3 |

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| | 0.75:1:1:1 | 75:0:70:60 | 39.6 | 42.3 | 45.0 |
| | 0.5:1:1:1 | 75:0:70:60 | 39.7 | 42.0 | 45.3 |

Risk to introduce hot spot

Decreased, but not sufficiently

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## On-line assistance in treatment guidance

- *Find more effective phase-amplitude settings*.
  - Hot spot at pubic bone close to top waveguide
  - Gradually reduce top power; keep total power constant
  - Risk of hot spot at the back
    - Reducing power bottom antenna will lower target temperature

## On-line assistance in treatment guidance

- *Find more effective phase-amplitude settings*.
  - Hot spot at pubic bone close to top waveguide
  - Gradually reduce top power; keep total power constant
  - Risk of hot spot at the back
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  - Try slight ‘defocusing’ to reduce hot spot and compensate for increased power at the back

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- *Find more effective phase-amplitude settings*.
  - Hot spot at pubic bone close to top waveguide
  - Gradually reduce top power; keep total power constant
  - Risk of hot spot at the back
    - Reducing power bottom antenna will lower target temperature
  - Try slight ‘defocusing’ to reduce hot spot and compensate for increased power at the back
    - Wavelength @ 70 MHz ~50 cm
    - 15° phase change will induce a small focus shift of ~1 cm
    - Apply phase shift to left/right waveguides

# On-line assistance in treatment guidance

- *Find more effective phase-amplitude settings*.
  - Hot spot at pubic bone close to top waveguide

| | Power ratios T:B:L:R | Phases T:B:L:R (°) | T90 (°C) | Hot spot (°C) | Overall max (°C) |
|---|---|---|---|---|---|
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| 400 W | 1:1:1:1 | 75:0:70:60 | 39.1 | 41.4 | 43.2 |
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| 500 W | 0.9:1:1:1 | 75:0:70:60 | 39.6 | 42.4 | 44.9 |
| | 0.75:1:1:1 | 75:0:70:60 | 39.6 | 42.3 | 45.0 |
| | 0.5:1:1:1 | 75:0:70:60 | 39.7 | 42.0 | 45.3 |
| | 0.5:1:1:1 | 75:0:55:45 | 39.5 | 41.6 | 45.1 |
| | 0.5:1:1:1 | 75:0:40:30 | 39.4 | 41.1 | 44.8 |

**Stepwise 15° phase reduction**

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# On-line assistance in treatment guidance

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| | 0.75:1:1:1 | 75:0:70:60 | 39.6 | 42.3 | 45.0 |
| | 0.5:1:1:1 | 75:0:70:60 | 39.7 | 42.0 | 45.3 |
| | 0.5:1:1:1 | 75:0:55:45 | 39.5 | 41.6 | 45.1 |
| | 0.5:1:1:1 | 75:0:40:30 | 39.4 | 41.1 | 44.8 |

**Higher T90**
**Comparable/better suppression**

**no additonal risk of new hot spots**

Kok *et al Int J Hyperthermia. 2021; 38(1): 532–551*

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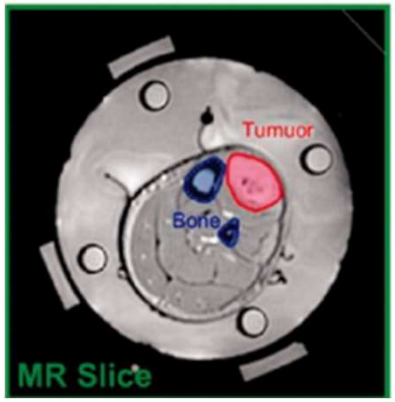
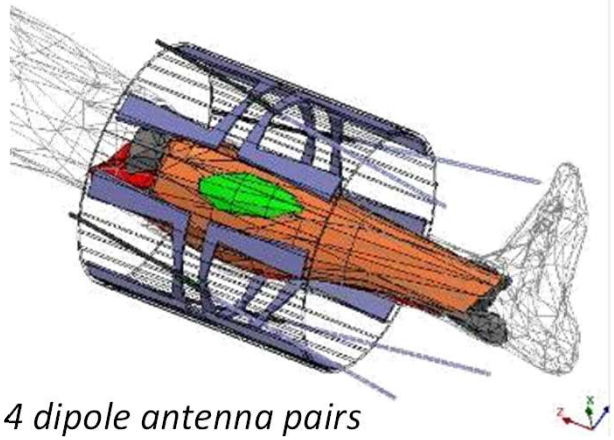
## On-line assistance in treatment guidance

- *Purpose:* phase-amplitude steering assisted by on-line planning predictions.

***Clinical problem:*** *Leg sarcoma heated with mini phased array. Realize optimal focusing*




*Leg sarcoma,*
*Mini Annular Phased Array, 140 MHz*



*4 dipole antenna pairs*

Li et al *Int J Hyperthermia* 2011; 27: 86-99

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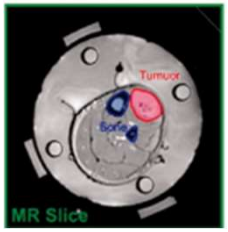
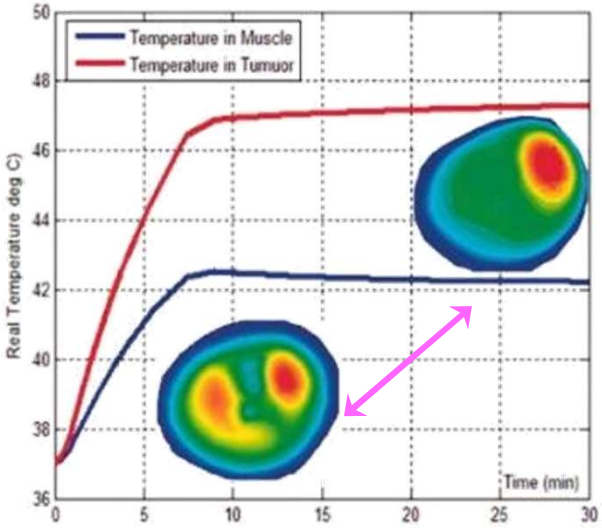
## On-line assistance in treatment guidance

- *Find more effective phase-amplitude settings*.
  - Hot spot at pubic bone close to top waveguide

*Leg sarcoma,*
*Mini Annular Phased Array, 140 MHz*




MR-thermometry feedback
+ treatment planning improve focusing during treatment




Li et al *Int J Hyperthermia* 2011; 27: 86-99

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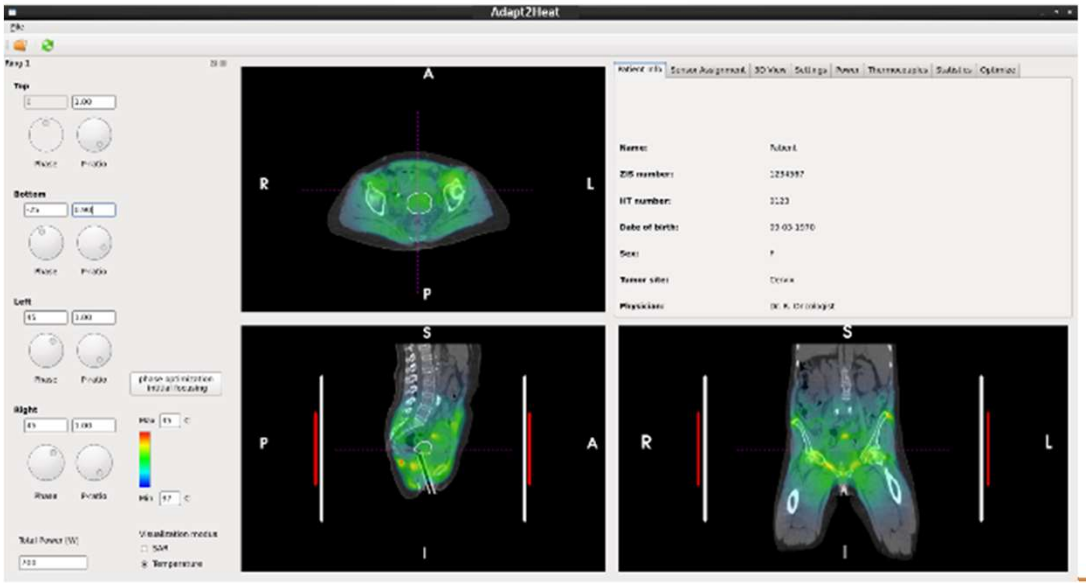
## Hyperthermia treatment planning

### On-line assistance in treatment guidance

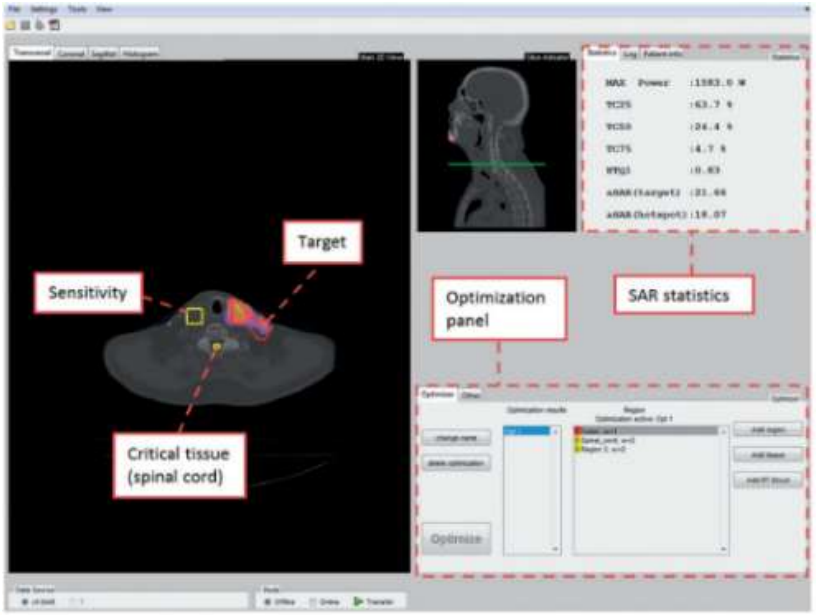
- Software tools developed for on-line use of planning

**Adapt2Heat (Amsterdam UMC)**




Kok *et al. Int. J. Hyperthermia.* 2022 vol. 39, pp. 265-277

**VEDO (Erasmus MC)**




Rijnen et al. *Int. J. Hyperthermia*; 2013: 29: 181-193.

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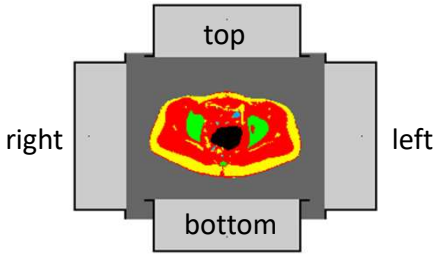
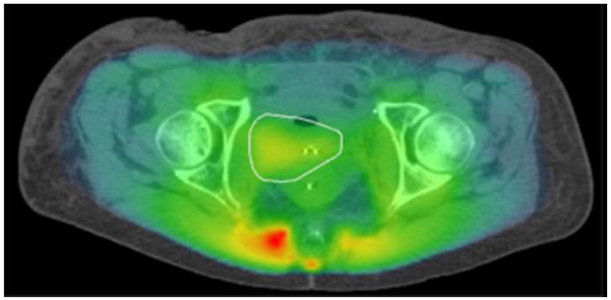
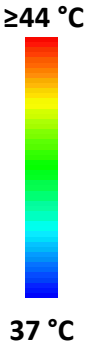
# On-line assistance in treatment guidance

- Adapt2Heat
  - Example: cervical cancer patient treated with ALBA-4D
    - Hot spot complaint at buttock




**Predicted temperature**








Kok et al. *Int. J. Radiation Oncology Biol. Phys.* 2017. 99(4):1039-1047

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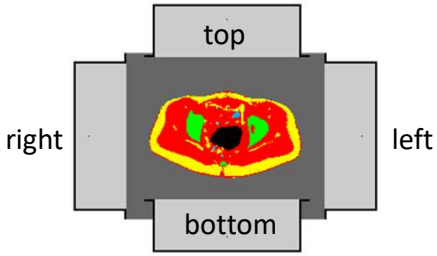


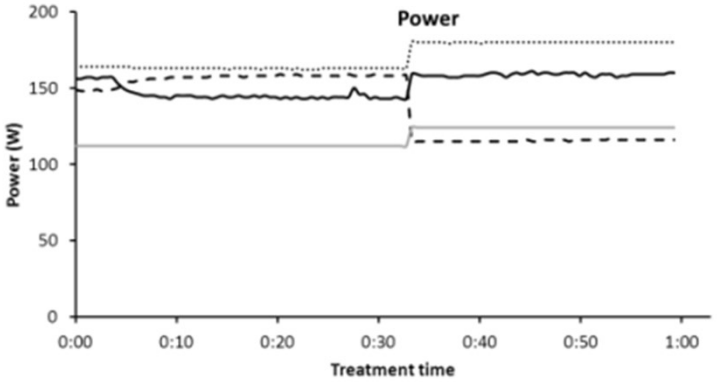


Amplitude change based on planning

Kok et al. *Int. J. Radiation Oncology Biol. Phys.* 2017. 99(4):1039-1047

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# On-line assistance in treatment guidance

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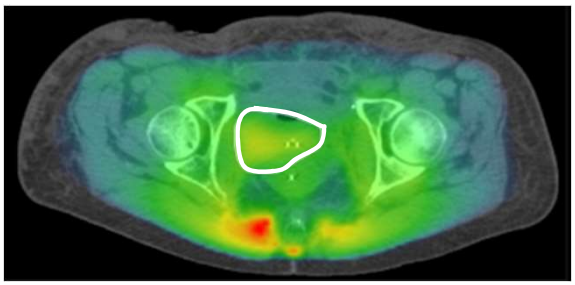
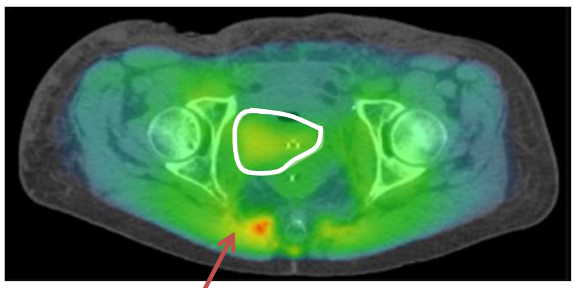
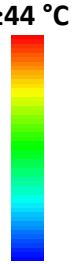
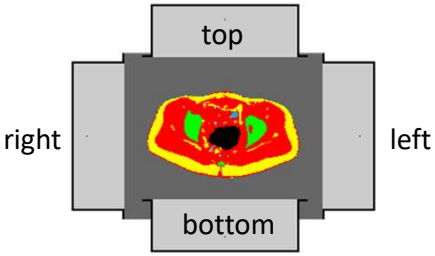


before HTP



after HTP




HTP predicts reduction hot spot



Kok et al. *Int. J. Radiation Oncology Biol. Phys.* 2017. 99(4):1039-1047

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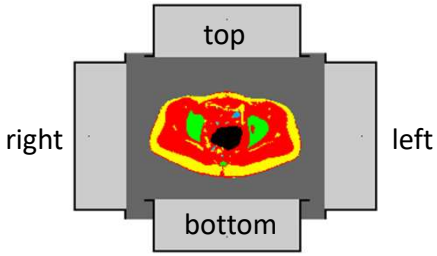


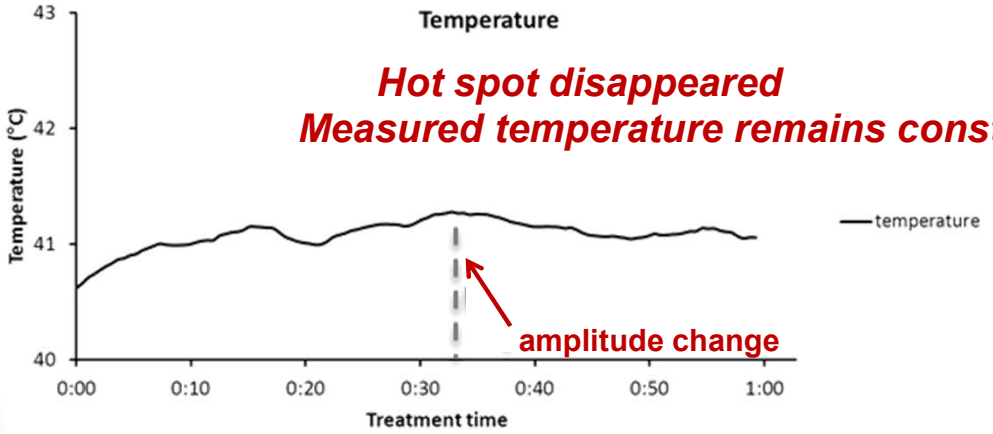


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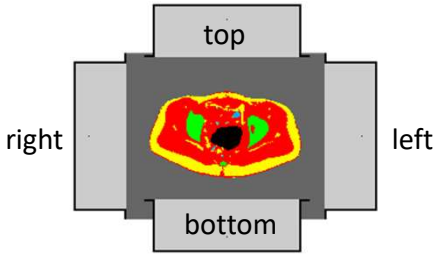
Kok et al. *Int. J. Radiation Oncology Biol. Phys.* 2017. 99(4):1039-1047

# On-line assistance in treatment guidance

- Adapt2Heat
  - Example 2: cervical cancer patient treated with ALBA-4D
    - Planning helpful to improve target heating



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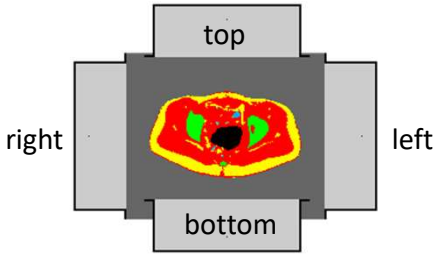


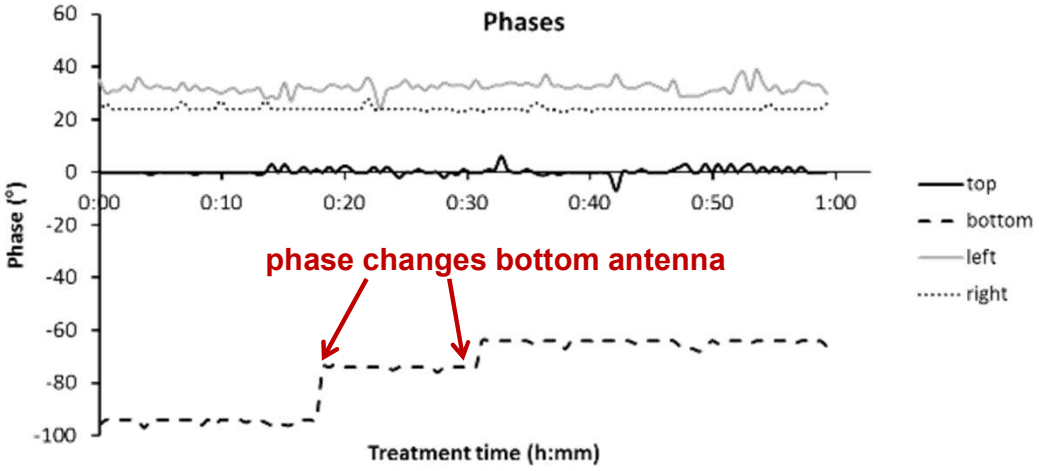


Kok et al. *Int. J. Hyperthermia.* 2018. 34(7):1082-1091

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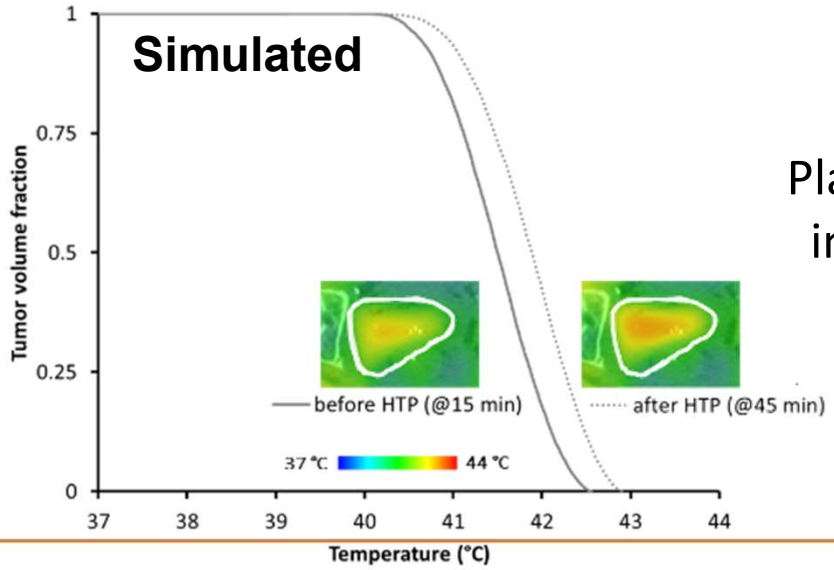


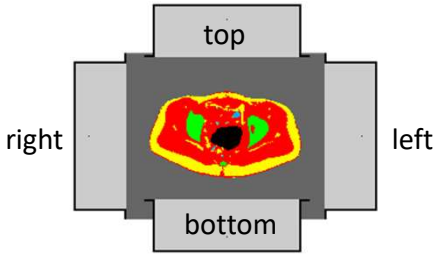


Planning predicts improvement

Kok et al. *Int. J. Hyperthermia.* 2018. 34(7):1082-1091

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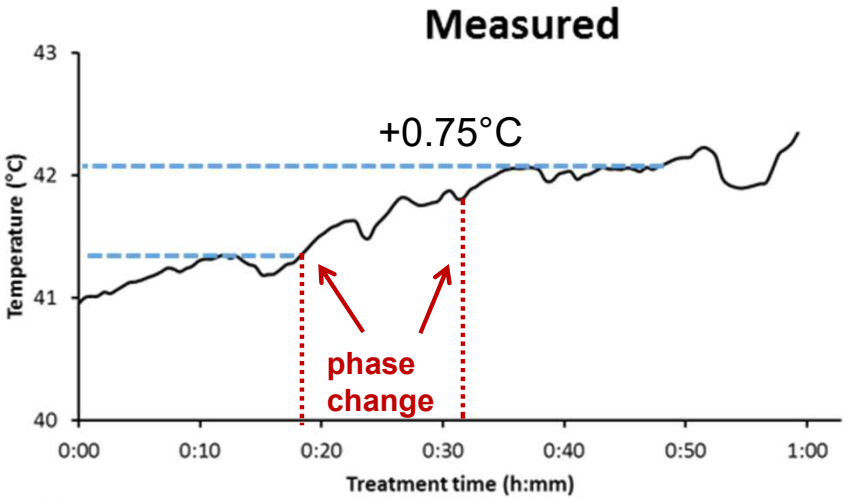
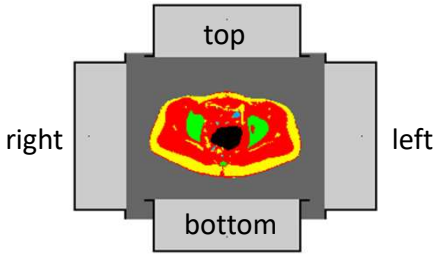



Improvement measured

average

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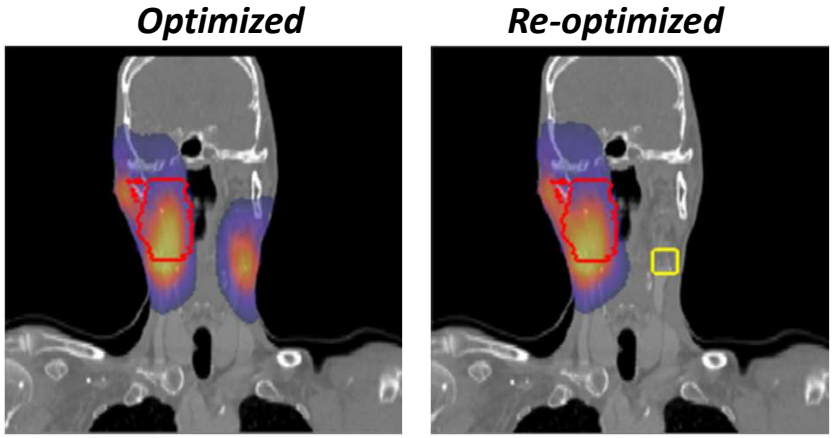
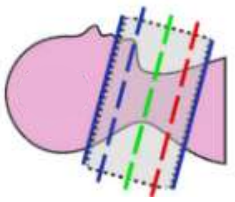
Kok et al. *Int. J. Hyperthermia.* 2018. 34(7):1082-1091

## On-line assistance in treatment guidance

- VEDO
  - Example: Head and neck cancer patient treated with HYPERcollar
    - Hot spot suppression



Rijnen et al. *Int. J. Hyperthermia*; 2013: 29: 181-193:

# Hyperthermia treatment planning

***Full treatment guidance***

## Full treatment guidance

- *Purpose:* Steering prescribed by planning instead of experience.

## Full treatment guidance

- *Purpose:* Steering prescribed by planning instead of experience.

*Study evaluating of steering prescribed by planning*

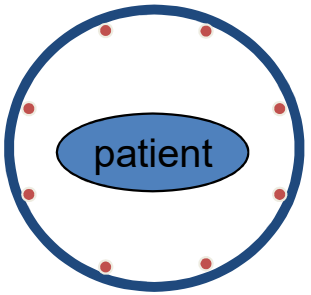
Erasmus MC

36 cervical cancer patients,

5 treatment sessions

***BSD Sigma-60***

4 paired dipoles






Franckena *et al Int J Hyperthermia. 2010; 26(2):145-157*

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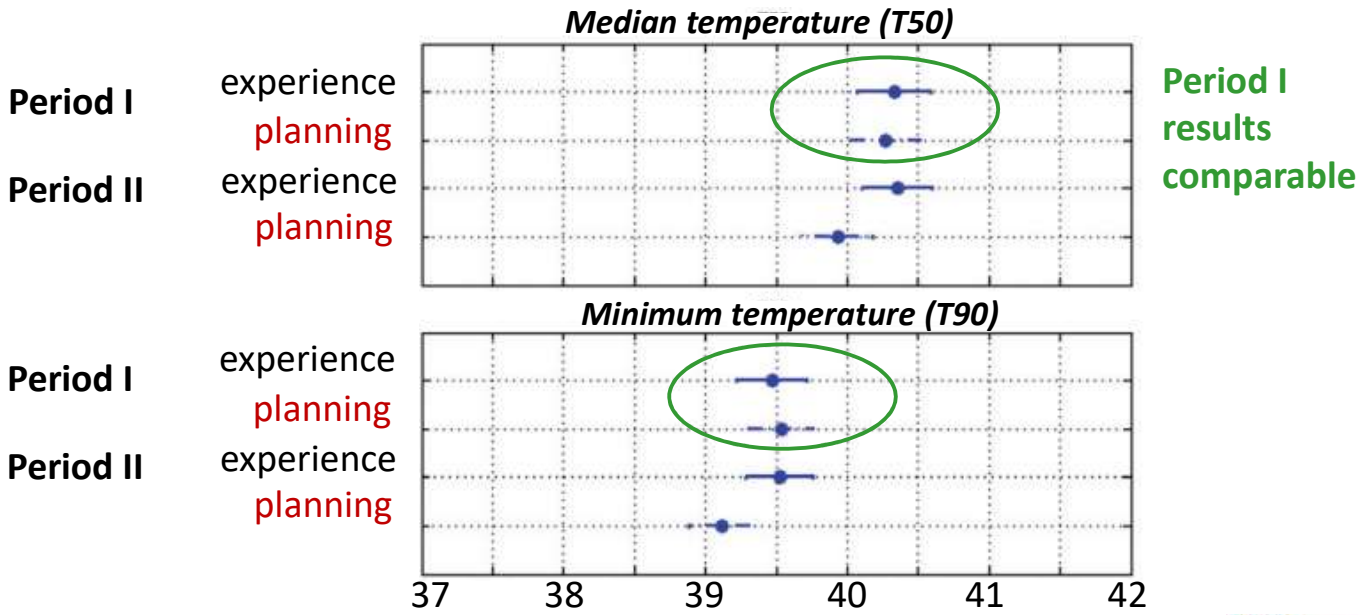




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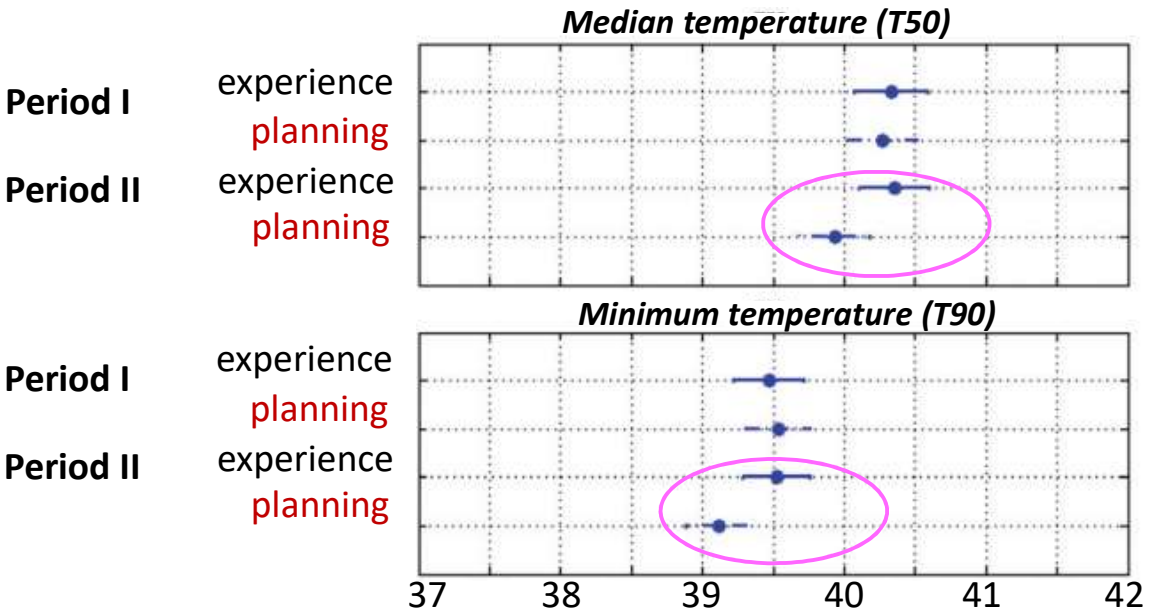


Period II planning yields lower temperatures

Franckena *et al Int J Hyperthermia. 2010; 26(2):145-157*

# Full treatment guidance

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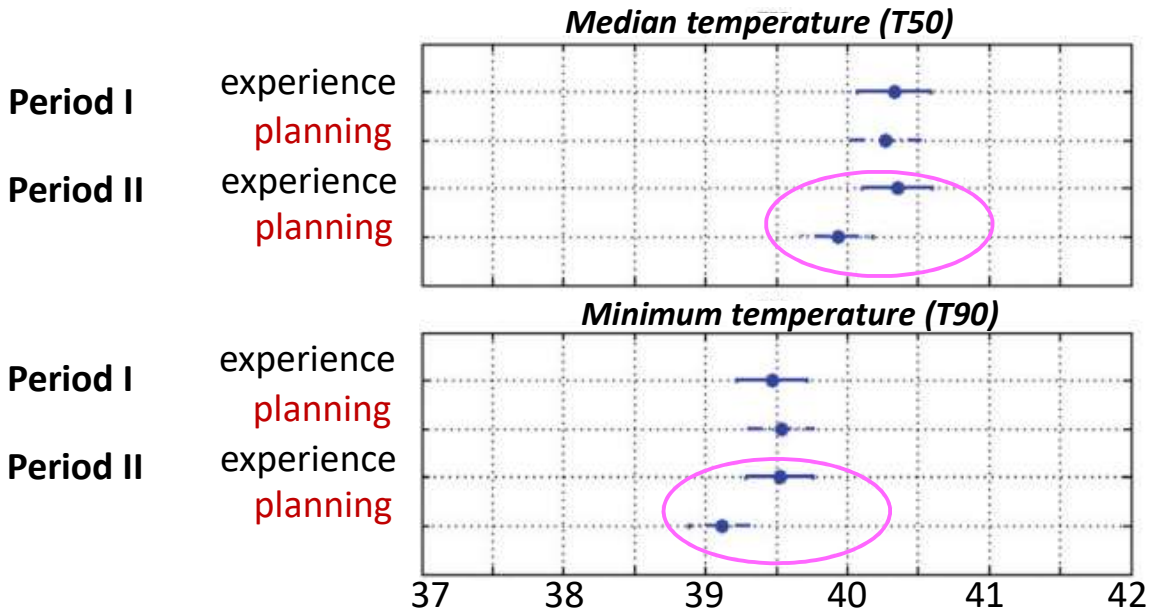


**Period II planning yields lower temperatures**

**New planning CT halfway treatment series ?**

Franckena *et al Int J Hyperthermia. 2010; 26(2):145-157*

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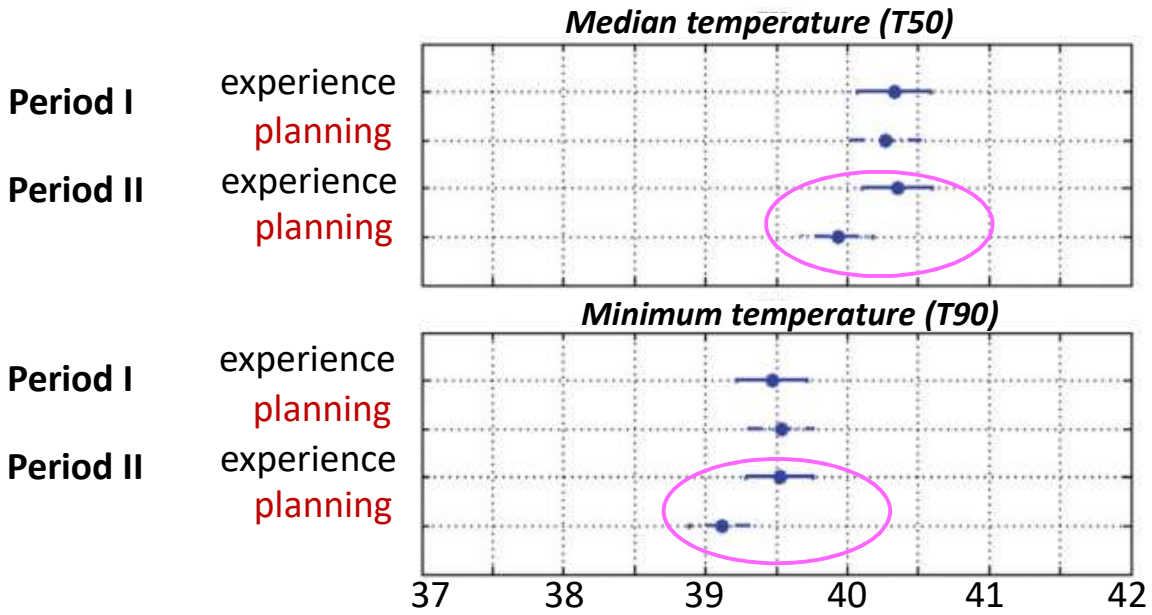
## Hyperthermia treatment planning

**Full treatment guidance** **Very challenging**

- *Purpose:* Steering prescribed by planning instead of experience.

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# Hyperthermia treatment planning

***Future perspectives***

## Future perspectives

- More widespread clinical use of planning
  - Planning is recommended in QA guidelines*

*Bruggmoser *et al Strahlenther Onkol. 2012;188(Suppl 2):198–211*

## Future perspectives

- More widespread clinical use of planning
  - Planning is recommended in QA guidelines*
- Further developments to improve quantitative reliability
  - Patient-specific tissue properties

*Bruggmoser *et al Strahlenther Onkol. 2012;188(Suppl 2):198–211*

## Future perspectives

- More widespread clinical use of planning
  - Planning is recommended in QA guidelines*
- Further developments to improve quantitative reliability
  - Patient-specific tissue properties
- Biological modelling
  - Translating the effect of hyperthermia into equivalent enhanced radiation dose
    - Language and evaluation tools of radiation oncologists

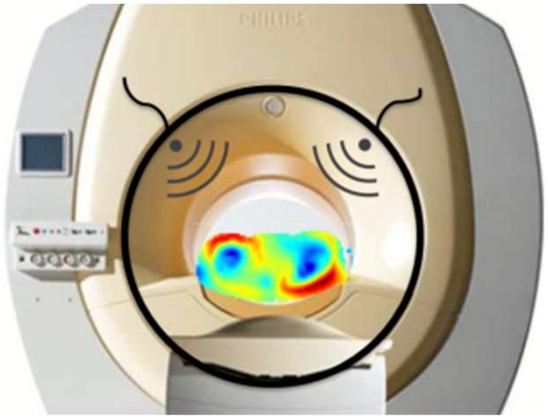
*Bruggmoser *et al Strahlenther Onkol. 2012;188(Suppl 2):198–211*

## Future perspectives

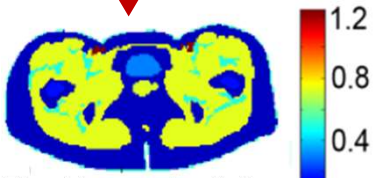
- Further developments to improve quantitative reliability
  - Patient-specific tissue properties
  - Dielectric imaging

## Future perspectives

- Further developments to improve quantitative reliability
  - Patient-specific tissue properties
  - Dielectric imaging
    - Reconstruct dielectric properties using MR imaging



3T
128 MHz



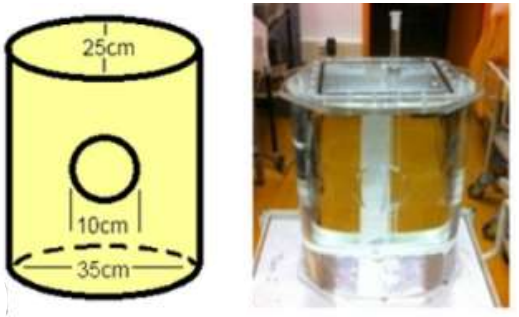
Electric conductivity




Inhomogeneous RF field ($B^{1+}$ field)

## Future perspectives

- Further developments to improve quantitative reliability
  - Patient-specific tissue properties
  - Dielectric imaging
    - Reconstruct dielectric properties using MR imaging
    - Phantom experiments
      - Homogeneous phantom
      - Spherical compartment filled with different saline content (conductivity 0.01 – 1.8 S/m)






Balidemaj et al. *Magnetic Resonance in Medicine 2015; 73(4):1505-1513*

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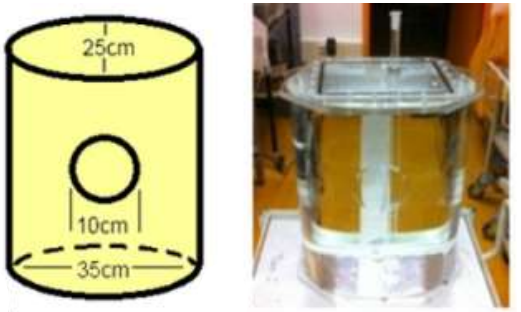
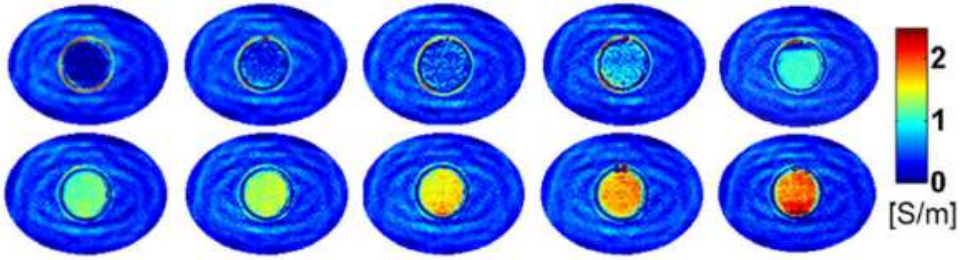



**Reconstructed conductivity**

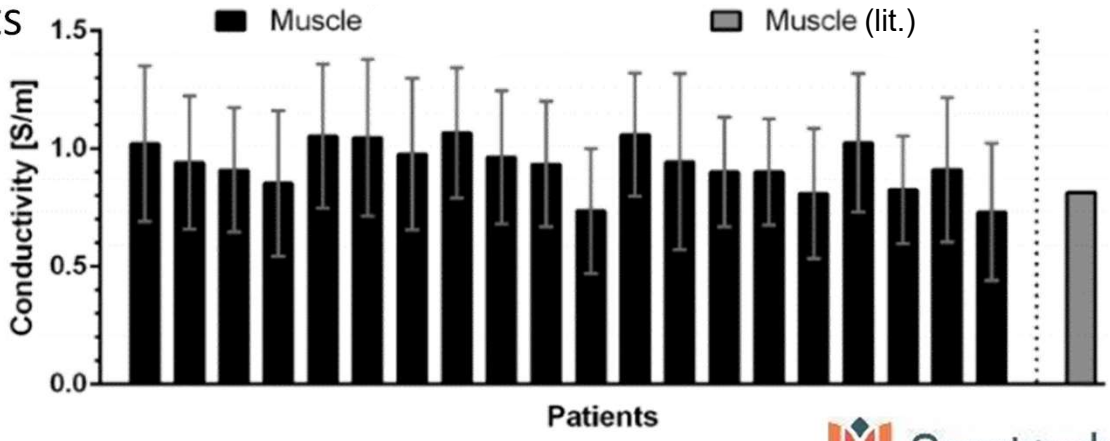


Balidemaj et al. *Magnetic Resonance in Medicine 2015; 73(4):1505-1513*

# Future perspectives

- Further developments to improve quantitative reliability
  - Patient-specific tissue properties
  - Dielectric imaging
    - Reconstruct dielectric properties using MR imaging
    - *In vivo* measurements

Large variation between patients




Balidemaj et al. *Phys Med Biol. 2016 21;61(4):1596-60*

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# Future perspectives

- Further developments to improve quantitative reliability
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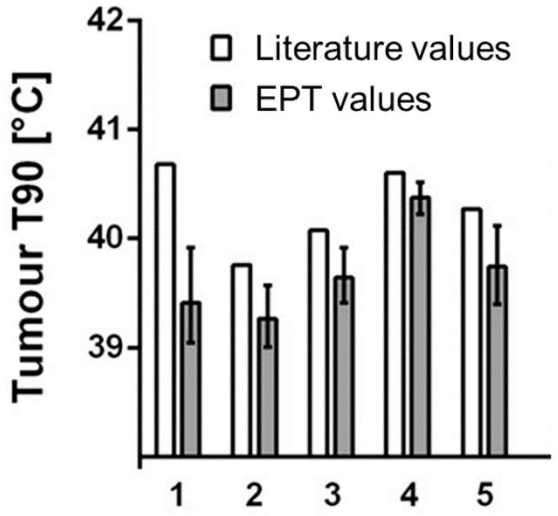
    - Reconstruct dielectric properties using MR imaging
    - *In vivo* measurements

***Differences literature – EPT values up to ~1.5°C***

Large variation between patients

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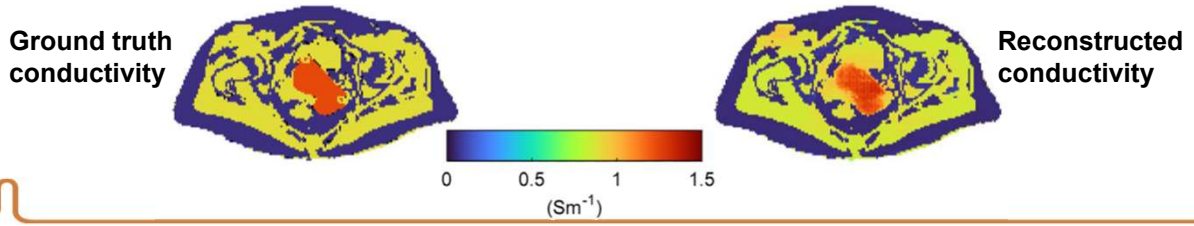
Balidemaj et al. *Phys Med Biol. 2016 21;61(4):1596-60*

# Future perspectives

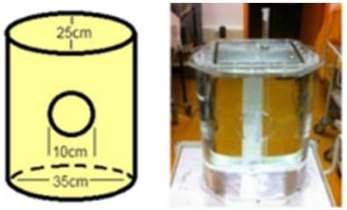
- Further developments to improve quantitative reliability
  - Patient-specific tissue properties
  - Dielectric imaging
    - Reconstruct dielectric properties using MR imaging
    - *In vivo* measurements
    - Deep learning
      - Training on large datasets of simulated $B^{1+}$ distributions

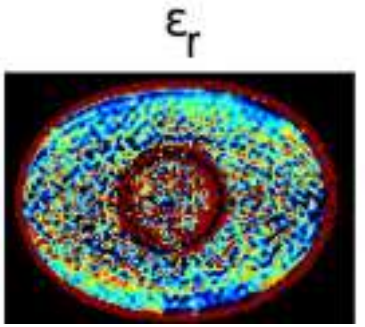



Gavazzi et al. *Magn Reson Med.* 2020.84(5):2772-2787

## Future perspectives

- Further developments to improve quantitative reliability
  - Patient-specific tissue properties
  - Dielectric imaging
    - Reconstruct dielectric properties using MR imaging
    - *In vivo* measurements
    - Deep learning
    - Reconstruction of permittivity remains challenging
      - Very sensitive to noise



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## Future perspectives

- Further developments to improve quantitative reliability
  - Patient-specific tissue properties
  - Dielectric imaging
  - Perfusion imaging
    - Patient specific 3D perfusion maps

# Future perspectives

- Further developments to improve quantitative reliability
  - Patient-specific tissue properties
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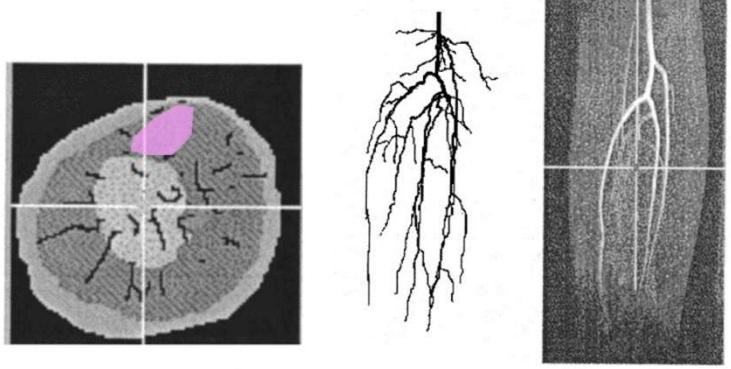
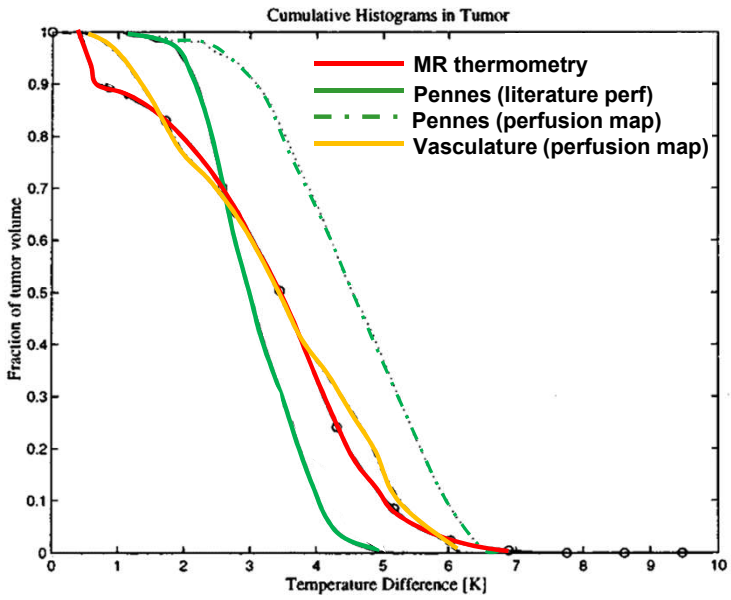
  - Perfusion imaging
    - Patient specific 3D perfusion maps

**Leg (sarcoma)**



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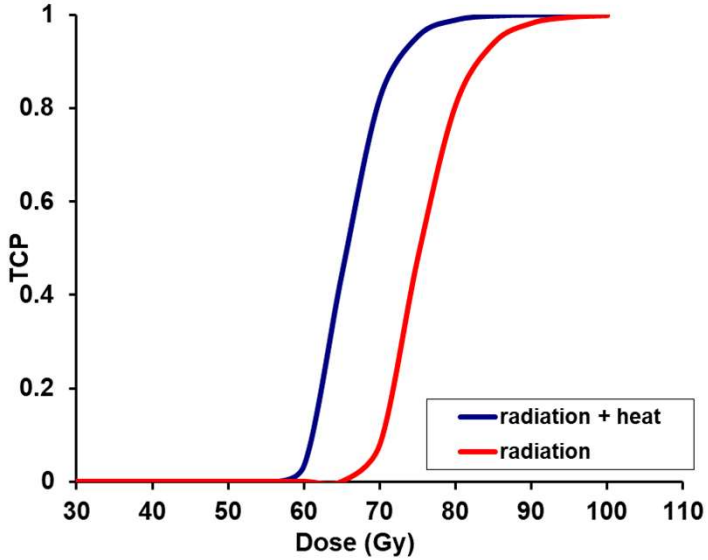
Craciunescu et al. Med. Phys. 2001 28(11): 2289-2296

## Future perspectives

- Further developments to improve quantitative reliability
  - Biological modelling




Kok et al, IJROBP 2014. 88(3):739-45

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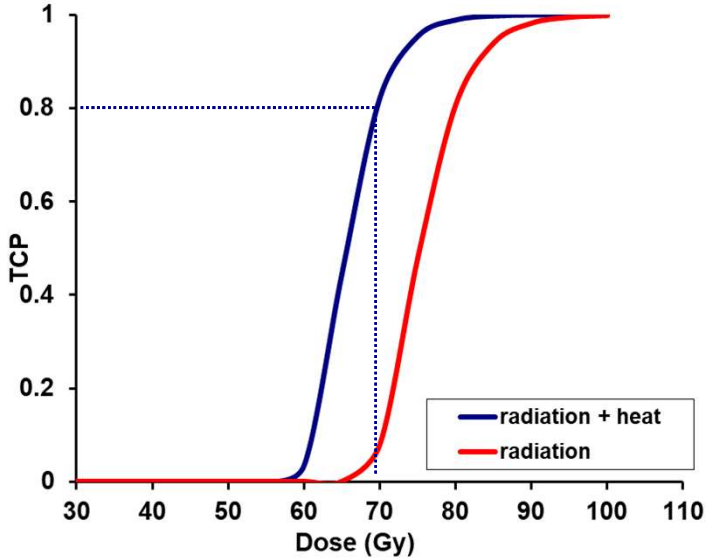


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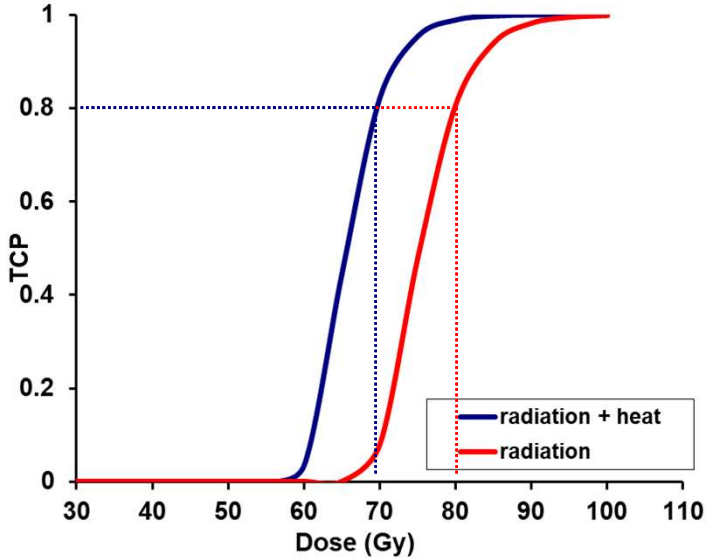


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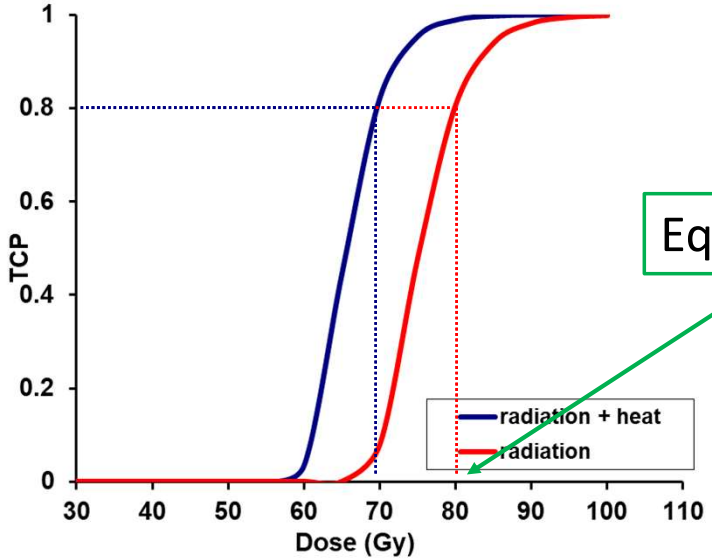
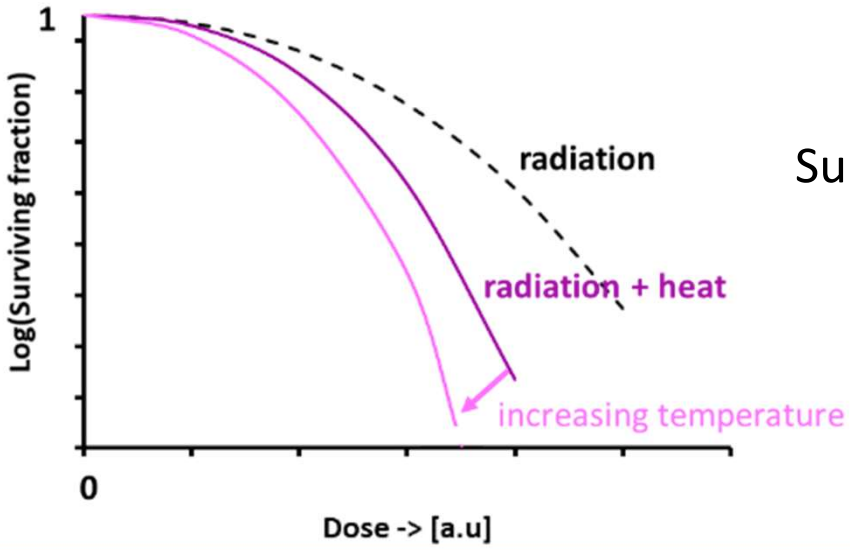



Equivalent radiation dose: $EQD_{RT}$

Kok et al, IJROBP 2014. 88(3):739-45

## Future perspectives

- Further developments to improve quantitative reliability
  - Biological modelling
  - Hyperthermia influences linear quadratic parameters α and β




***LQ-model:***

Survival fraction $= \exp[-\alpha D - \beta D^2]$

Kok et al, IJROBP 2014. 88(3):739-45

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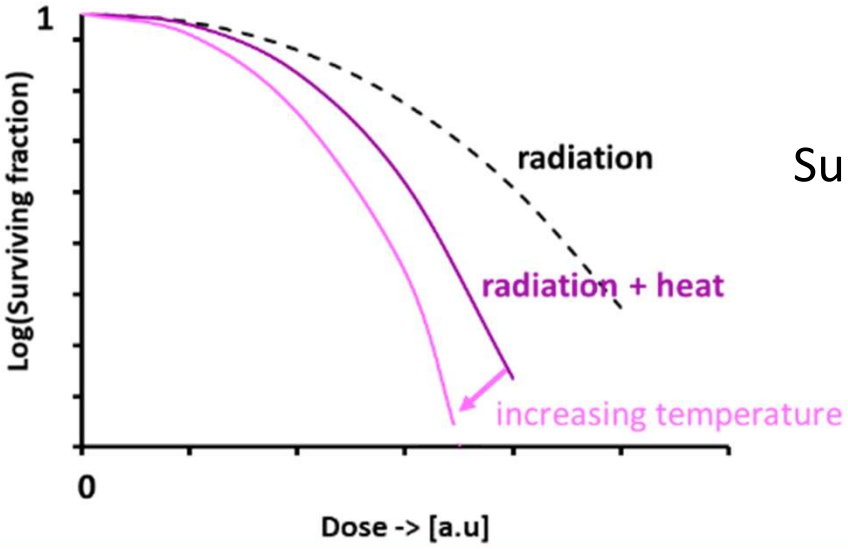


***LQ-model:***

Survival fraction $= \exp[-\alpha D - \beta D^2]$

Dependent on
- tumor type
- temperature
- time interval

Kok et al, IJROBP 2014. 88(3):739-45

# Future perspectives

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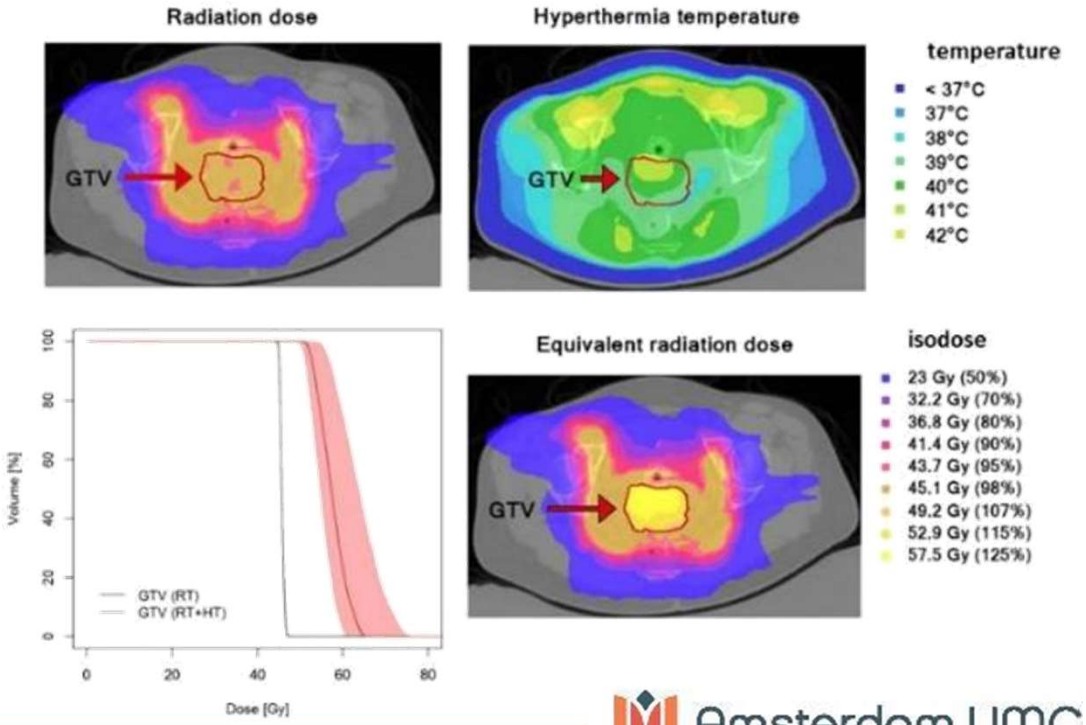
    - Equivalent dose prediction

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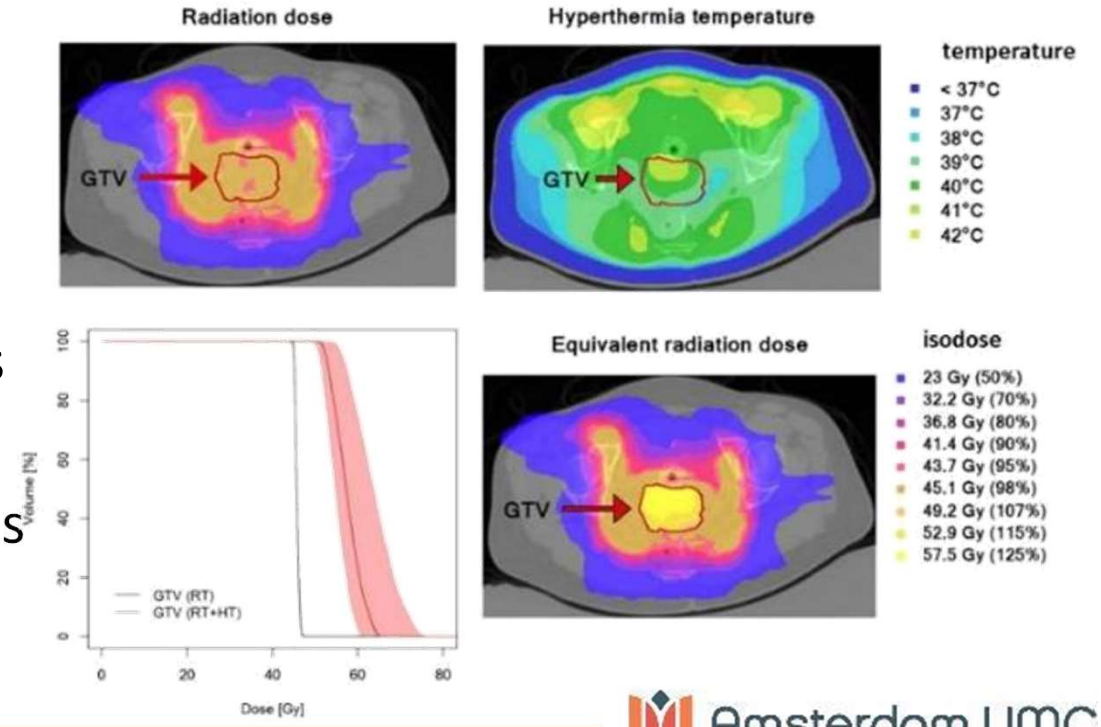
Van Leeuwen et al. *Int. J. Hyperthermia*; 2017; 33(2): 160-169

# Future perspectives

- Further developments to improve quantitative reliability
  - Biological modelling
    - Equivalent dose prediction
  - Language and evaluation tools of radiation oncologists
  - Useful to qualitatively compare treatment strategies
    - Impact of time interval




Van Leeuwen et al. *Int. J. Hyperthermia*; 2017; 33(2): 160-169

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# Hyperthermia treatment planning

***Summary & conclusions***

# Take home messages

- Treatment planning is:
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    - Always *compare* two or more strategies/ scenarios

# Take home messages

- Treatment planning is:
  - A powerful instrument
    - Sophisticated simulation techniques available
  - Very supportive to improve treatment quality when applied adequately
- Treatment planning is **NOT**:
  - Quantitatively reliable
    - Uncertainties in tissue properties
    - Always *compare* two or more strategies/ scenarios
  - Just launching a package and pushing buttons
    - Always *think* about the best evaluation strategy to answer your question
      - » Which metrics ? SAR or also temperature ?


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