भारतीय प्रौद्योगिकी संस्थान तिरुपति

TIRUPATI

Mathematical Modelling of Differential Equations and its Applications in Biomedical Industry

Panchatcharam Mariappan

Associate Professor

Department of Mathematics and Statistics,
IIT Tirupati

Recap

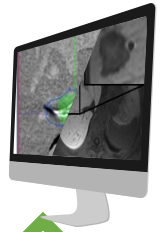
Cancer Treatments

Common Liver Cancers

HCCs

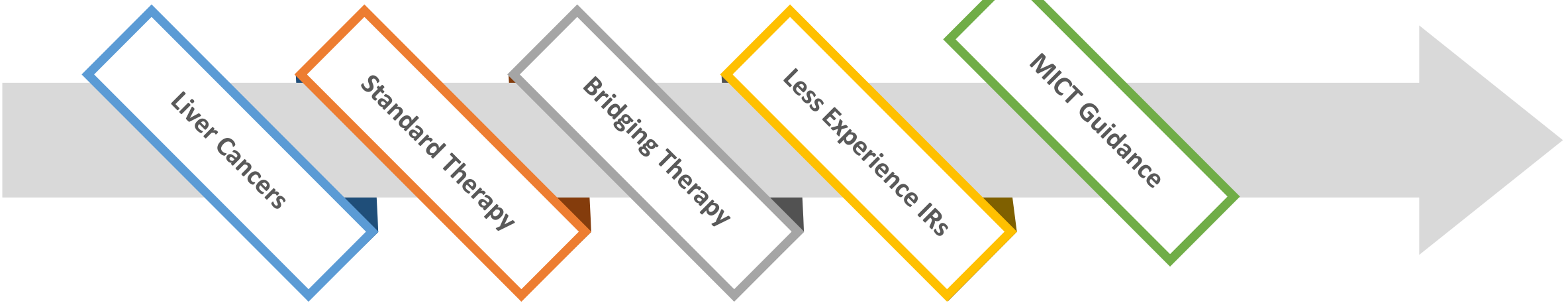
Bridging Therapy

RFA, MWA
IRE, Cryo
FUS, Laser



MICT Guidance

Help IRs
Change of parameters



Standard Therapy

- Surgical Treatments: 75-90% unsuitable[1]
- Transplantation

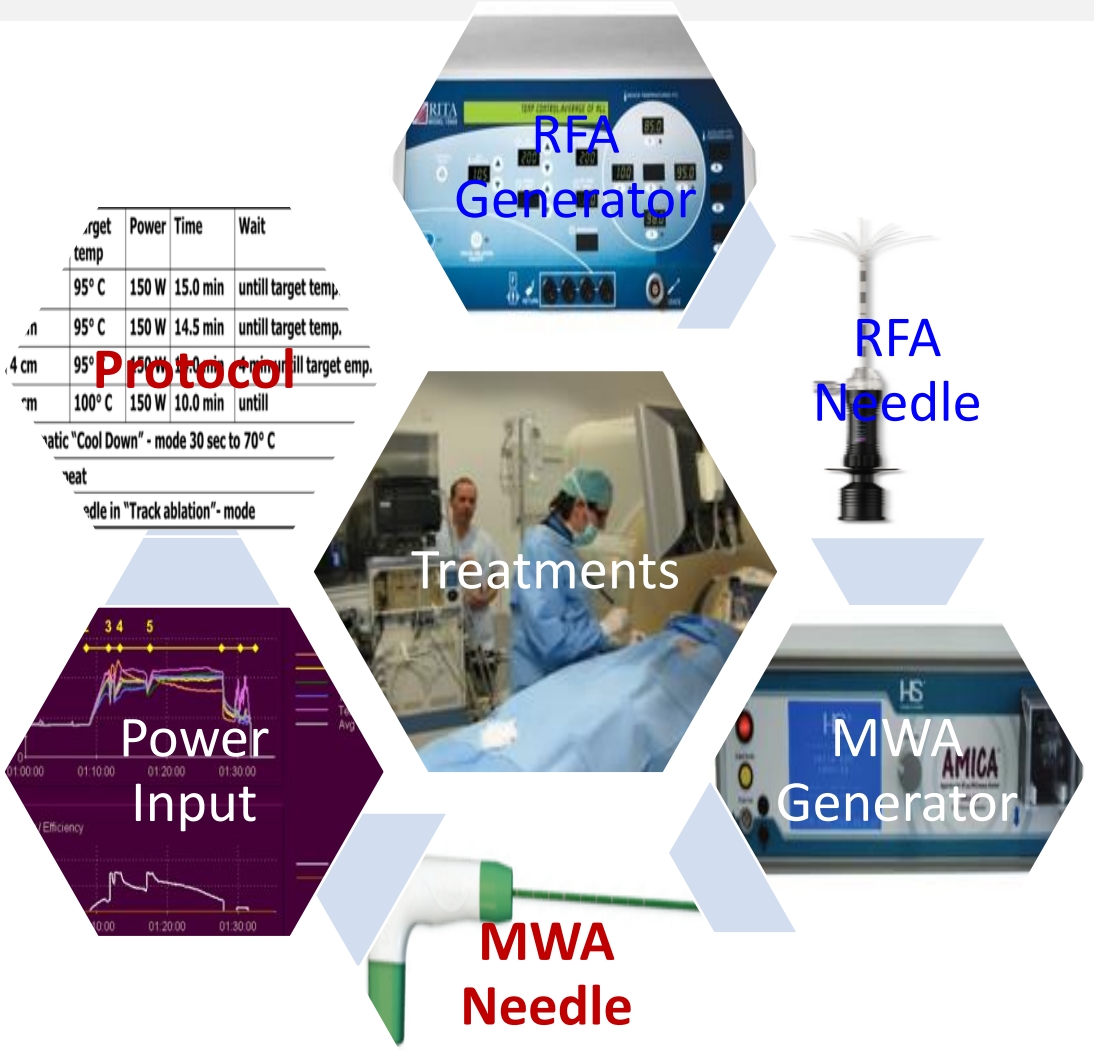
Less Experienced IRs

Under treatment: Recurrence
Over Treatment: Death

1. Bruix J, Sherman M (2011) Management of hepatocellular carcinoma: an update. Hepatology 53(3):1020–1022

Image Sources: https://angiodynamics.com
https://http://www.mermaidmedical.dk/

Patient-, Device-Specific Parameters



	Power	Time	Wait
temp			
95° C	150 W	15.0 min	untill target temp.
95° C	150 W	14.5 min	untill target temp.
95°			untill target emp.
100° C	150 W	10.0 min	untill

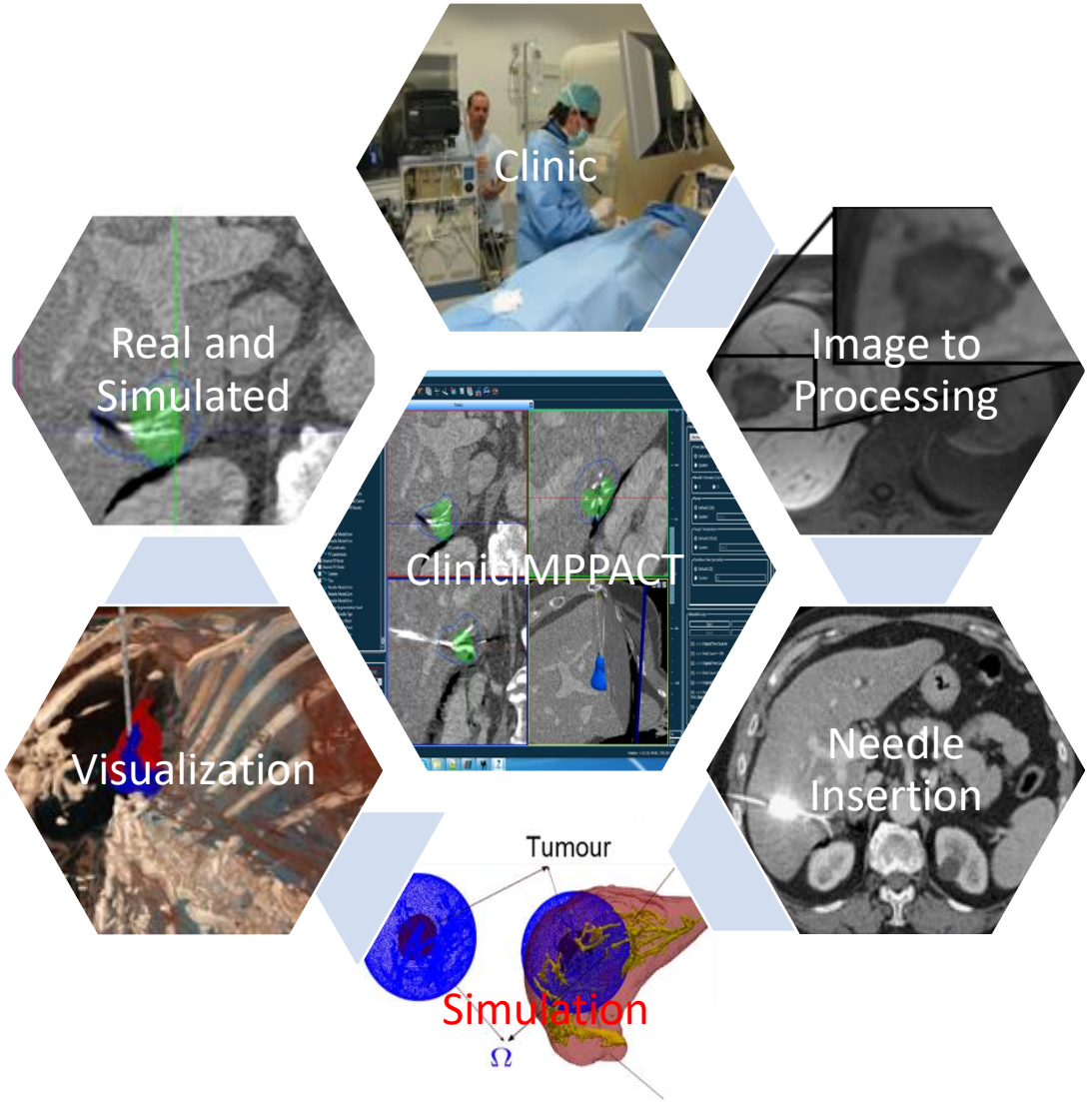
"Cool Down" - mode 30 sec to 70° C

"Track ablation" - mode

Image Sources: https://angiodynamics.com
https://http://www.mermaidmedical.dk/

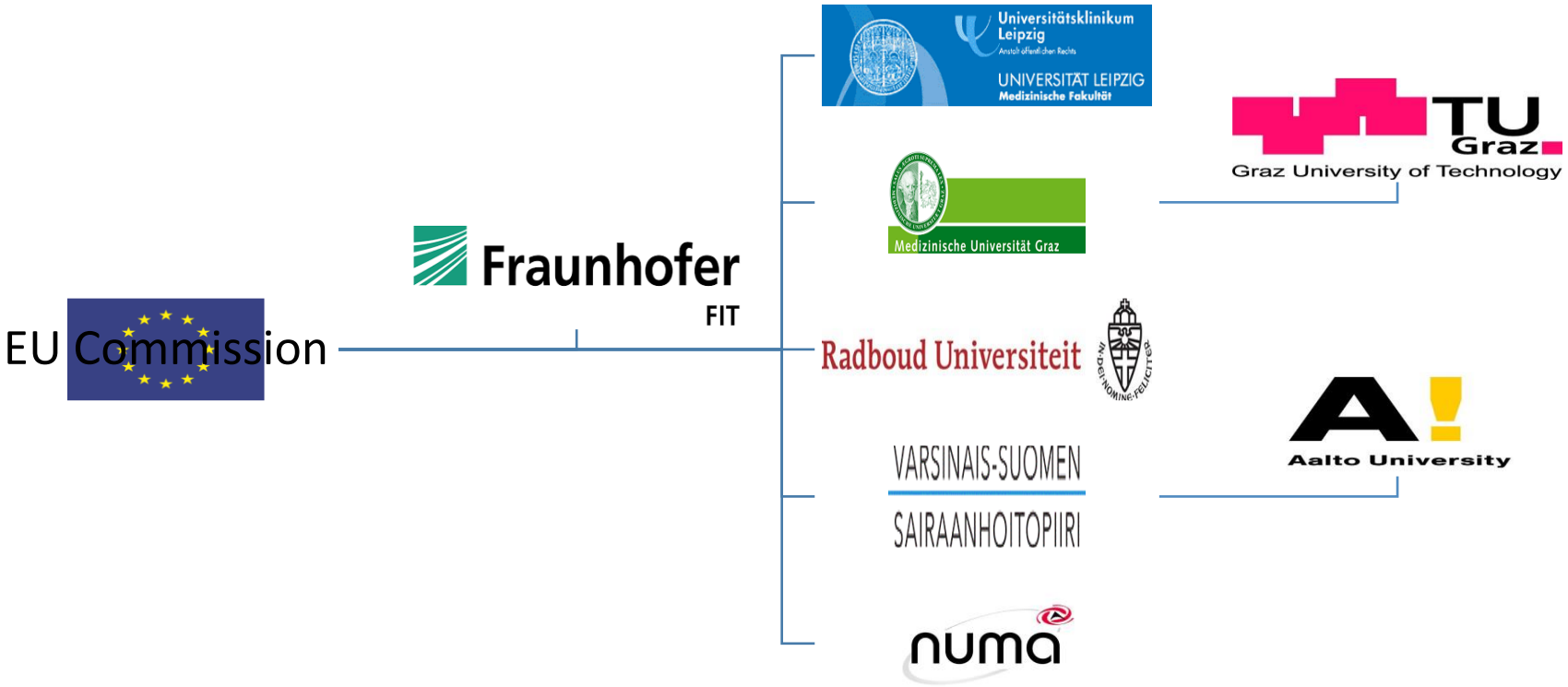
Objective

- Developed a software tool such that
  - Useful for the RFA treatment of liver cancer
  - Runs on a Single-PC
  - Usable at clinical environment
  - Predicts the lesion on the day of the treatment within few seconds
  - Accepts Patient-Specific parameters
  - Accepts Device-Specific parameters
  - Cost-efficient



ClinicIMPPACT Project

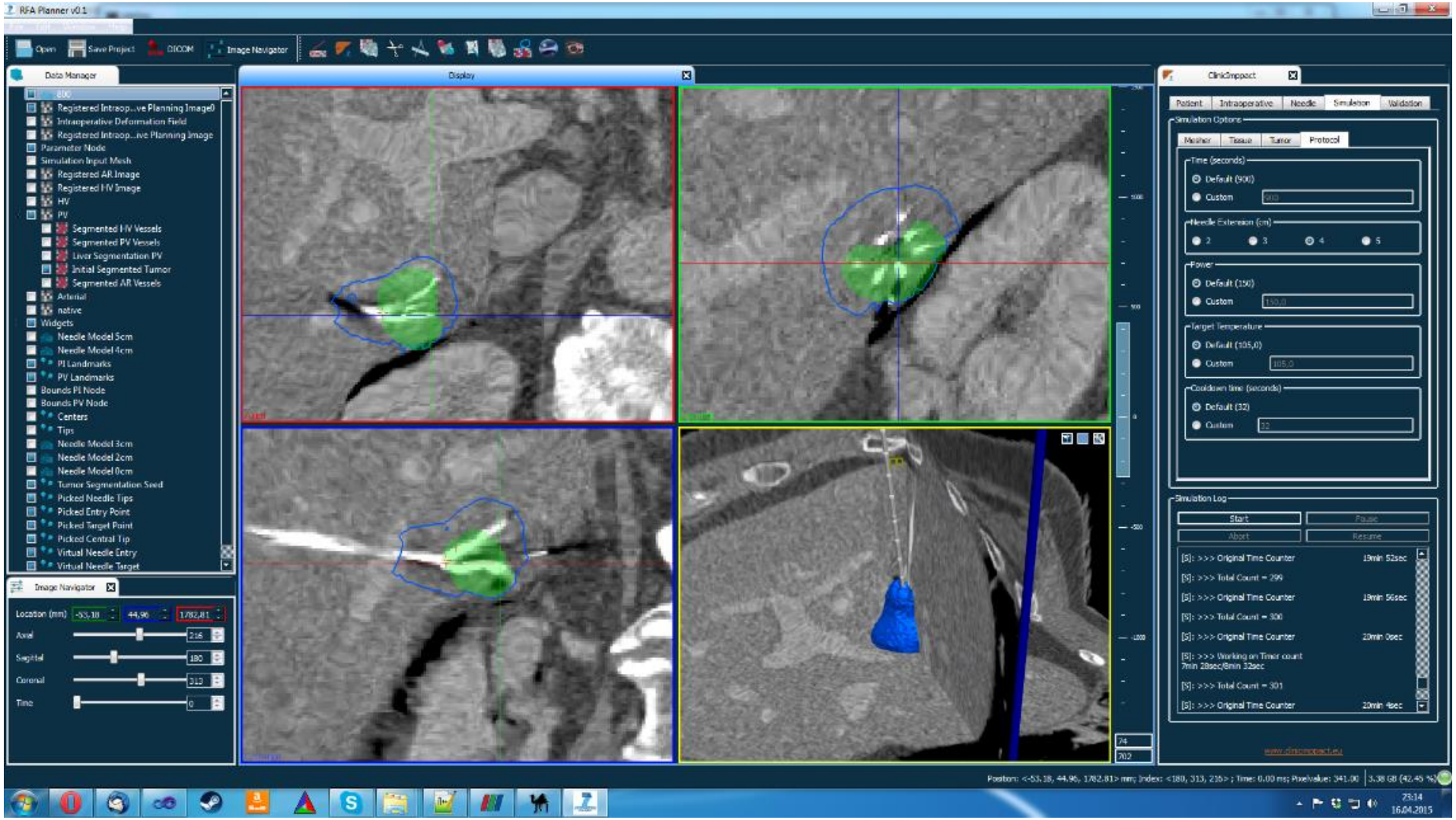
Clinical Intervention Modelling, Planning and Proof for Ablation Cancer Treatment



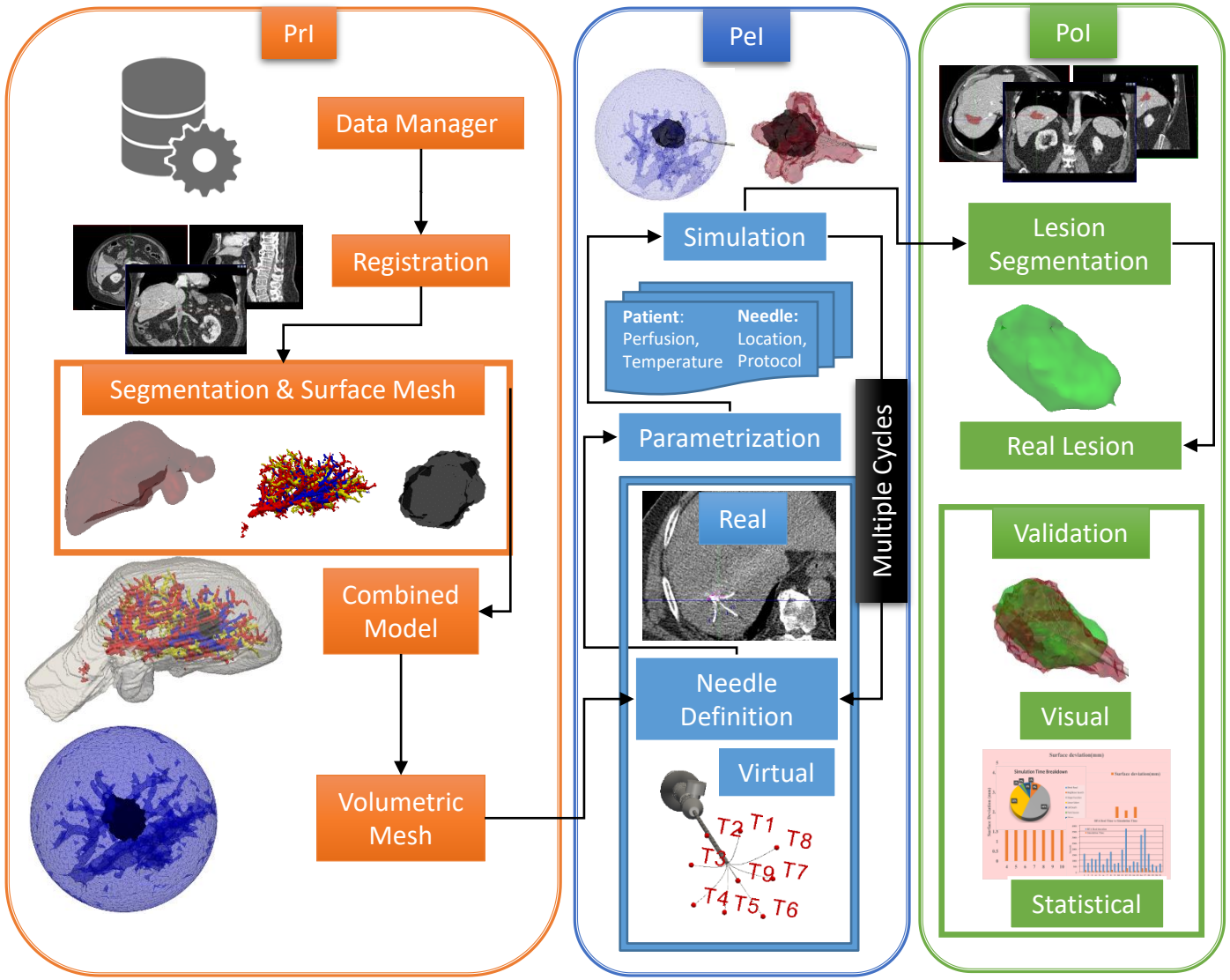
Rs.~41 Crores

http://www.clinicimppact.eu

RFA Guardian



Workflow


PrI
Data Manager
Registration
Segmentation & Surface Mesh
Combined Model
Volumetric Mesh
PeI
Simulation
Patient: Perfusion, Temperature
Needle: Location, Protocol
Parametrization
Real
Needle Definition
Virtual
T1 T2 T3 T4 T5 T6 T7 T8 T9
Multiple Cycles
PoI
Lesion Segmentation
Real Lesion
Validation
Visual
Statistical

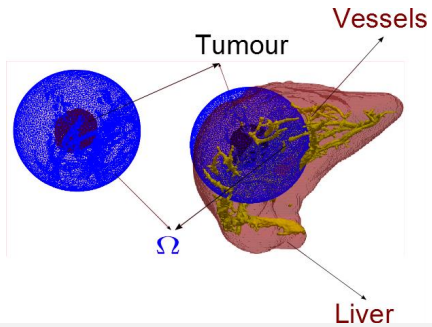
Governing Equations

Bioheat Equation[1]

$$\rho C \frac{\partial T}{\partial t} = k\Delta T + \omega_b \rho_b C_b (T_a - T) + Q_r \; on \; \Omega$$

$$h_c T + k \frac{\partial T}{\partial \vec{n}} = h_c T_\infty \text{ on vessels boundary}$$

$$T = T_0 \text{ on } \partial\Omega$$



Cell Death Model[2]

$$\frac{dA}{dt} = -k_f e^{\frac{T}{T_k}}(1-A)A + k_b(1-A-D)$$

$$\frac{dD}{dt} = k_f e^{\frac{T}{T_k}}(1-A)\,(1-A-D)$$

$$A(0) = 0.99, D(0) = 0.0$$

1. H. H. Pennes, Analysis of tissue and arterial blood temperature in the resting human forearm, J. Appl. Physio. 85(1):93-102, 1948
2. O'Neill DP, Peng T et al (2011) A three-state mathematical model of hyperthermic cell death. Ann Biomed Eng 39(1):570-579

भारतीय प्रौद्योगिकी संस्थान तिरुपति

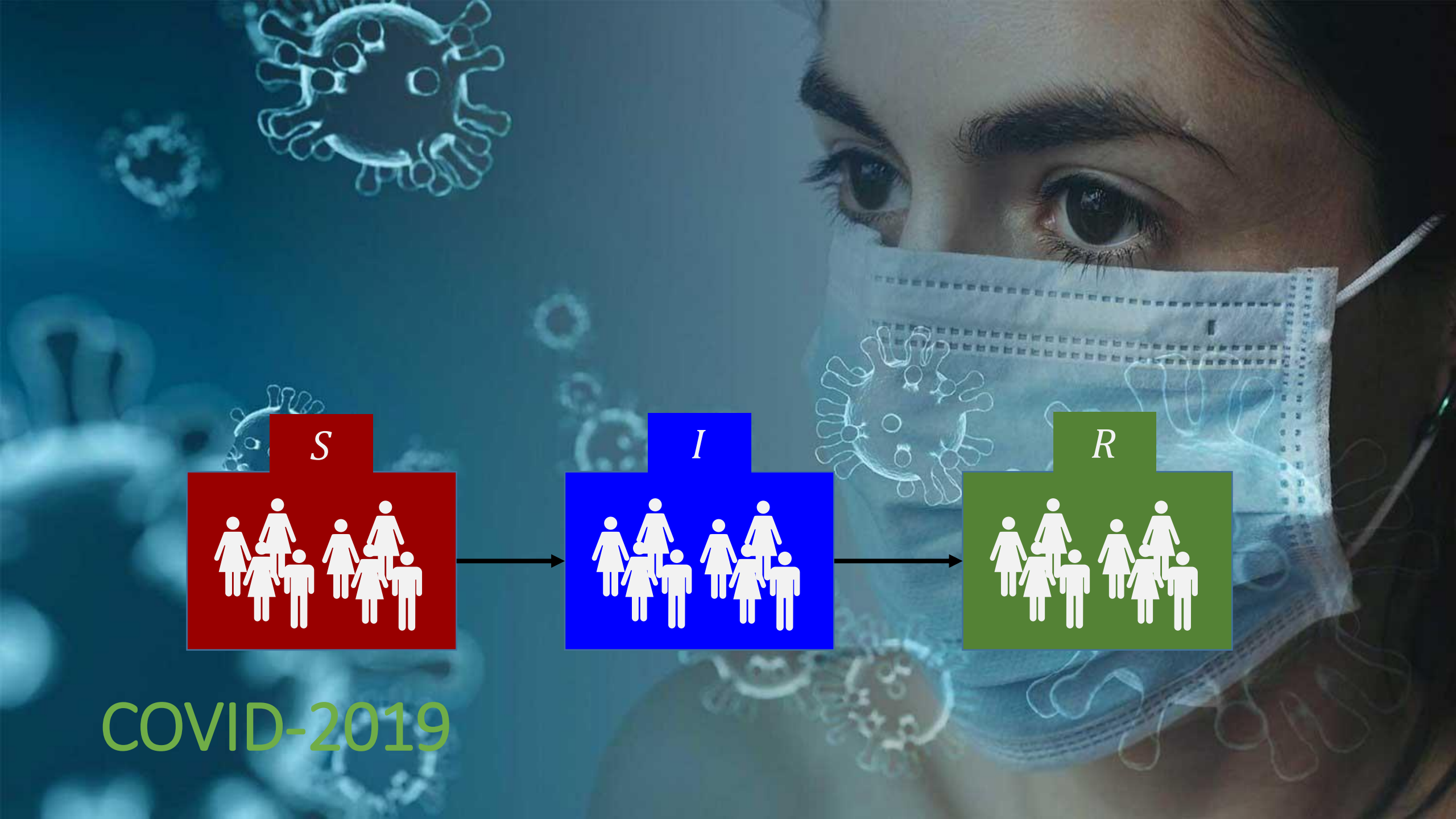
TIRUPATI

SIR Model for COVID-19

Panchatcharam Mariappan

Associate Professor

Department of Mathematics and Statistics,
IIT Tirupati

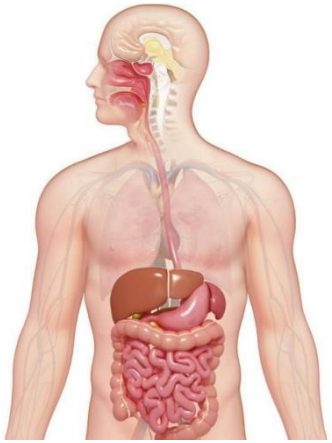

S
I
R
COVID-2019

Simple Example

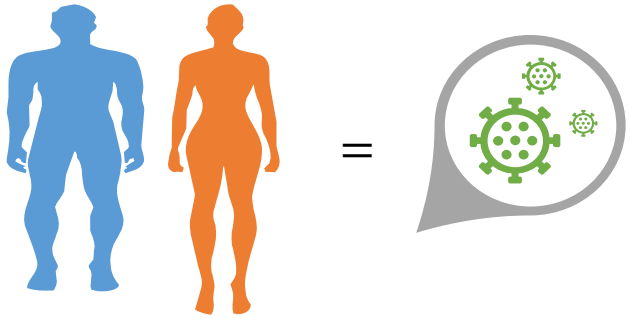
S

I

R



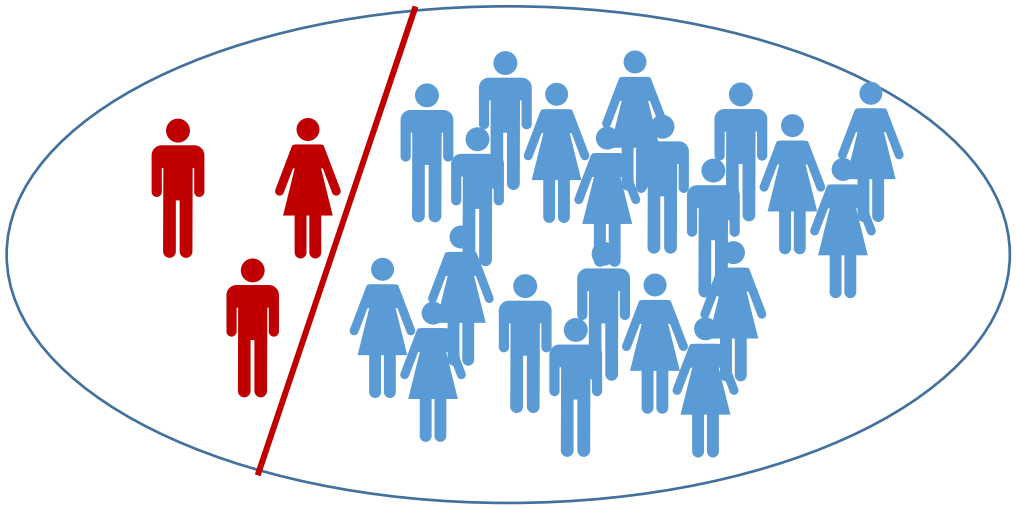
rice from the Sack taken
In the cooker, cooked and
Reached my mouth



Susceptible

The class of individuals who are healthy but can contract the disease.

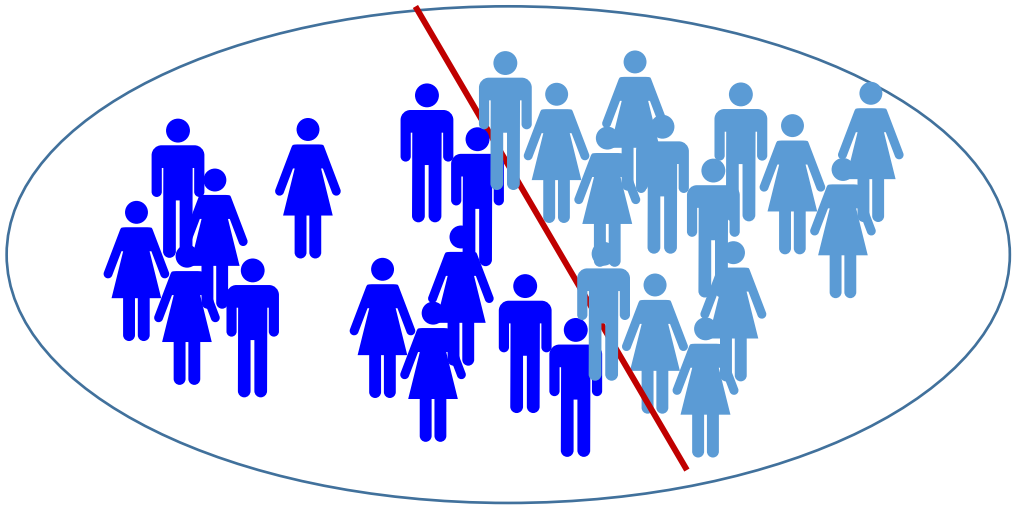
Denoted by S



Infectious

The class of individuals who have contracted the disease and are now sick with it.

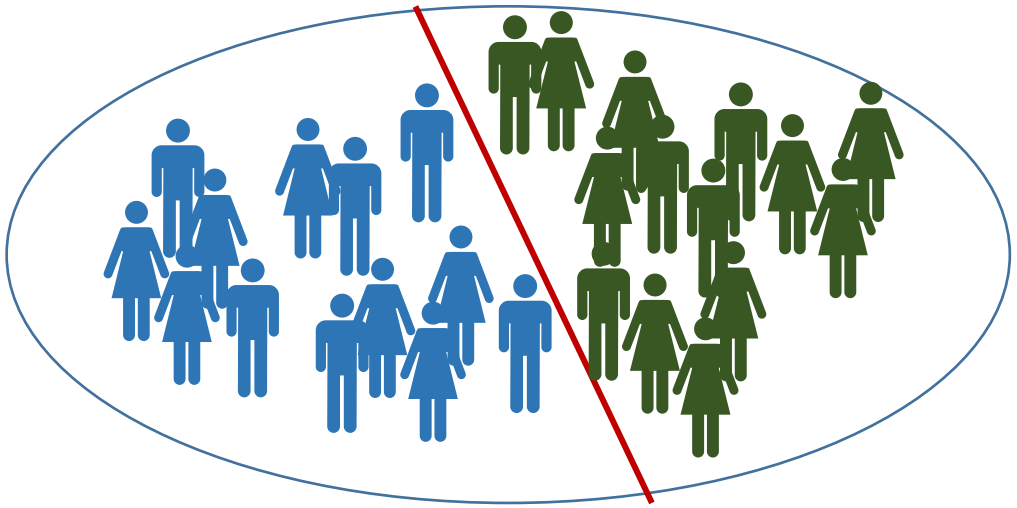
Denoted by I



Recovered/Removed

The class of individuals who have recovered and cannot contract the disease again.

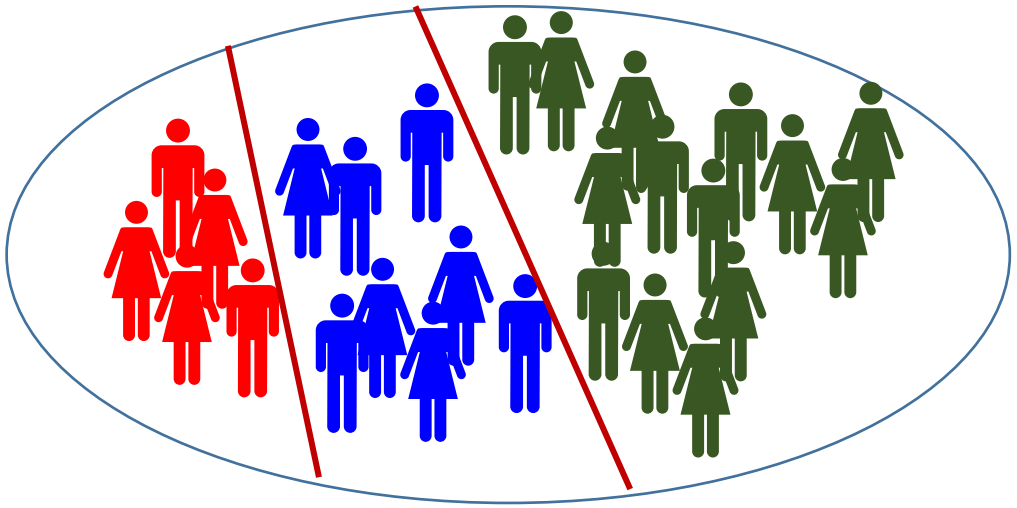
Denoted by R

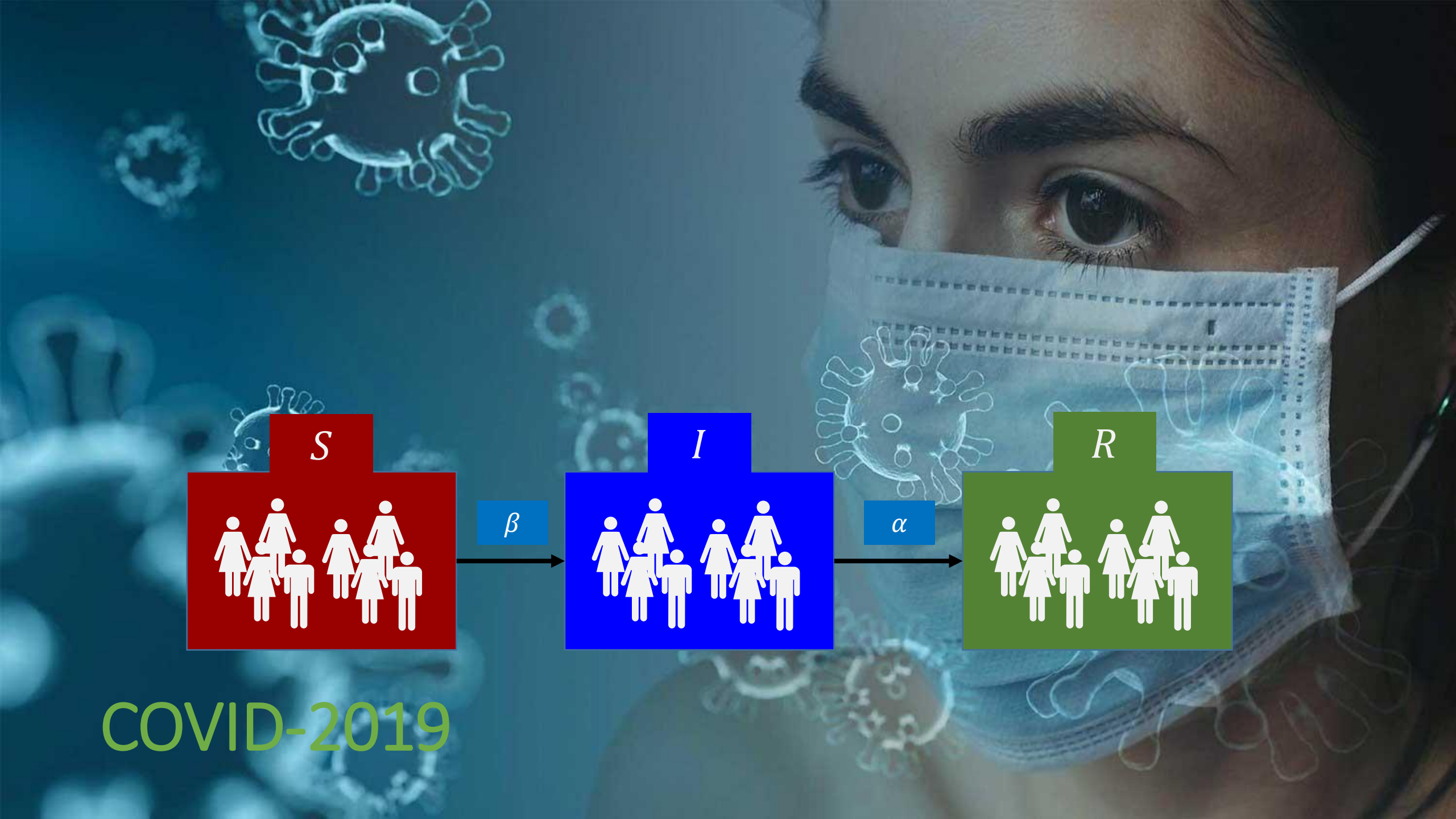


Total Population

The total population size is the sum of susceptible, infectious and recovered

Denoted by N



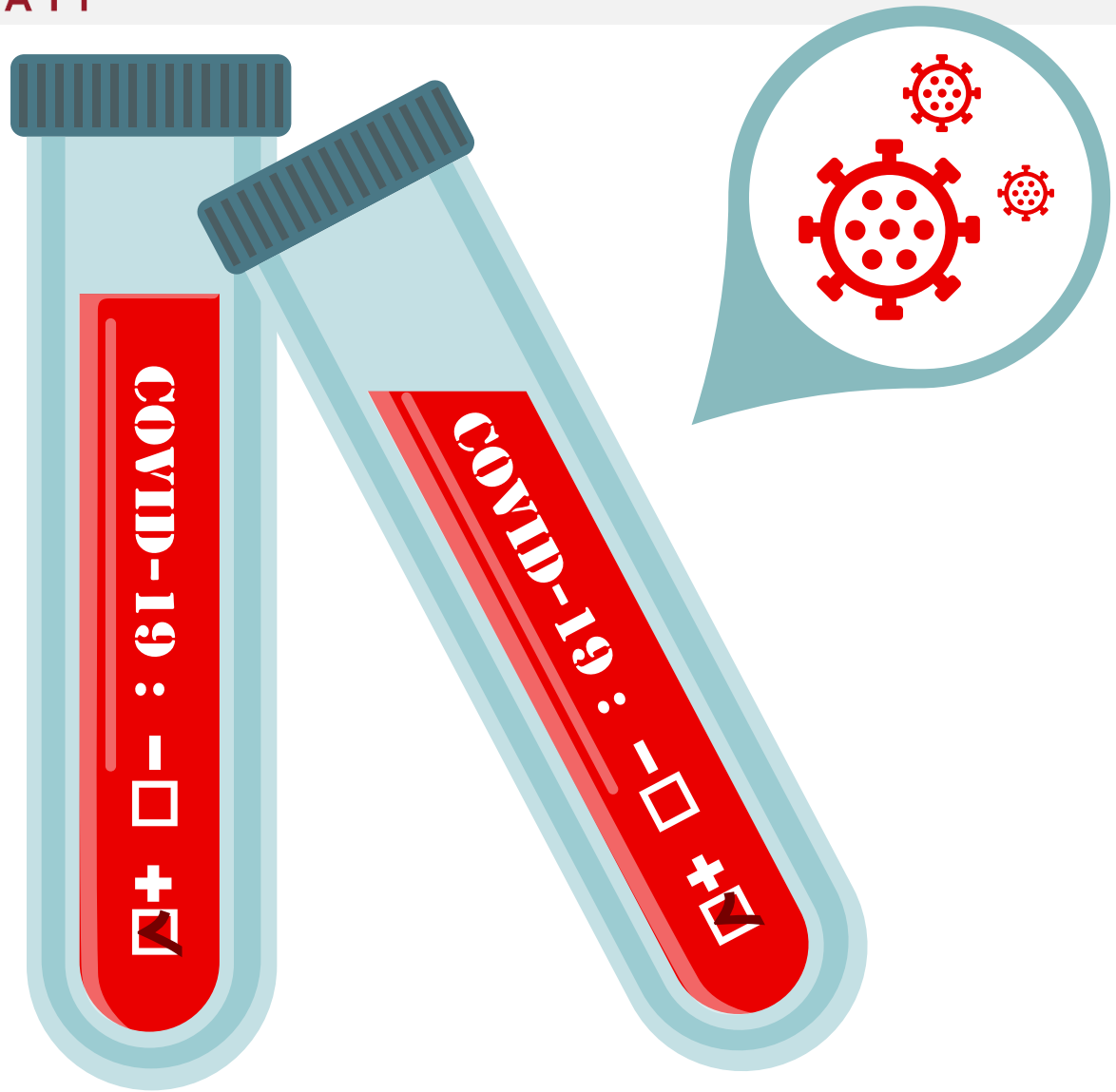


COVID-2019

2019-2020

COVID-19

Assumptions



We assume the following

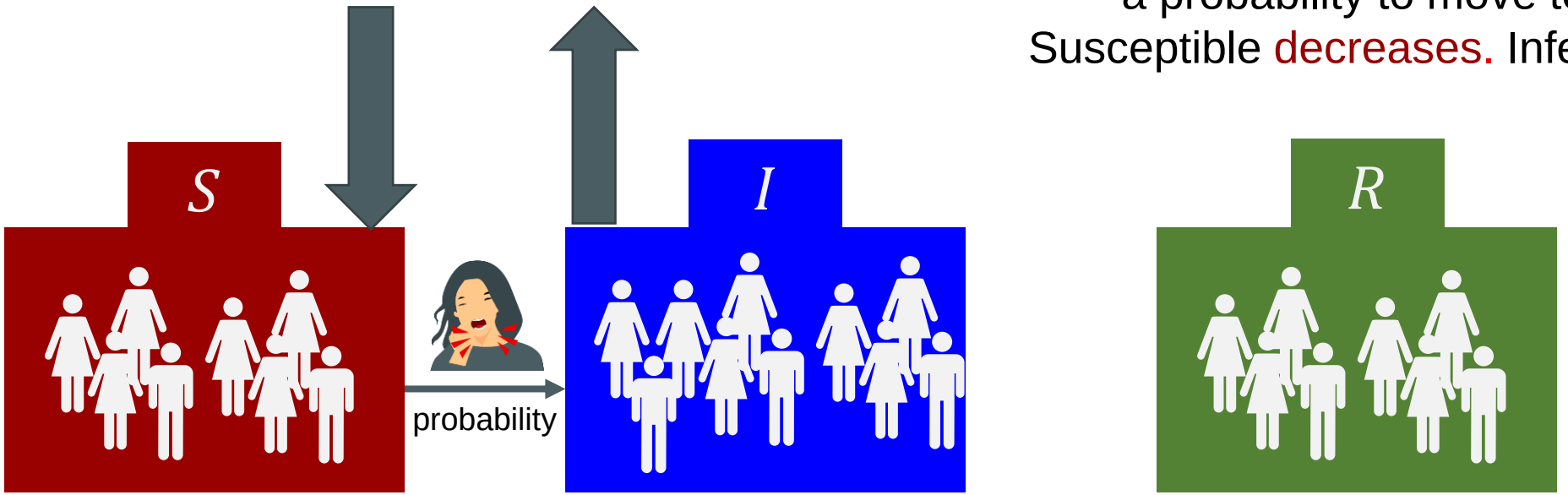
Infected individual becomes infectious

Total Population size is constant

COVID-19

Differential Equation

Observe how the classes change over time.
When a susceptible contact with infectious, there is a probability to move to infected class
Susceptible decreases. Infected increases



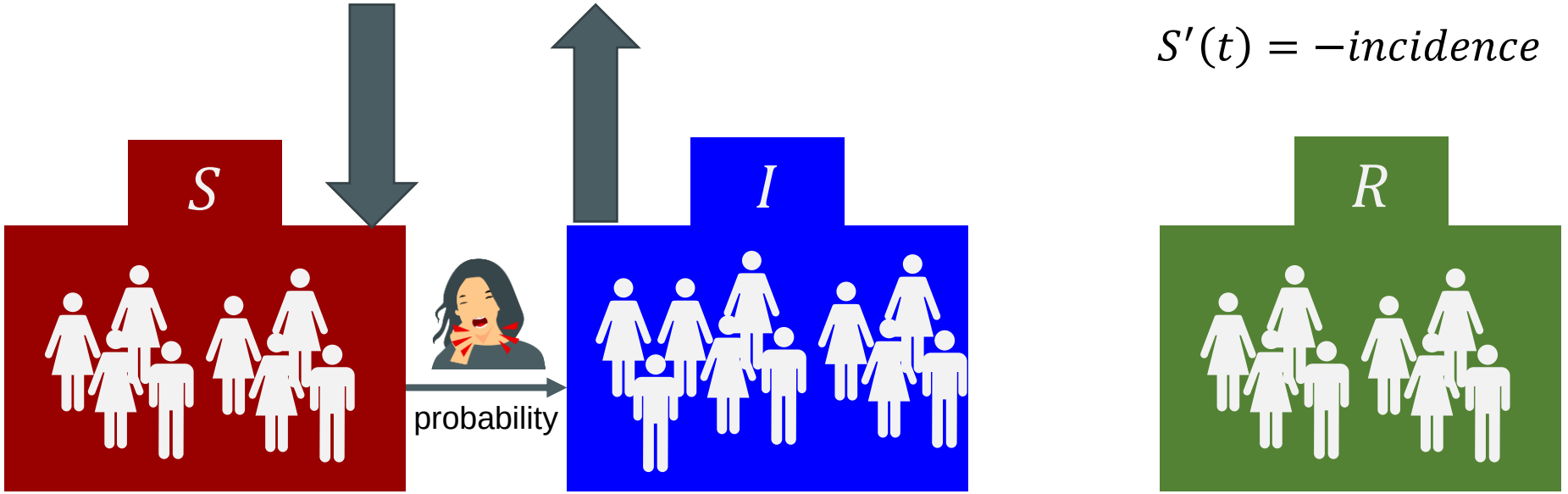
COVID-19

Differential Equation

Incidence

The number of individuals who become infected per unit of time

$$S'(t) = -incidence$$



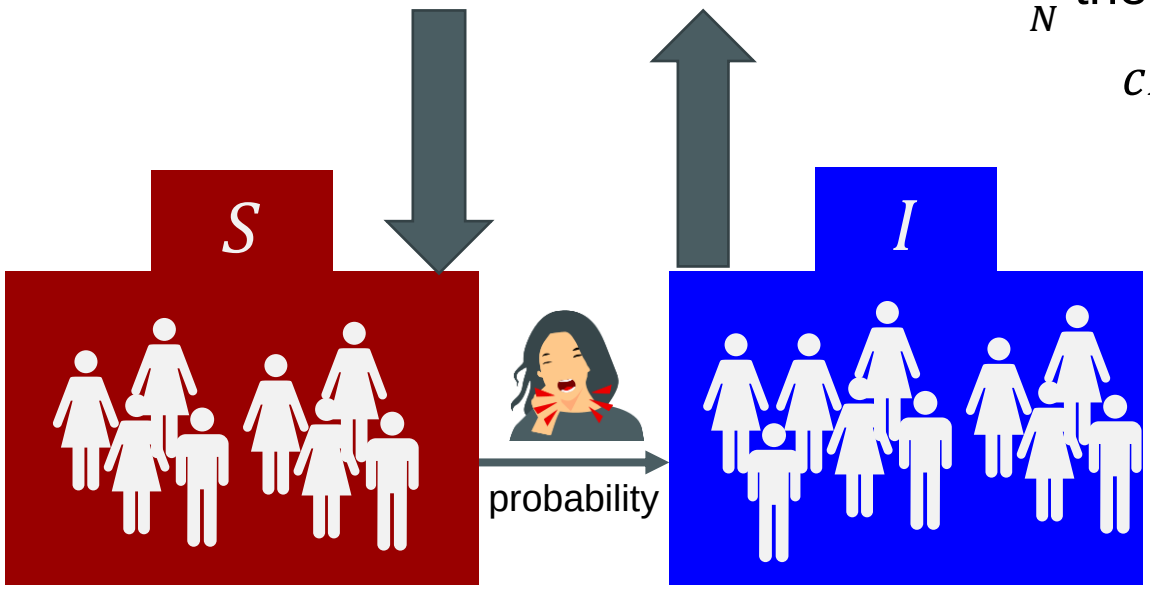
COVID-19

Differential Equation

Incidence

Let cN denote the number of contacts per unit time infected contacts. Where c denotes per capita rate $\frac{S}{N}$ the probability that a contact is with a susceptible

$cN\frac{S}{N}$ is number of contacts with susceptible per infected per unit time.



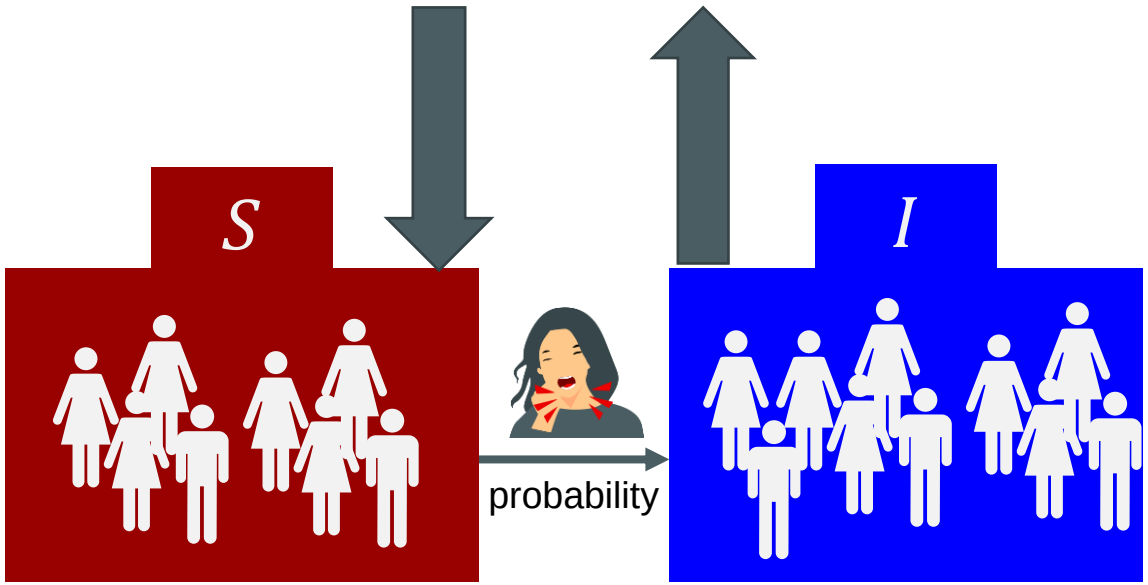
COVID-19

Differential Equation

Incidence

If p is the probability that a contact with a susceptible results in transmission, then pcS is the number of susceptible moves to infected per unit time per infected persons.

$\beta = pc$ the transmission rate constant



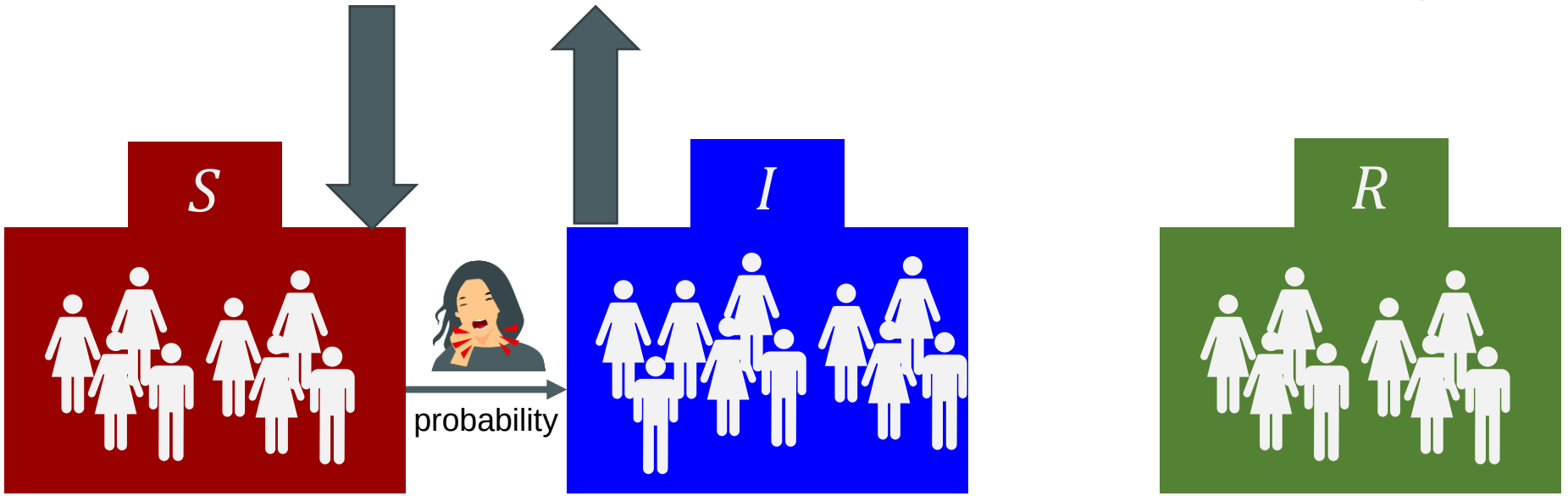
COVID-19

Differential Equation

Incidence

βSI denote the number of people who become infected per unit time = incidence

$$S'(t) = -\beta IS$$

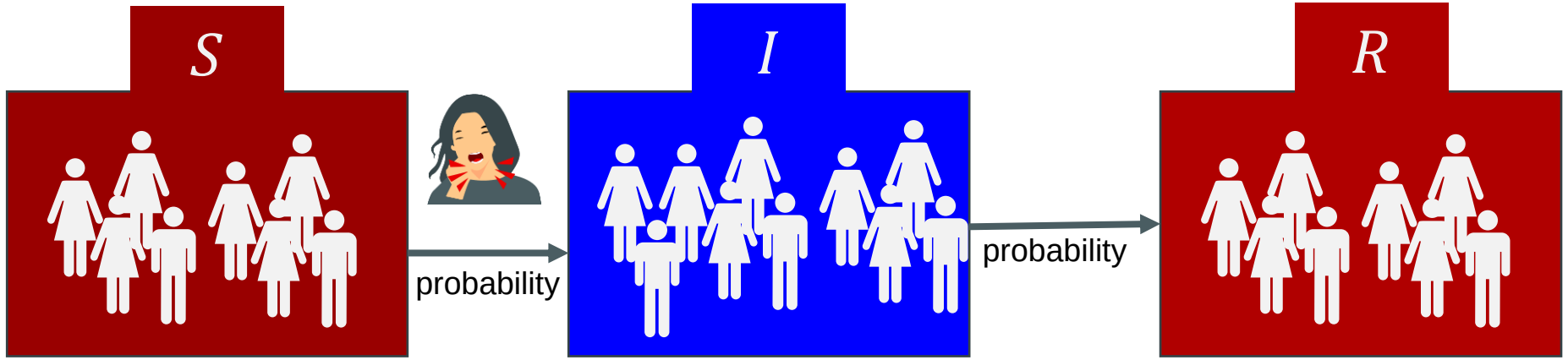


COVID-19

Differential Equation

Recovery Rate

Similarly, infected may move to recovery or removed class at a constant rate per capita probability per unit time α



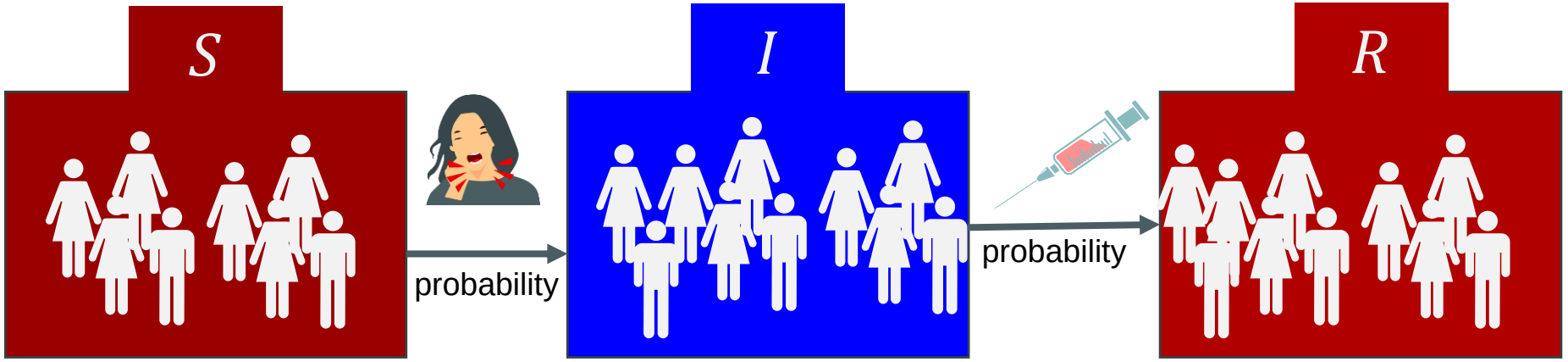
COVID-19

Differential Equation

Recovery Rate

αI is the number of infected moved to recover/remove
Since from susceptible, βIS moved to infected and αI moved from infected to recovered, we have

$$I'(t) = \beta IS - \alpha I$$



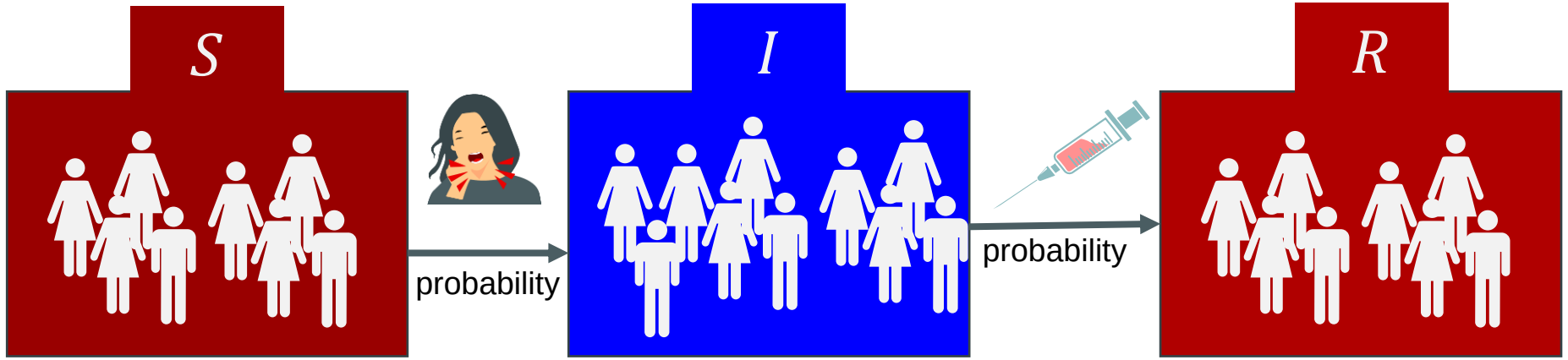
COVID-19

Differential Equation

Recovery Rate

Recovered persons move from infected to recover class is given by

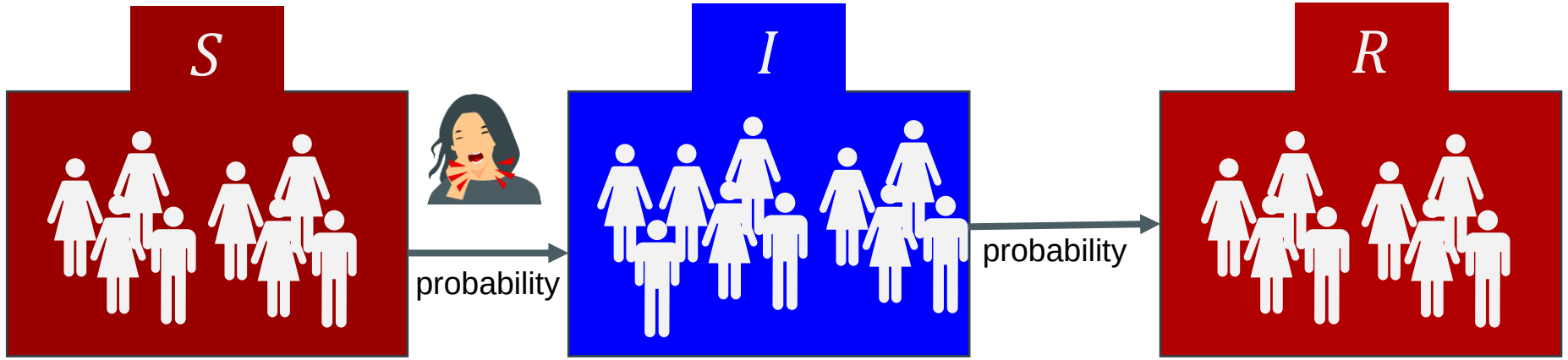
$$R'(t) = \alpha I$$



COVID-19

SIR Model

$$S'(t) = -\beta IS$$
$$I'(t) = \beta IS - \alpha I$$
$$R'(t) = \alpha I$$
$$S(0), I(0), R(0)$$
$$N = S(0) + I(0) + R(0)$$

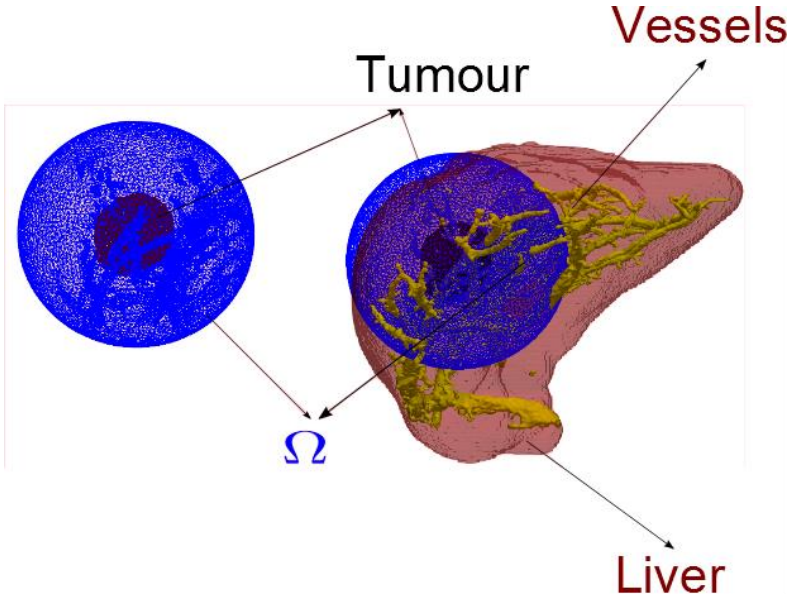


Bioheat Equation[1]

$$\rho C \frac{\partial T}{\partial t} = k\Delta T + \omega_b \rho_b C_b (T_a - T) + Q_r \; on \; \Omega$$

$$h_c T + k \frac{\partial T}{\partial \vec{n}} = h_c T_\infty \text{ on vessels boundary}$$

$$T = T_0 \text{ on } \partial\Omega$$



1. H. H. Pennes, Analysis of tissue and arterial blood temperature in the resting human forearm, J. Appl. Physio. 85(1):93-102, 1948

भारतीय प्रौद्योगिकी संस्थान तिरुपति

TIRUPATI

Cell Death Model

Panchatcharam Mariappan

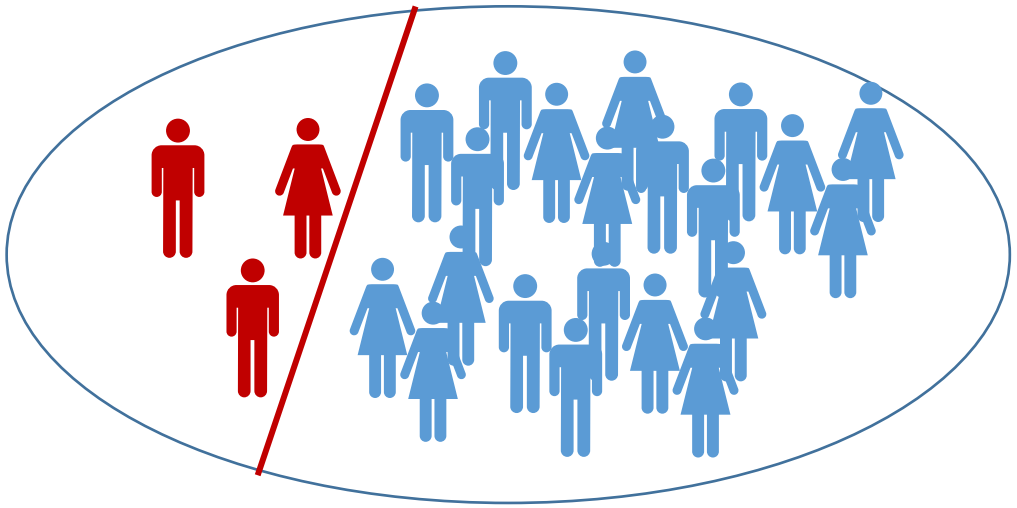
Associate Professor

Department of Mathematics and Statistics,
IIT Tirupati

Ablation Zone

The class of individuals who are healthy but can contract the disease.

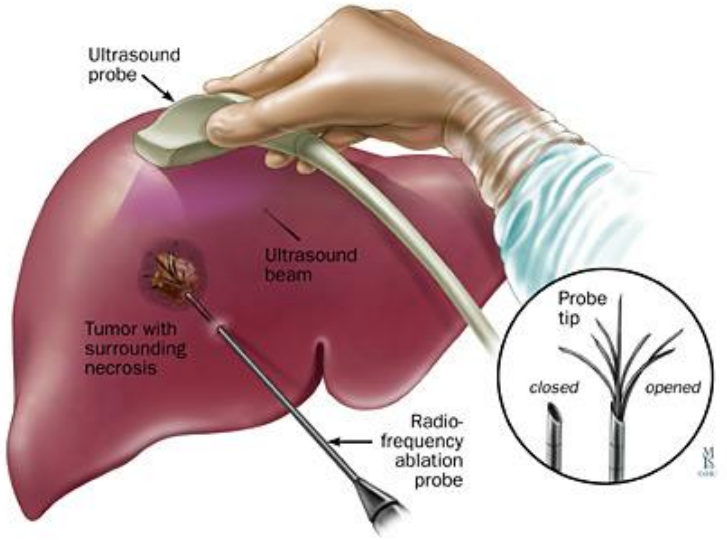
Denoted by S



Ablation Zone

- Area of coagulative necrosis created by the RFA procedure
- Region covered by dead and damaged cells due to heat

Success of the RFA is decided by the ablation zone

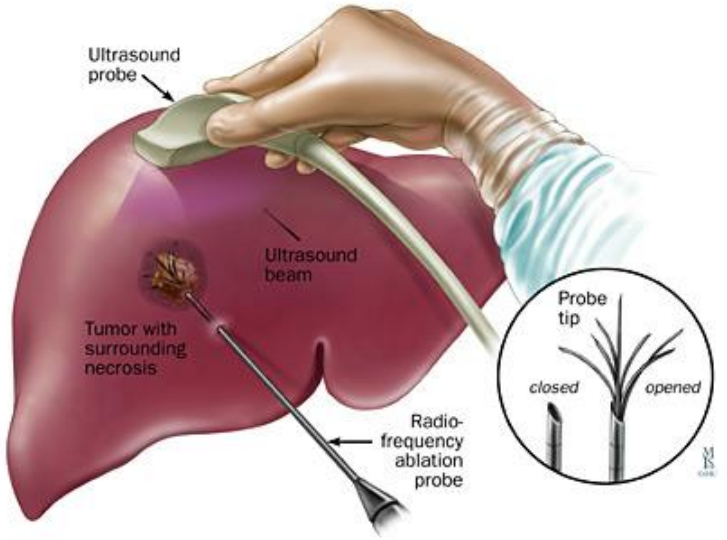


Simplest Model

- **Cell damage occurs when temperature rises above $43℃$**
  - ❑ **Temperature and Heating time plays vital role**

Simplest model:

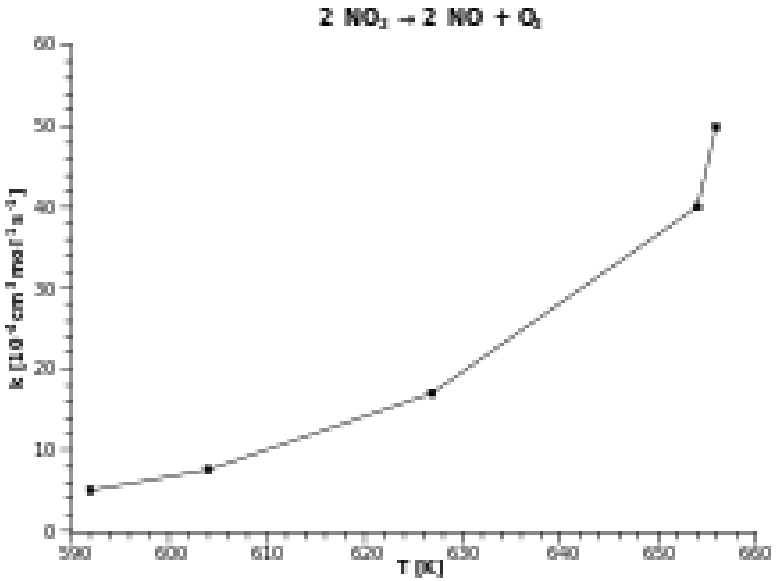
- **Single temperature threshold ($50℃ - 60℃$)**
  - **Below threshold active cells**
  - **Above threshold dead cells**



Arrehenius Model

$$k = Ae^{-\frac{E_a}{RT}}$$

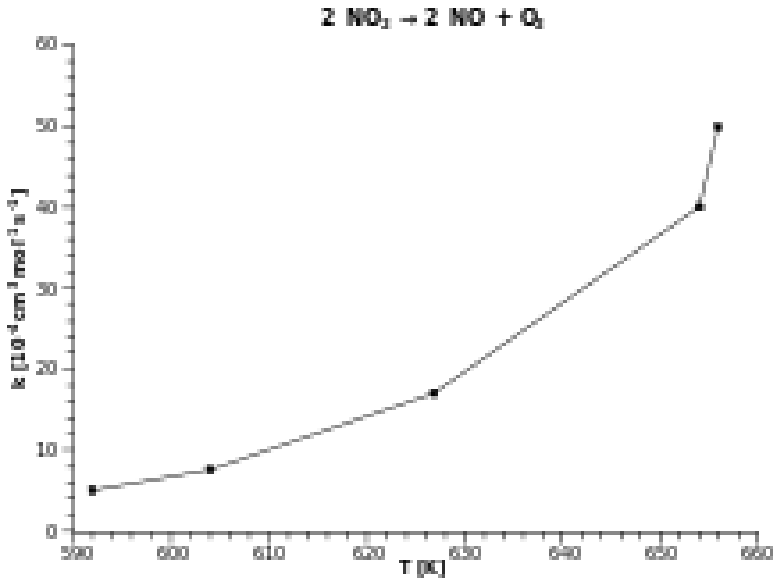
- E_a: activation energy
- T: temperature
- R: universal constant
- A: exponential factor



Survival Fraction

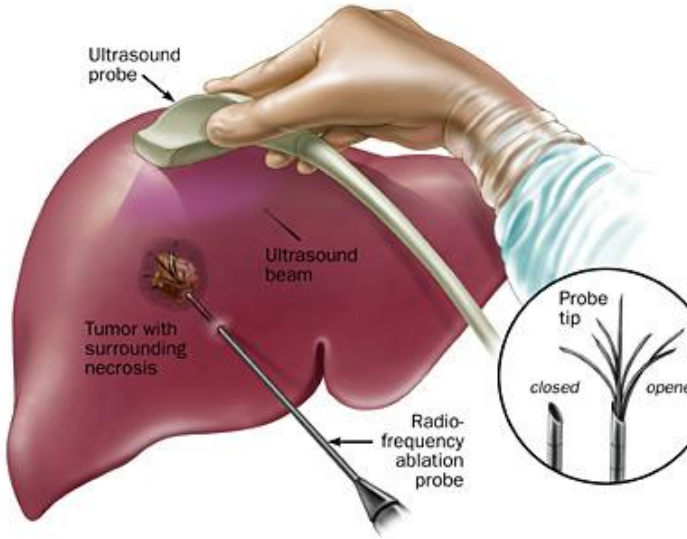
$$\Omega(\mathrm{t}) = \int_0^{\tau} A exp\left(-\frac{E_a}{RT(t)}\right) dt$$

- E_a: activation energy
- T: temperature
- R: universal constant
- A: exponential factor



Cell Death Model[1]

Cell Death Model



1. O'Neill DP, Peng T et al (2011) A three-state mathematical model of hyperthermic cell death. Ann Biomed Eng 39(1):570-579

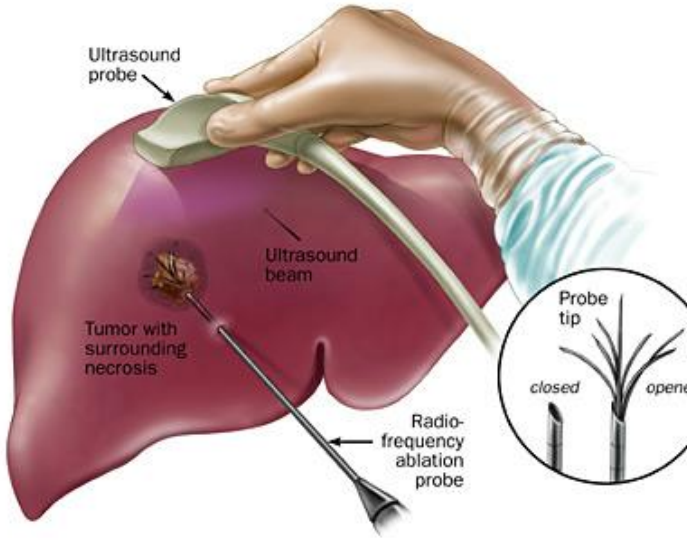
Cell Death Model[1]

Cell Death Model

$$\frac{dA}{dt} = -k_f e^{\frac{T}{T_k}}(1-A)A + k_b(1-A-D)$$

$$\frac{dD}{dt} = k_f e^{\frac{T}{T_k}}(1-A)\,(1-A-D)$$

$$\mathrm{A}(0) = 0.99, D(0) = 0.0$$



1. O'Neill DP, Peng T et al (2011) A three-state mathematical model of hyperthermic cell death. Ann Biomed Eng 39(1):570-579

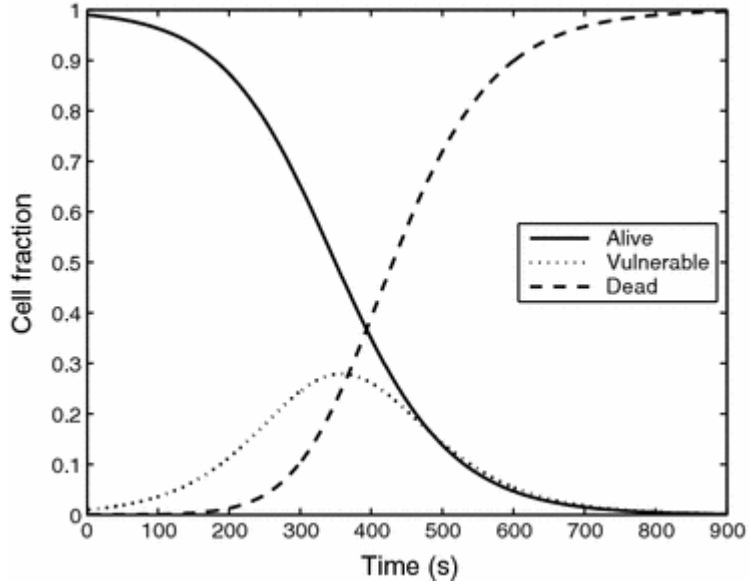
Cell Death Model[1]

Cell Death Model

$$\frac{dA}{dt} = -k_f e^{\frac{T}{T_k}}(1-A)A + k_b(1-A-D)$$

$$\frac{dD}{dt} = k_f e^{\frac{T}{T_k}}(1-A)\,(1-A-D)$$

$$\mathrm{A}(0) = 0.99, D(0) = 0.0$$



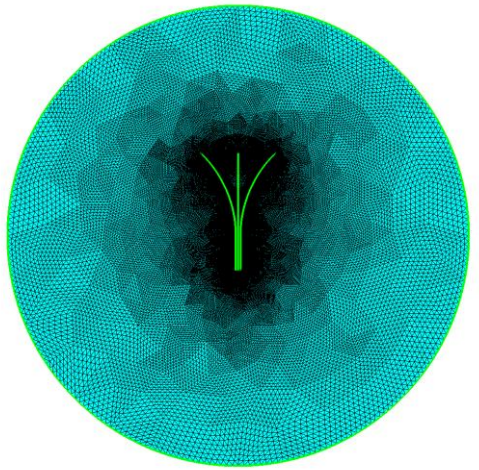
1. O'Neill DP, Peng T et al (2011) A three-state mathematical model of hyperthermic cell death. Ann Biomed Eng 39(1):570-579

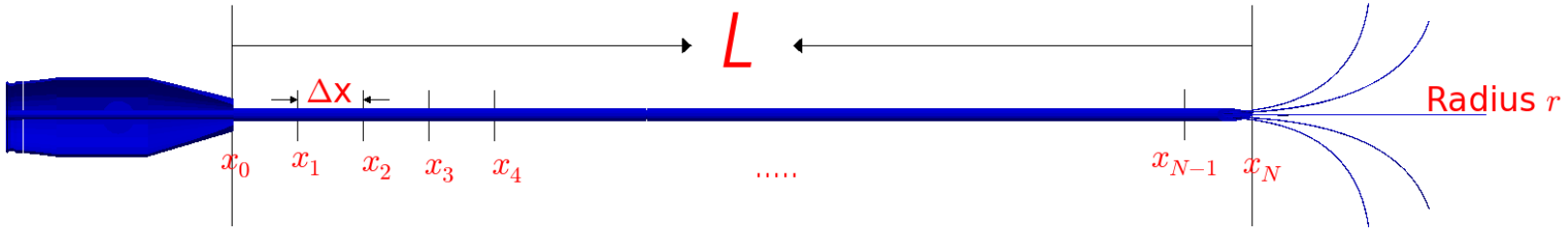
Joule Heat Model

$$\sigma \Delta \phi = 0 \quad on \quad \Omega$$

$$\phi = \begin{cases} \phi_r & on \quad Needle\ Tips \\ \phi_c & on \quad Circular\ boundary \end{cases}$$

$$\frac{\partial \phi}{\partial \vec{n}} = 0 \quad on \quad Needle\ Shaft$$





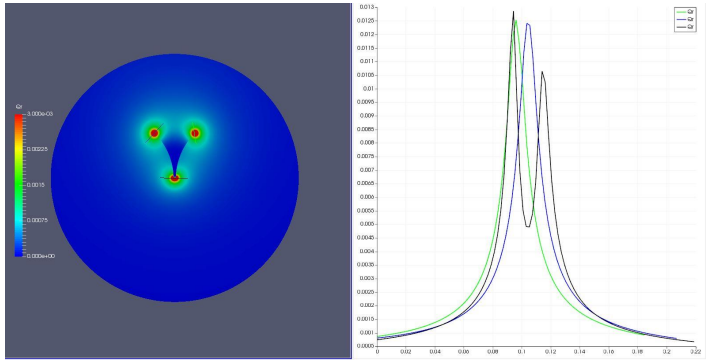
$$Q_r = \sigma |\nabla \phi|^2$$

Point Source Model

Gaussian:

$$P(\vec{x}) = \frac{\sum_{tip} \alpha_{tip} \exp(-\frac{\|\vec{x} - \vec{x}_{tip}\|^2}{2\sigma^2})}{\sum_{tip} \alpha_{tip} (\sigma\sqrt{2\pi})^3}$$

Heat Source: $Q_r = \sum P(\vec{x}) * power$



Power Adjustment: PID Controller

भारतीय प्रौद्योगिकी संस्थान तिरुपति

TIRUPATI

Joule Heat/Point Source Model

Panchatcharam Mariappan

Associate Professor

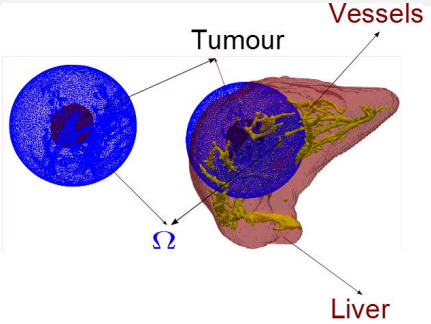
Department of Mathematics and Statistics,
IIT Tirupati

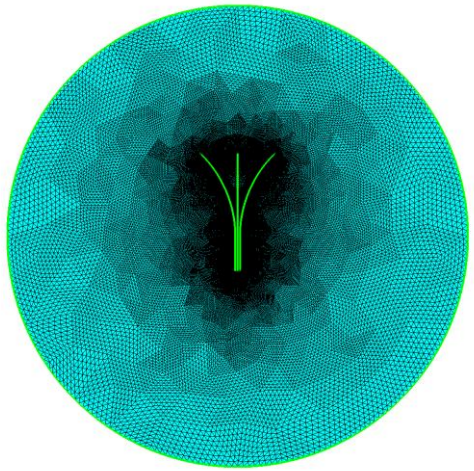
What is the Model?

Joule Heat Model

Bioheat Equation[1]

$$\rho C \frac{\partial T}{\partial t} = k\Delta T + \omega_b \rho_b C_b (T_a - T) + Q_r \; on \; \Omega$$





Joule Heat Model

$$\sigma\Delta\phi = 0 \text{ on } \Omega$$

$$\varphi = \begin{cases} \varphi_r \; on \; NeedleTips \\ \varphi_c \; on \; Circularboundary \end{cases}$$

$$\frac{\partial \phi}{\partial \boldsymbol{n}} = 0 \text{ on Needle shaft}$$

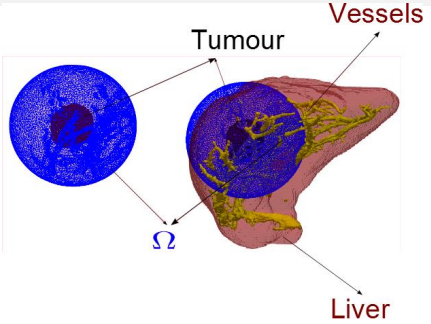
$$Q_r = \sigma(|\nabla\phi|^2)$$

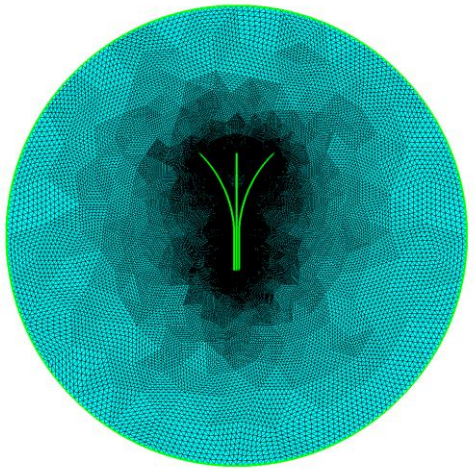
1. H. H. Pennes, Analysis of tissue and arterial blood temperature in the resting human forearm, J. Appl. Physio. 85(1):93-102, 1948
2. O'Neill DP, Peng T et al (2011) A three-state mathematical model of hyperthermic cell death. Ann Biomed Eng 39(1):570-579

Point Source Model

Bioheat Equation[1]

$$\rho C \frac{\partial T}{\partial t} = k\Delta T + \omega_b \rho_b C_b (T_a - T) + Q_r \; on \; \Omega$$





Point Source Model

$$P(\vec{x}) = \frac{\sum_{tip} \alpha_{tip} \exp(-\frac{\|\vec{x} - \vec{x}_{tip}\|^2}{2\sigma^2})}{\sum_{tip} \alpha_{tip} (\sigma\sqrt{2\pi})^3}$$

$$Q_r = \sum P(\vec{x}) * power$$

1. H. H. Pennes, Analysis of tissue and arterial blood temperature in the resting human forearm, J. Appl. Physio. 85(1):93-102, 1948
2. O'Neill DP, Peng T et al (2011) A three-state mathematical model of hyperthermic cell death. Ann Biomed Eng 39(1):570-579

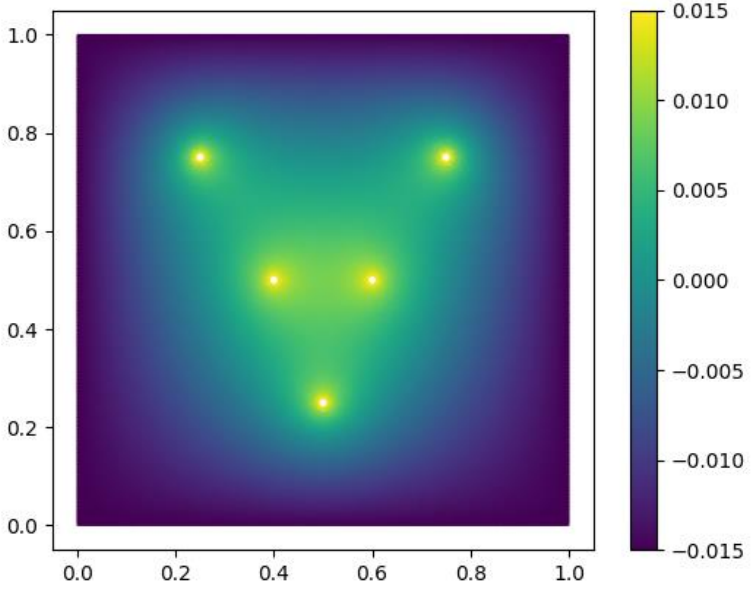
How?

Joule Heat Model

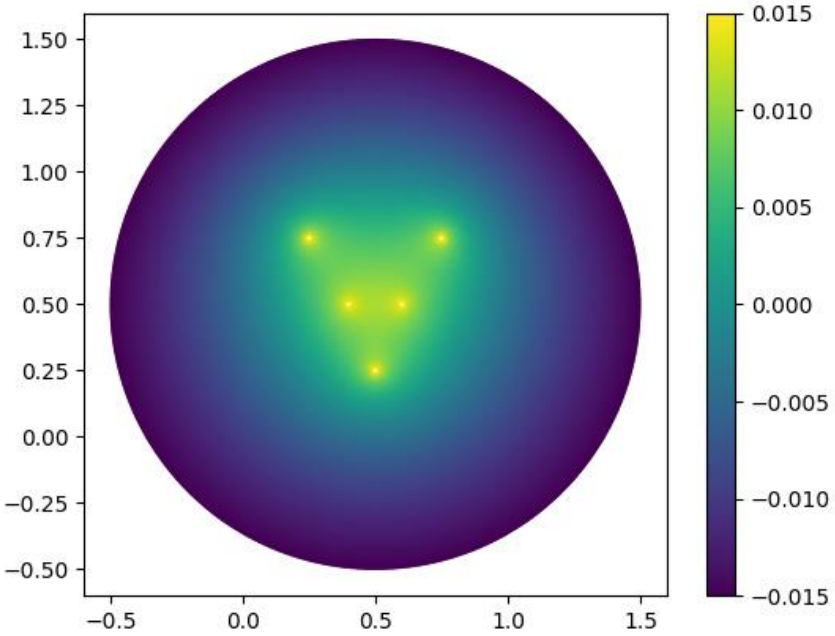
$$\varphi = \begin{cases} 0.015 & on\ needle\ tips \\ -0.015 & on\ rectangular\ boundary \end{cases}$$

$$\sigma = 0.4$$

Using FeniCS software



φ Visualization on unit square

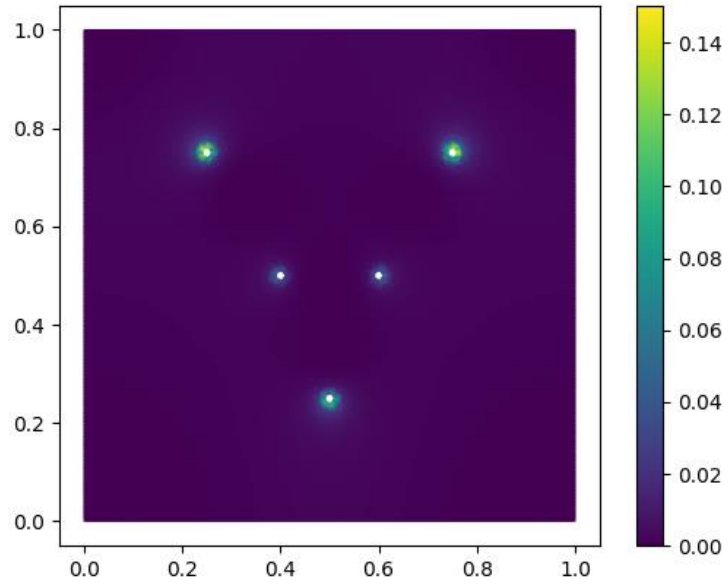


φ Visualization on circle

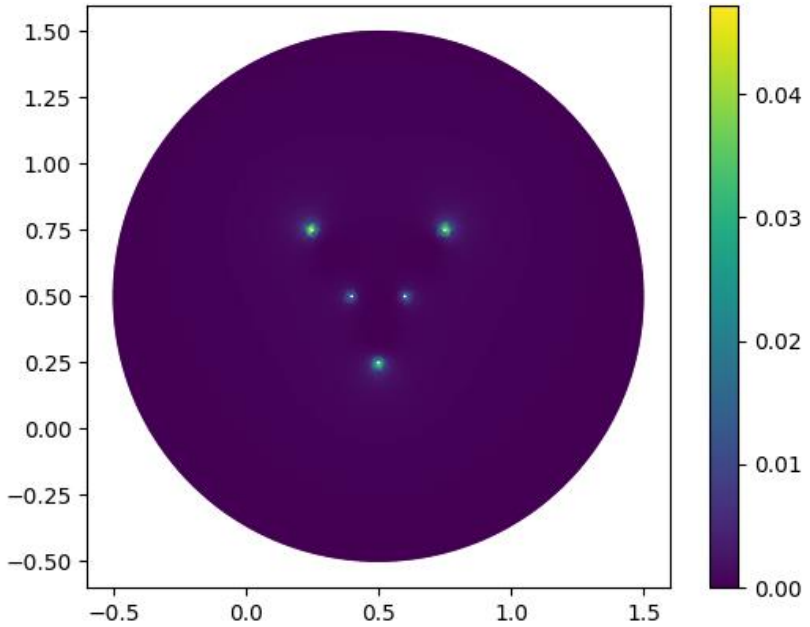
Joule Heat Model

$$Q_r = \sigma(|\nabla\phi|^2) \qquad \sigma = 0.4$$

Using FeniCS software



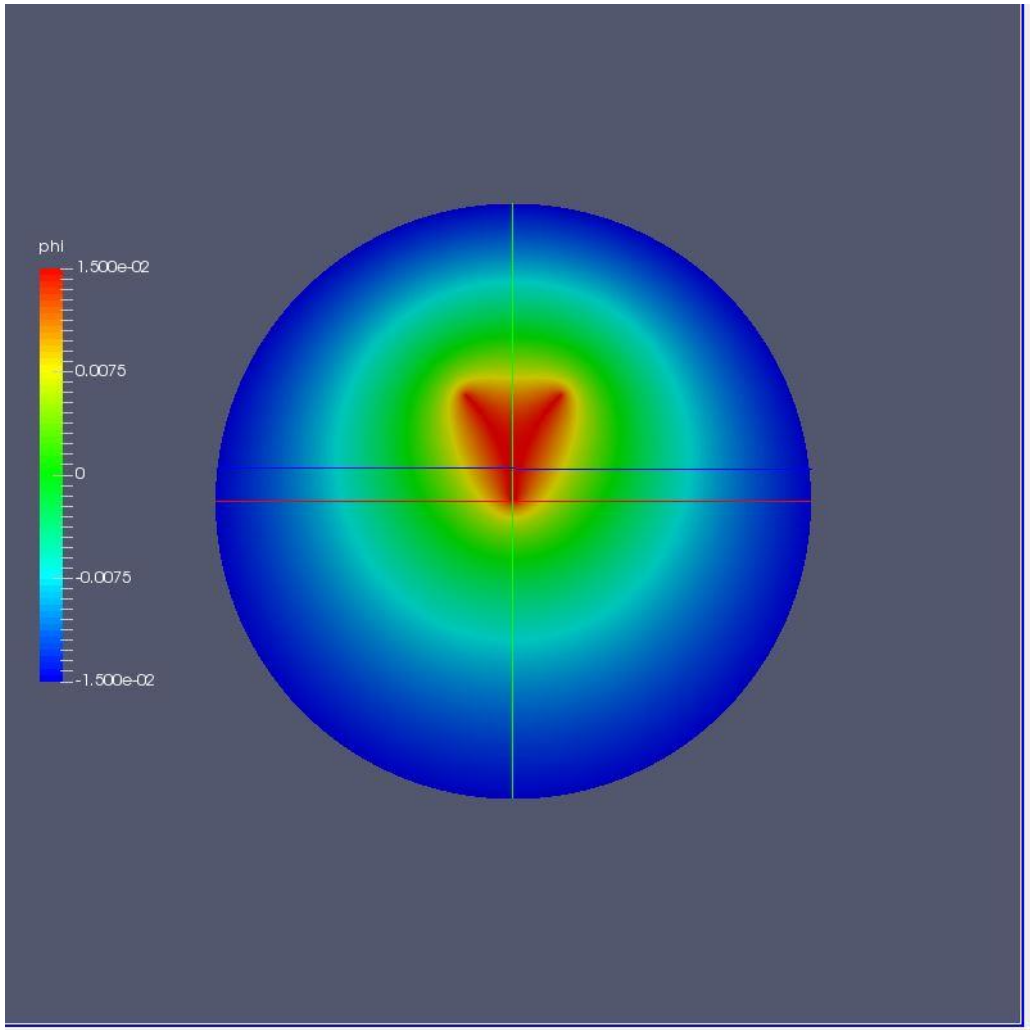
Q_r Visualization on unit square

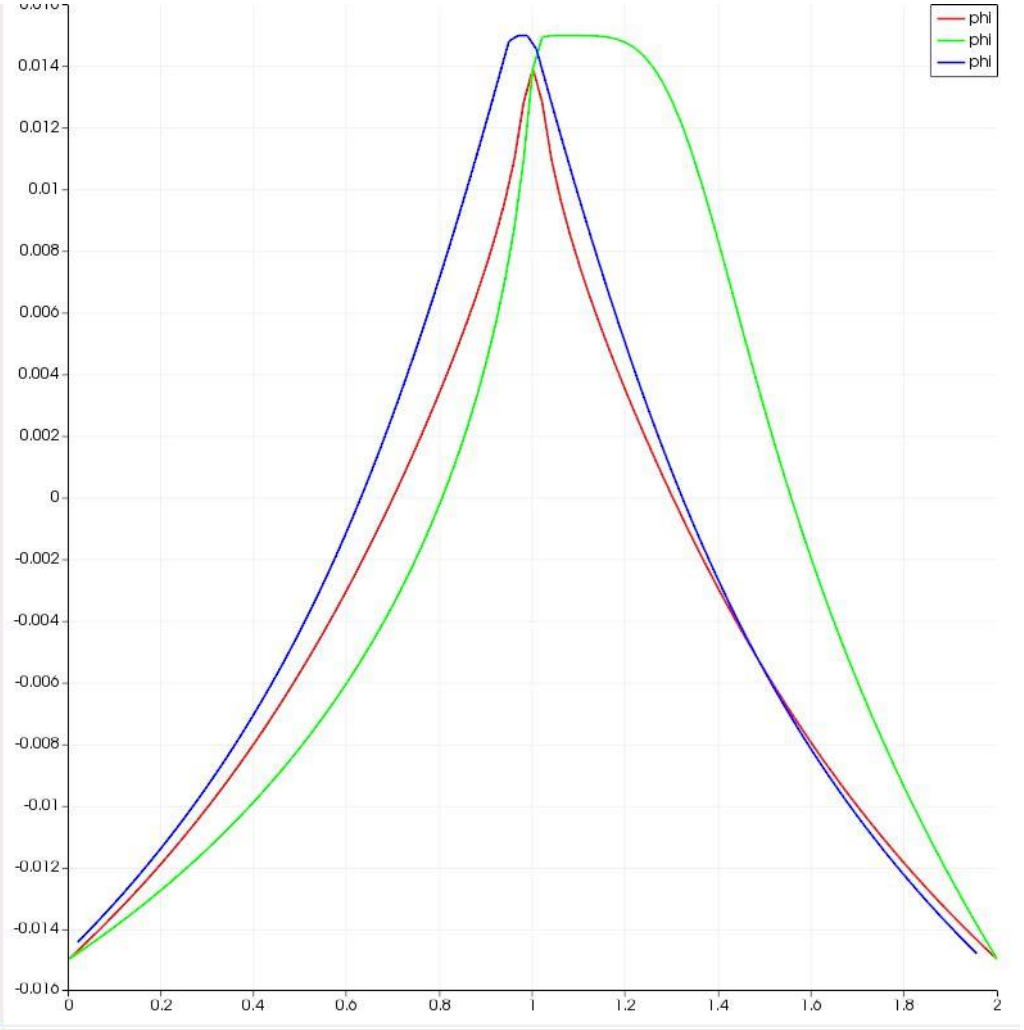


Q_r Visualization on circle

Joule Heat Model

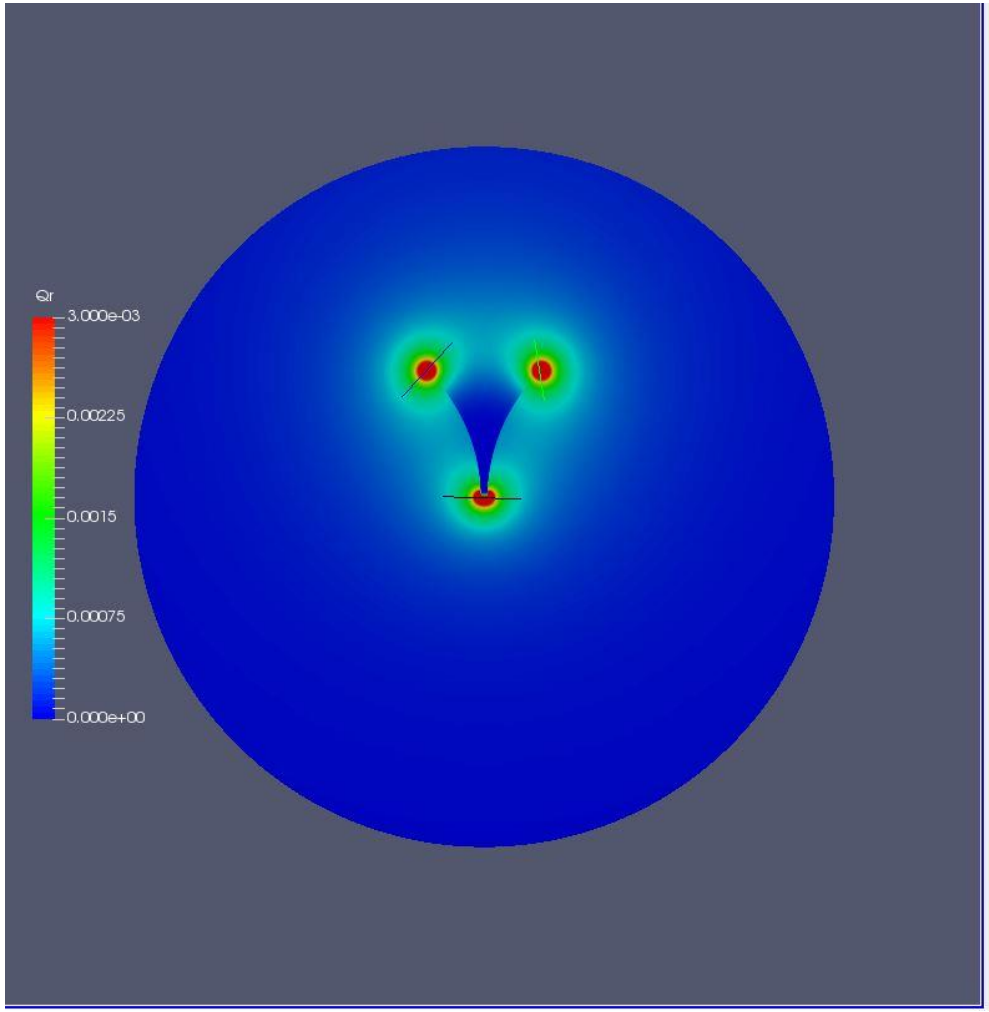
Using Elmer software

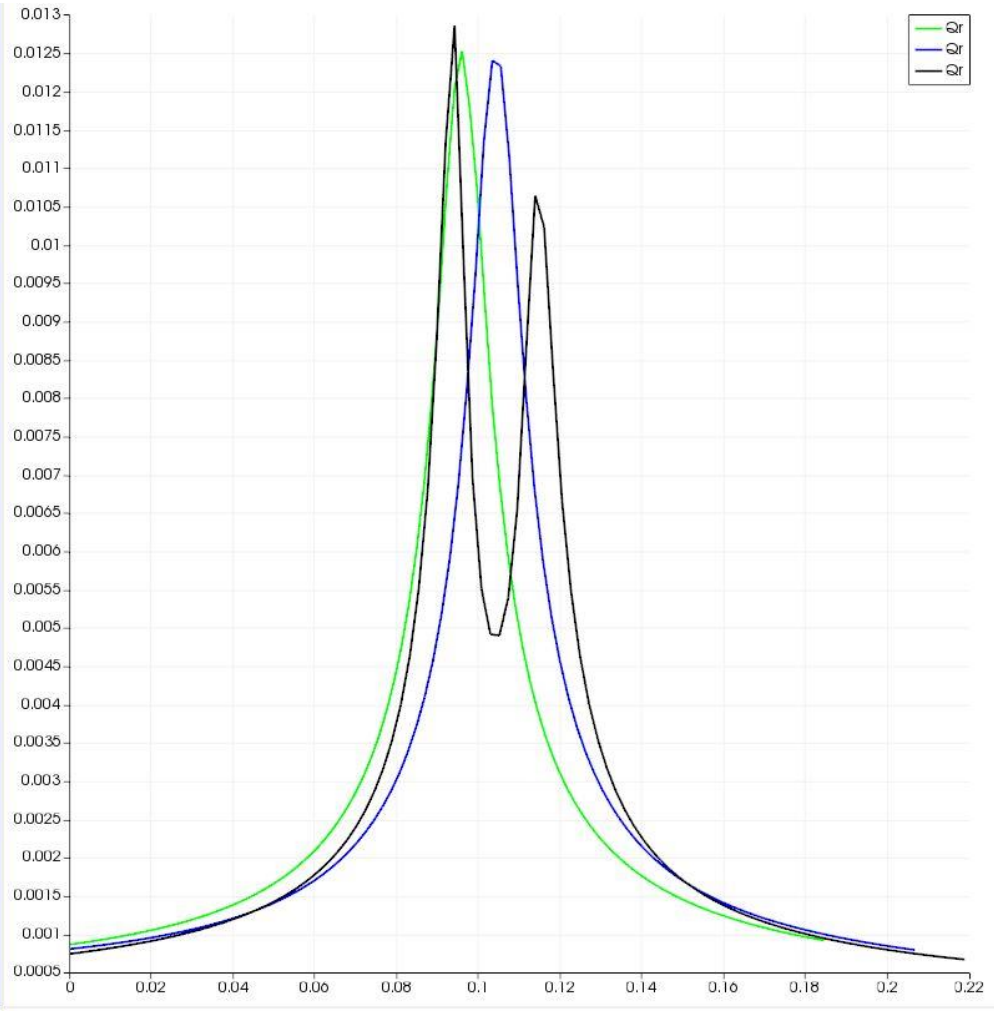




Joule Heat Model

Using Elmer software

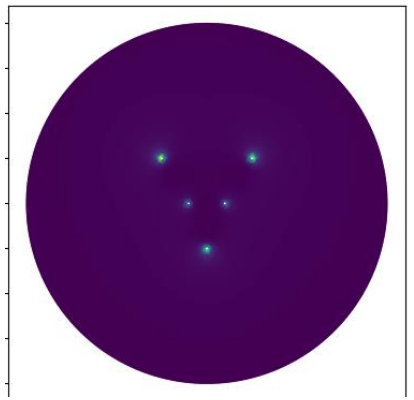


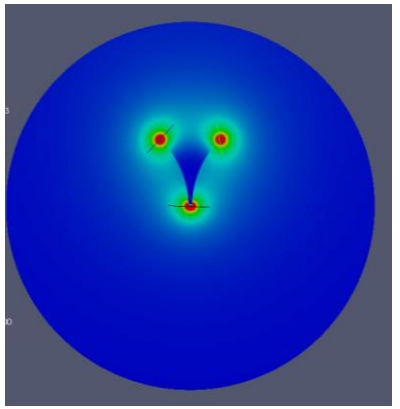


Joule Heat Model

$$\sigma\Delta\phi = \delta_0 \text{ on } \Omega$$

$$\delta_0 = \frac{1}{2\sqrt{\pi\epsilon}} e^{-\frac{|x|^2}{\epsilon}}$$





Theorem (Smoothness[1]): If $u \in C(\Omega)$ satisfies the mean value property for each ball $B(\boldsymbol{x}, r) \subset \Omega$, then $u \in C^{\infty}(\Omega)$

In Proof:

$$u^{\epsilon}(\boldsymbol{x}) = \int_{\Omega} \eta_{\epsilon}(\boldsymbol{x} - \boldsymbol{y}) u(\boldsymbol{y}) d\boldsymbol{y}$$

$$\Omega_{\epsilon} = \{\boldsymbol{x} \in \Omega : dist(\boldsymbol{x}, \partial\Omega) > \epsilon\}$$

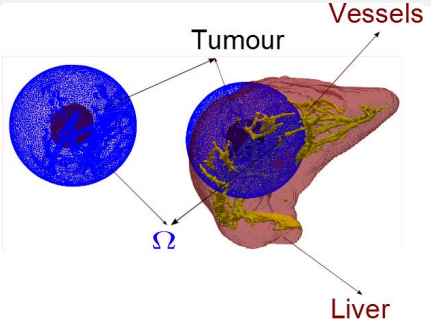
$$u^{\epsilon} = u \text{ in } \Omega_{\epsilon}$$

1. Evans, Partial Differential Equations, AMS, 2010, Page 28

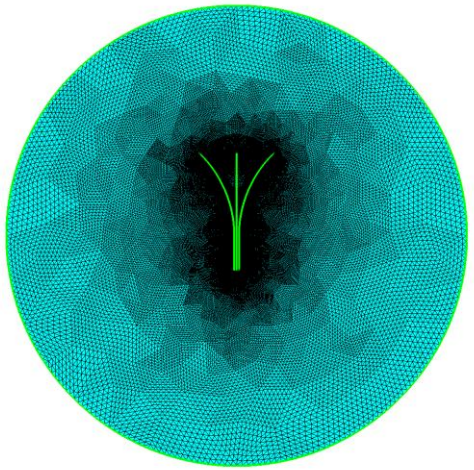
Point Source Model

Bioheat Equation[1]

$$\rho C \frac{\partial T}{\partial t} = k\Delta T + \omega_b \rho_b C_b (T_a - T) + Q_r \; on \; \Omega$$



Point Source Model

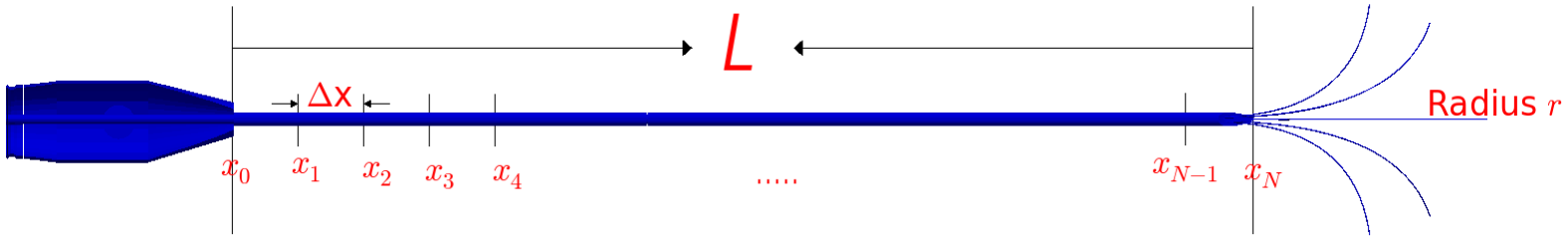


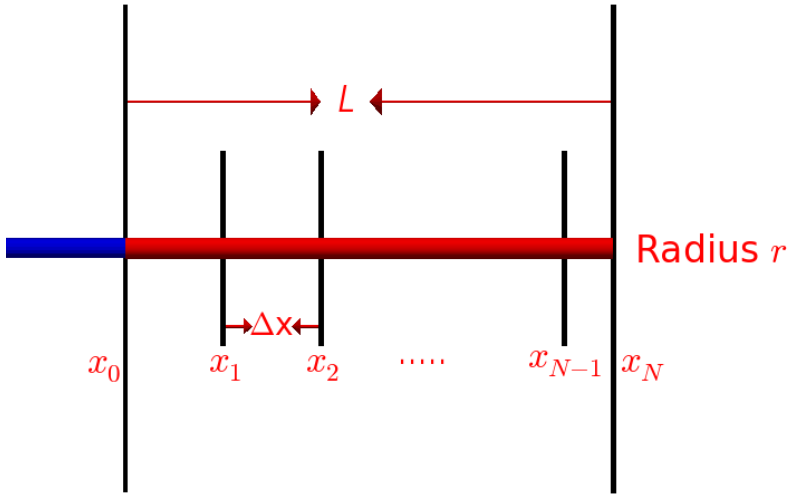
$$P(\vec{x}) = \frac{\sum_{tip} \alpha_{tip} \exp\left(-\frac{\left\|\vec{x} - \vec{x}_{tip}\right\|^2}{2\sigma^2}\right)}{\sum_{tip} \alpha_{tip} \left(\sigma\sqrt{2\pi}\right)^3}$$

$$Q_r = \sum P(\vec{x}) * power$$

1. H. H. Pennes, Analysis of tissue and arterial blood temperature in the resting human forearm, J. Appl. Physio. 85(1):93-102, 1948
2. O'Neill DP, Peng T et al (2011) A three-state mathematical model of hyperthermic cell death. Ann Biomed Eng 39(1):570-579

Joule Heat Model





$$\phi_e(\vec{x}) = \int_0^L \frac{q_e(x')dx'}{4\pi\epsilon|x-x'|} = \frac{2\pi r}{4\pi\epsilon}\sum_{j=1}^{N} q_j \int_{I_j} \frac{dx'}{|\vec{x}-x'|}$$

$$q_j = \begin{cases} q_a, & j = 2,3,\ldots,N-1 \\ q_b, & j = 1,N \end{cases}$$

Joule Heat Model

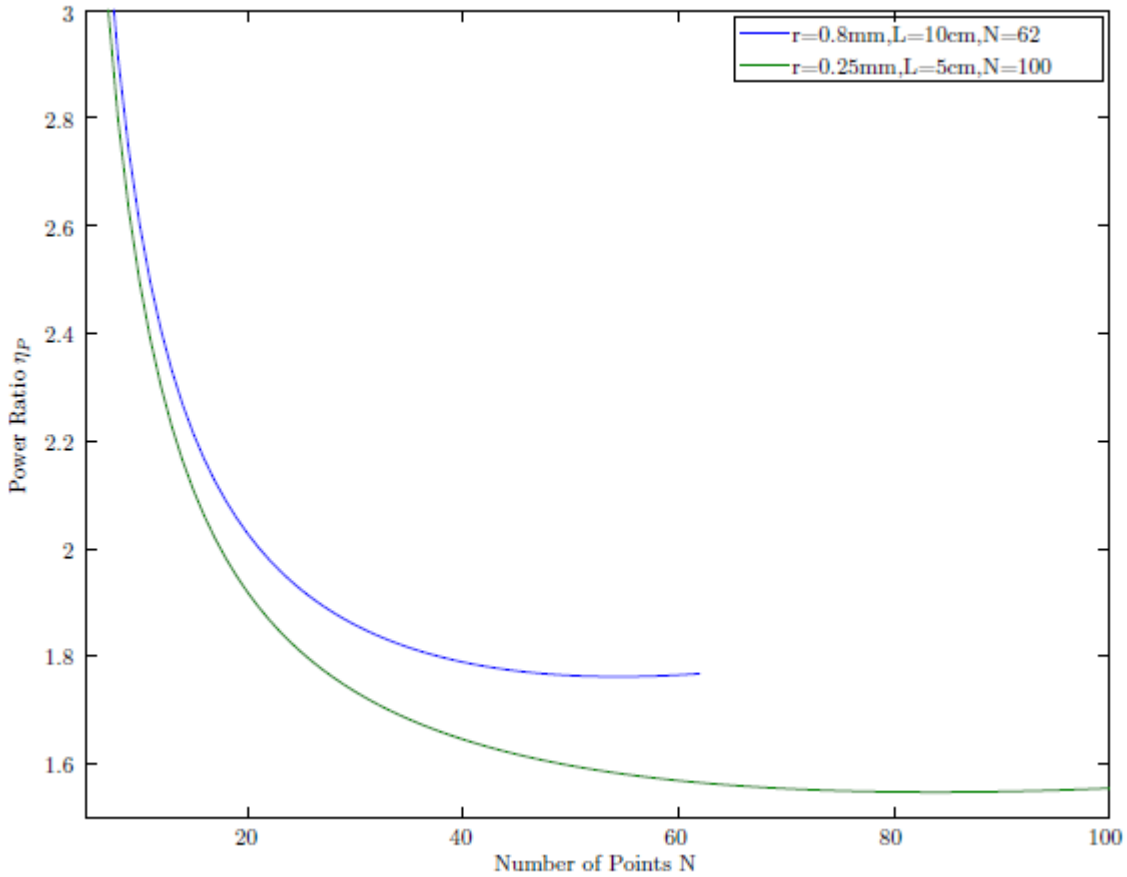
Alternatively when number of points known(k):$k \leq N$

$$\eta_P = \frac{Power\ deposition\ at\ ends}{Power\ deposition\ at\ middle} = \frac{\mathrm{P_{end}}}{\mathrm{P_{mid}}}$$

$$\eta_P = \frac{\mathrm{P_{end}}}{\mathrm{P_{mid}}} = \frac{\mathrm{P_b} + \left(\frac{\mathrm{N}}{\mathrm{k}} - 1\right)\mathrm{P_a}}{\frac{\mathrm{N}}{\mathrm{k}}\mathrm{P_a}}$$

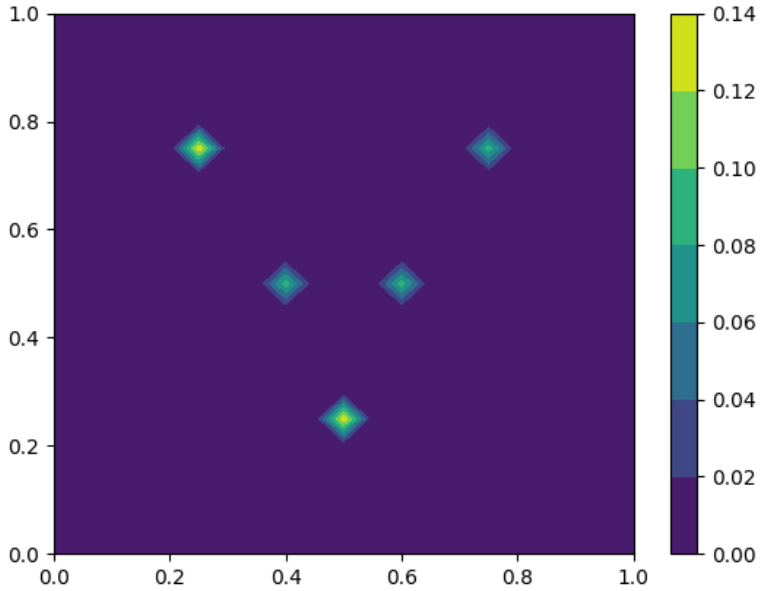
$$\eta_P = \begin{cases} 1.76 & L = 10cm, r = 0.8mm \\ 1.5 & r = 0.25mm, L = 5cm \end{cases}$$

$$\alpha_{tip} = \begin{cases} 1.5 & end\ tips \\ 1.0 & middle\ tips \end{cases}$$

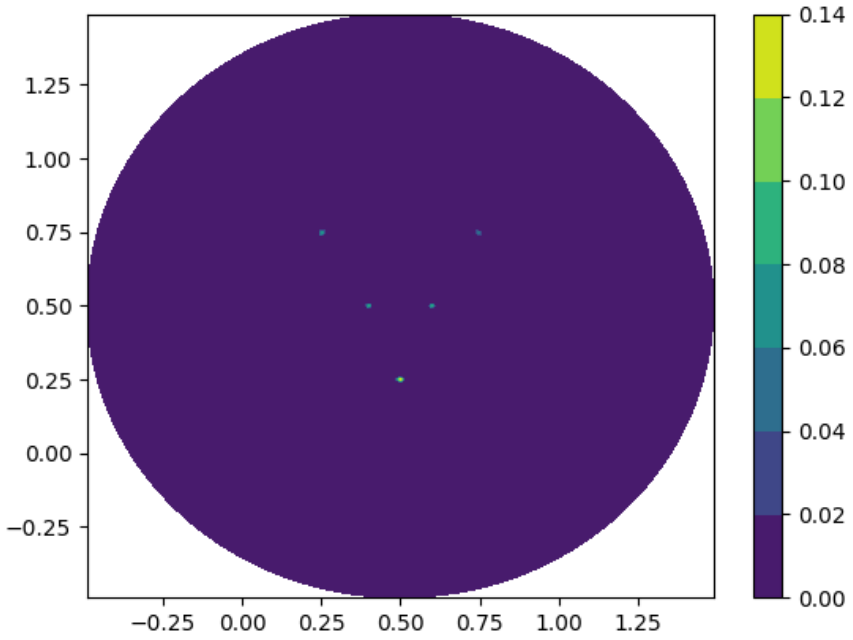


Point Source

Using FeniCS software



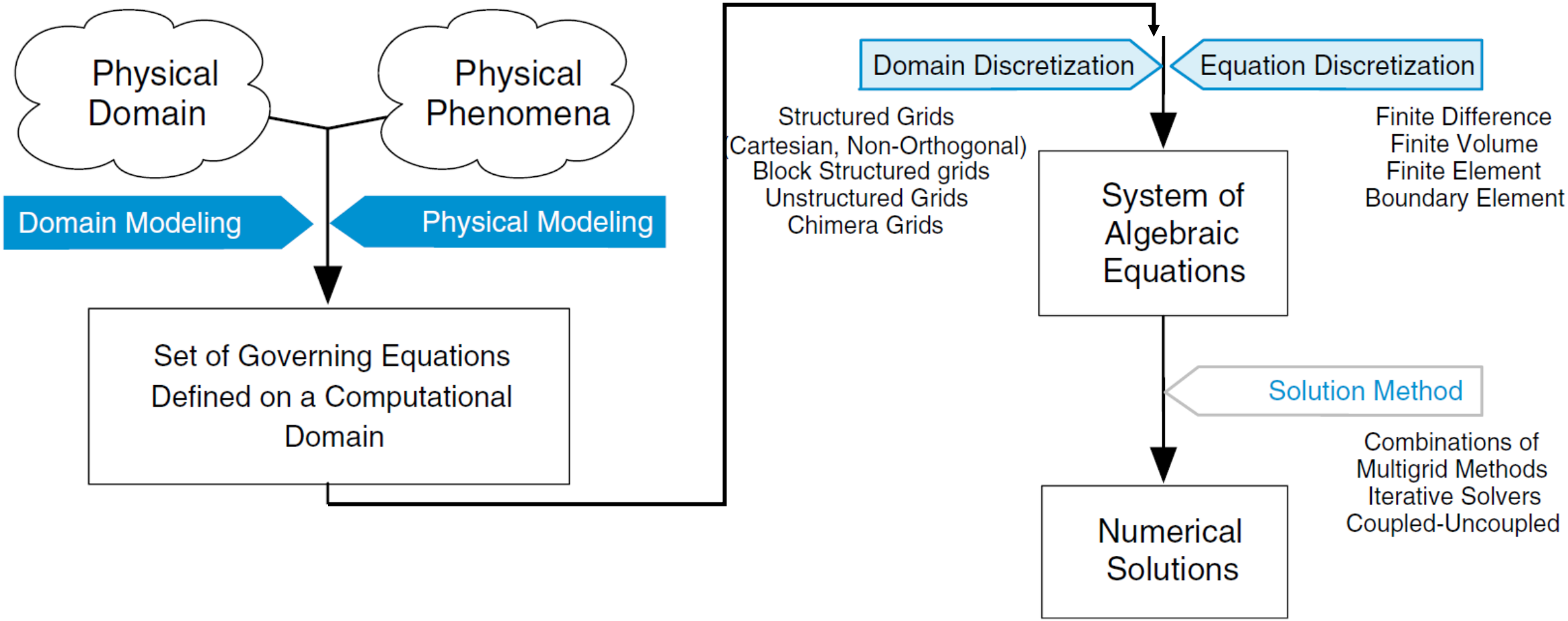
Q_r Visualization on unit square



Q_r Visualization on circle

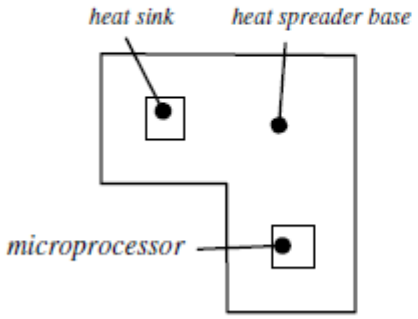
Numerical PDEs: General Idea

Discretization Process



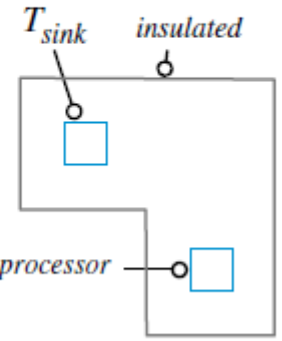
Discretization Process

Domain Modeling

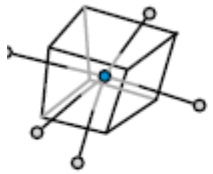


Physical Modeling

$$-\nabla \cdot (k \nabla T) = \dot{q}$$



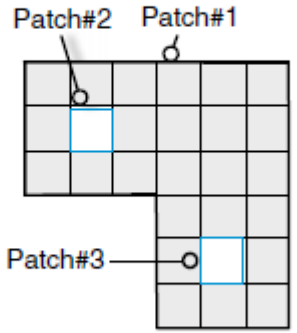
Equations Discretization



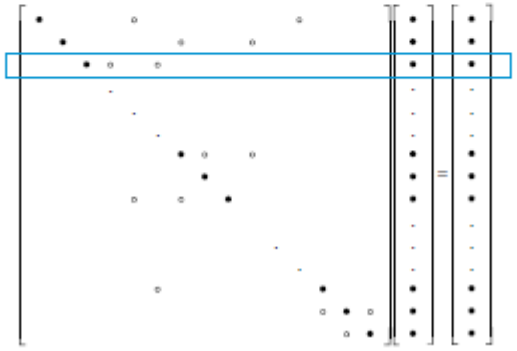
$$\underbrace{\frac{\partial(\rho\phi)}{\partial t}}_{\text{transient term}} + \underbrace{\nabla \cdot (\rho \mathbf{v} \phi)}_{\text{convection term}} = \underbrace{\nabla \cdot (\Gamma \nabla \phi)}_{\text{diffusion term}} + \underbrace{Q}_{\text{source term}}$$

$$a_C \phi_C + \sum_{F \sim NB(C)} a_F \phi_F = b_C$$

Domain Discretization



Solution Method



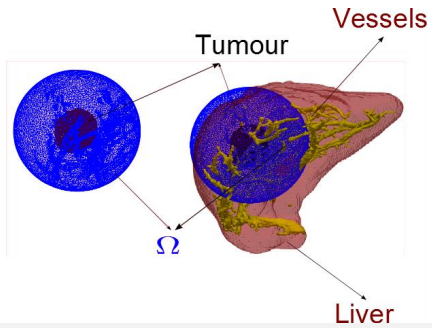
Governing Equations

Bioheat Equation[1]

$$\rho C \frac{\partial T}{\partial t} = k\Delta T + \omega_b \rho_b C_b (T_a - T) + Q_r \; on \; \Omega$$

$$h_c T + k \frac{\partial T}{\partial \vec{n}} = h_c T_\infty \text{ on vessels boundary}$$

$$T = T_0 \text{ on } \partial\Omega$$



Cell Death Model[2]

$$\frac{dA}{dt} = -k_f e^{\frac{T}{T_k}}(1-A)A + k_b(1-A-D)$$

$$\frac{dD}{dt} = k_f e^{\frac{T}{T_k}}(1-A)\,(1-A-D)$$

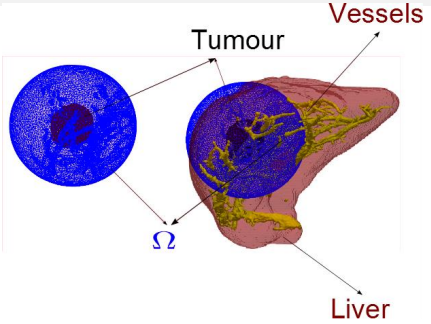
$$A(0) = 0.99, D(0) = 0.0$$

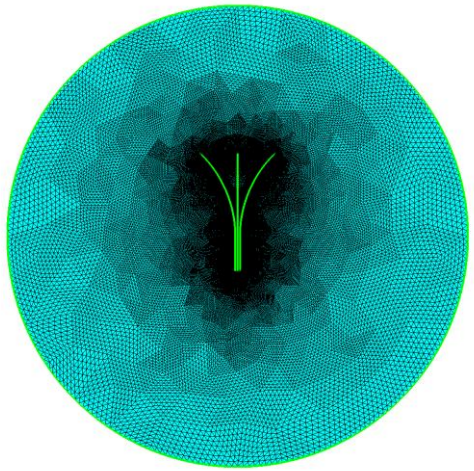
1. H. H. Pennes, Analysis of tissue and arterial blood temperature in the resting human forearm, J. Appl. Physio. 85(1):93-102, 1948
2. O'Neill DP, Peng T et al (2011) A three-state mathematical model of hyperthermic cell death. Ann Biomed Eng 39(1):570-579

Joule Heat Model

Bioheat Equation[1]

$$\rho C \frac{\partial T}{\partial t} = k\Delta T + \omega_b \rho_b C_b (T_a - T) + Q_r \; on \; \Omega$$





Joule Heat Model

$$\sigma\Delta\phi = 0 \text{ on } \Omega$$

$$\varphi = \begin{cases} \varphi_r \; on \; NeedleTips \\ \varphi_c \; on \; Circularboundary \end{cases}$$

$$\frac{\partial \phi}{\partial \boldsymbol{n}} = 0 \text{ on Needle shaft}$$

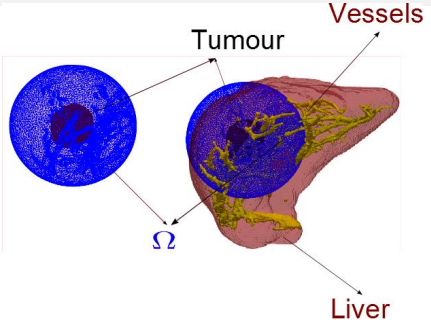
$$Q_r = \sigma(|\nabla\phi|^2)$$

1. H. H. Pennes, Analysis of tissue and arterial blood temperature in the resting human forearm, J. Appl. Physio. 85(1):93-102, 1948
2. O'Neill DP, Peng T et al (2011) A three-state mathematical model of hyperthermic cell death. Ann Biomed Eng 39(1):570-579

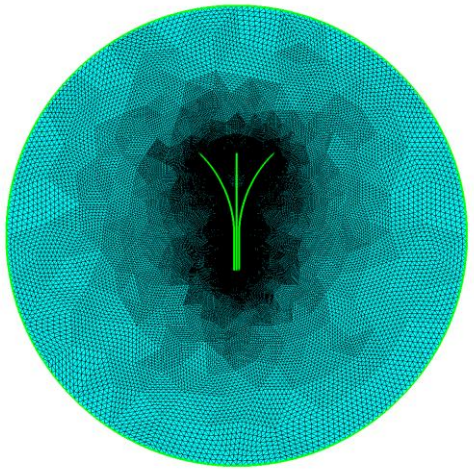
Point Source Model

Bioheat Equation[1]

$$\rho C \frac{\partial T}{\partial t} = k\Delta T + \omega_b \rho_b C_b (T_a - T) + Q_r \; on \; \Omega$$



Point Source Model



$$P(\vec{x}) = \frac{\sum_{tip} \alpha_{tip} \exp\left(-\frac{\left\|\vec{x} - \vec{x}_{tip}\right\|^2}{2\sigma^2}\right)}{\sum_{tip} \alpha_{tip} \left(\sigma\sqrt{2\pi}\right)^3}$$

$$Q_r = \sum P(\vec{x}) * power$$

1. H. H. Pennes, Analysis of tissue and arterial blood temperature in the resting human forearm, J. Appl. Physio. 85(1):93-102, 1948
2. O'Neill DP, Peng T et al (2011) A three-state mathematical model of hyperthermic cell death. Ann Biomed Eng 39(1):570-579

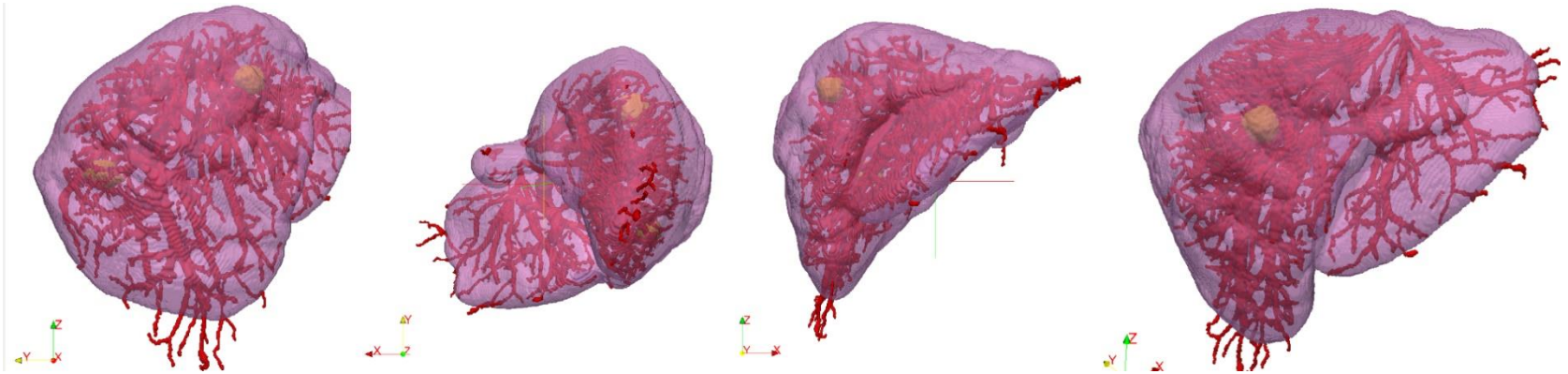
Validation Phase

Simulation Accuracy

Validation

RFA Validation Study:

- RFA simulation has been tested using over 100 meshes
- Patient data used for each was the same



- Report filled out by physicians who conducted the procedure used to replicate protocol as accurately as possible

Validation

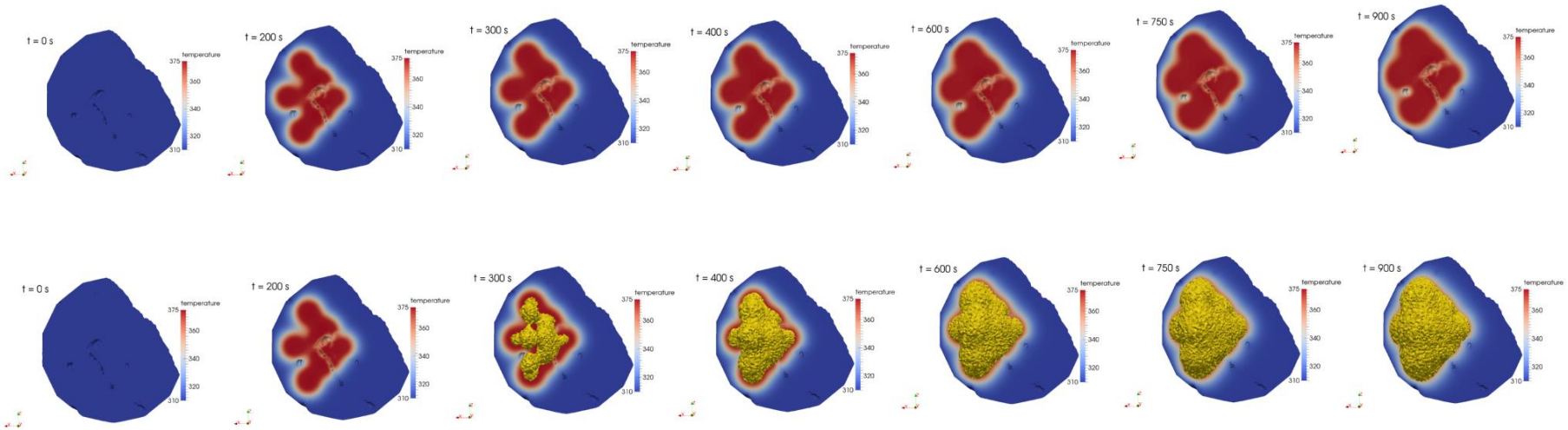
Simulation parameters:

- As well as same patient data used for each simulation, identical input values were used for following parameters:
  - Input power = 150 Watts
  - Spherical domain centred on tumour location with 30mm radius
  - Simulation ran for 225 4 second timesteps
- Meshing parameters varied as follows:
  - Nearfield = 0.1 – 2.0
  - Farfield = 0.4 – 5.0
  - Zonefield = 0.5 – 5.0

Validation

Lesion growth:

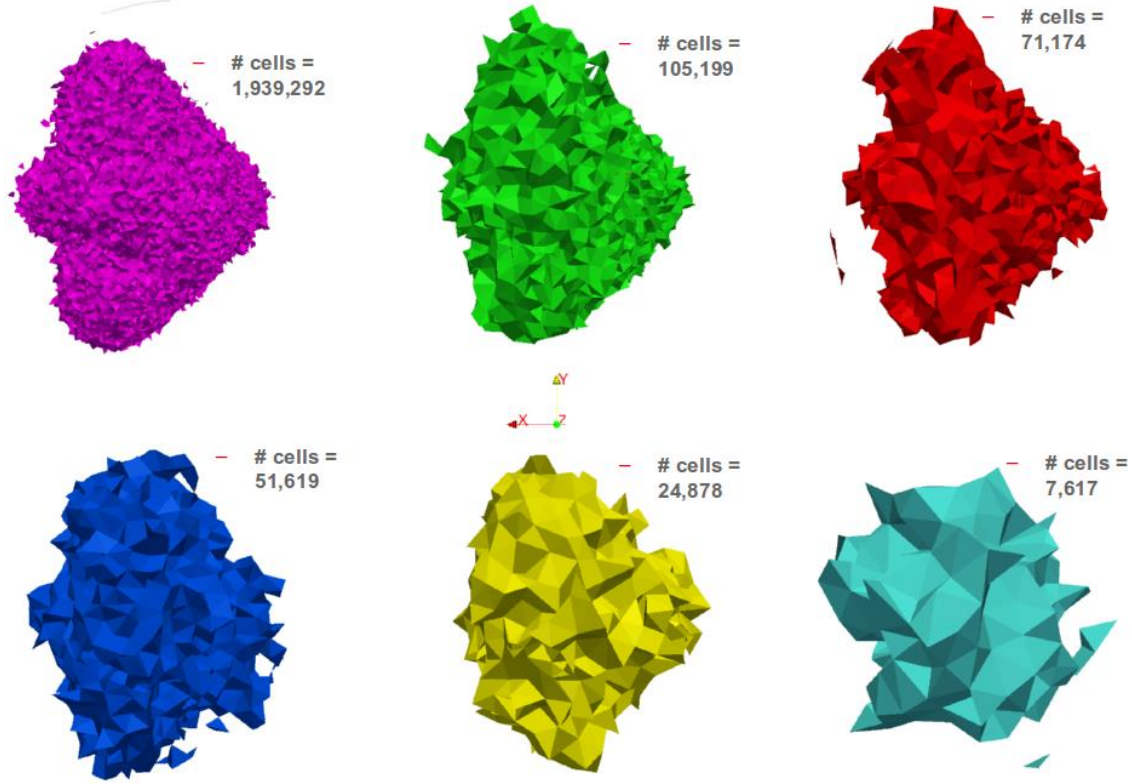
- The growth of the lesion during the procedure is shown below:



Validation

Results:

- Predicted lesion of each simulation compared to lesion of finest mesh – influence of increasing mesh density clear:



Evaluation Metrics

Volume Deviation

$$DSC = \frac{2|V_{se} \cap V_{si}|}{|V_{se}| + |V_{si}|}$$

$$RVD = \left|\frac{|V_{se}|}{|V_{si}|} - 1\right|$$

$$SN = \frac{|V_{se} \cap V_{si}|}{|V_{se}|}$$

$$VOE = \frac{|V_{si} \cap V_{se}|}{|V_{si} \cup V_{se}|}$$

$$PPV = \frac{|V_{se} \cap V_{si}|}{|V_{si}|}$$

V_{Se}: Segmented lesion volume
V_{Si}: Simulated lesion volume

Surface Deviation

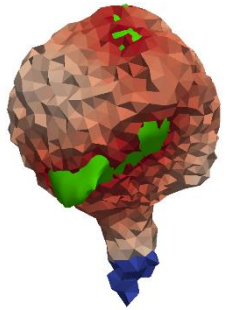
$\overrightarrow{\boldsymbol{p}_i} = (p_{ix}, p_{iy}, p_{iz})$: point at the surface of the simulated lesion
$\boldsymbol{R}$: Segmented lesion surface

$$d_i = d(\overrightarrow{\boldsymbol{p}_i}, \boldsymbol{R}) = \min_j \left\{ \sqrt{(p_{ix} - r_{jx})^2 + (p_{iy} - r_{jy})^2 + (p_{iz} - r_{jz})^2} \right\}$$

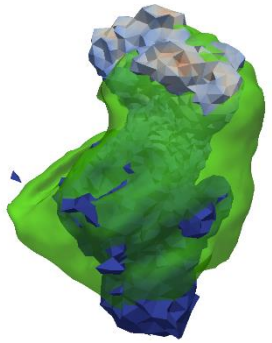
$$AAE = \frac{\sum w_i |d_i|}{\sum w_i}$$

Simulated Lesion matches with Segmented lesion only if
AAE < 3.5mm
RVD < 30%, DSC, SN, PPV > 70% or VOE>70%

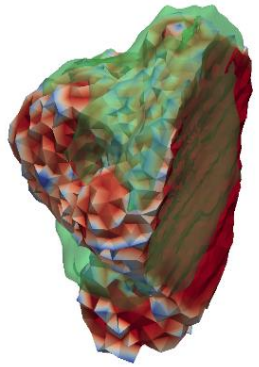
Simulation Result



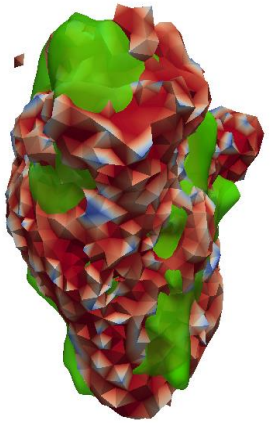
RVD: 18
Surf Dev: 2.28



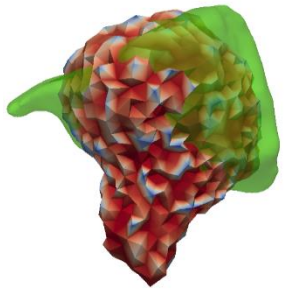
RVD: 74
Surf Dev: 3.09



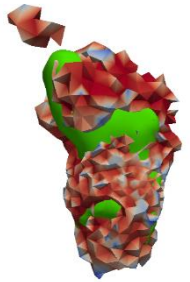
RVD: 6.67
Surf Dev: 2.88



RVD: 0.003
Surf Dev: 4.57

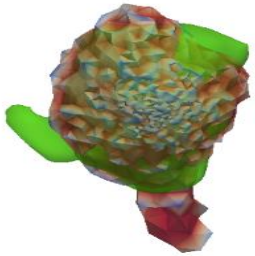


RVD: 0.61
Surf Dev: 2.74

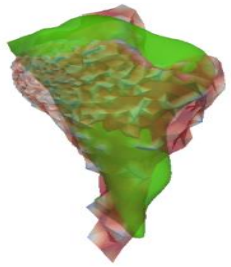


RVD: 55.71
Surf Dev: 1.88

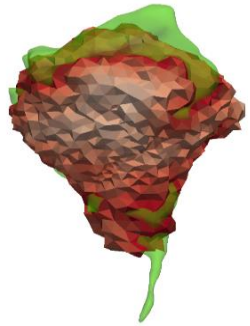
RVD: 0.58
Surf Dev: 2.37



RVD: 3.56
Surf Dev: 1.53



RVD: 7.94
Surf Dev: 1.79

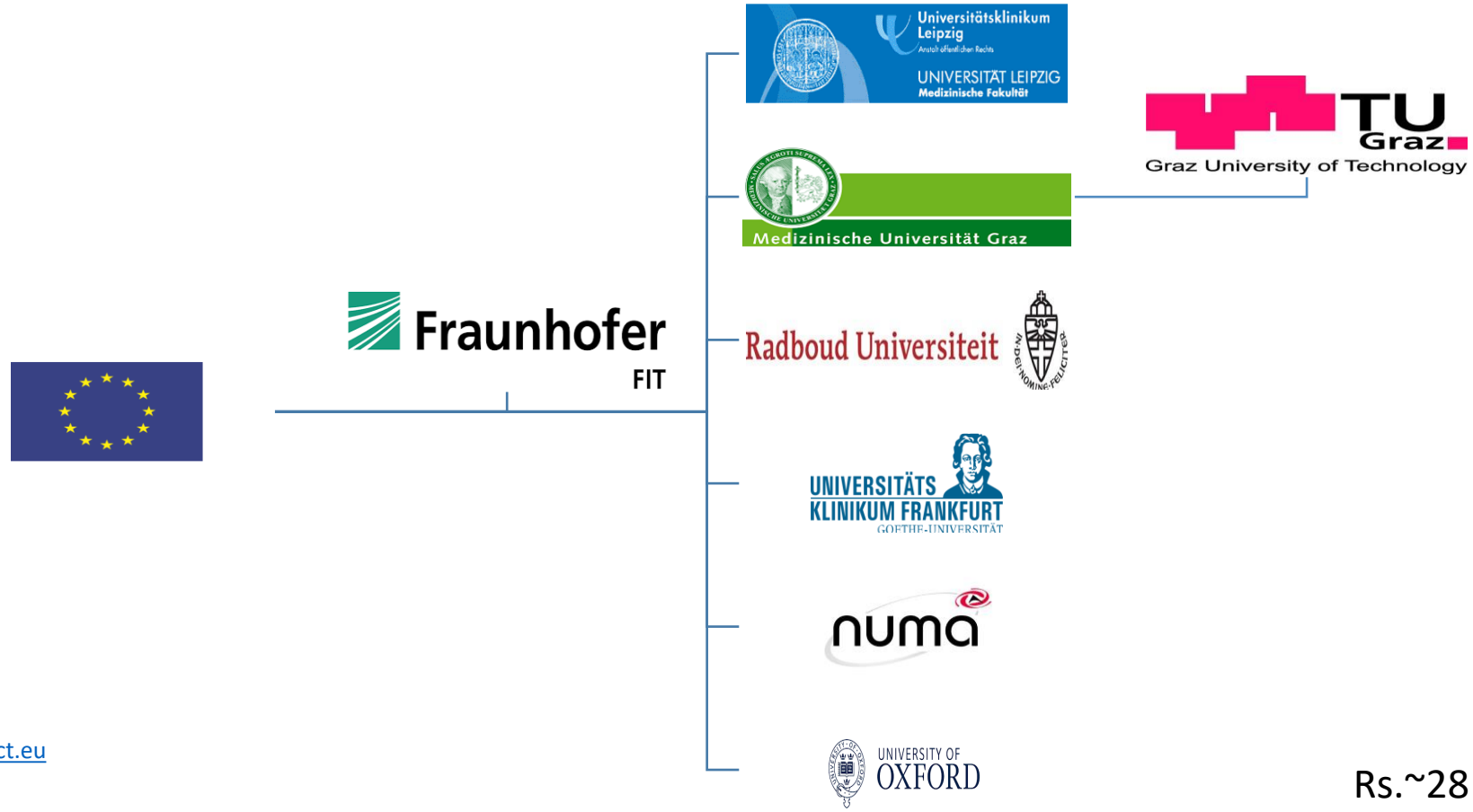


RVD: 21.64
Surf Dev: 2.57

Microwave Ablation

GoSmart Project

Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment



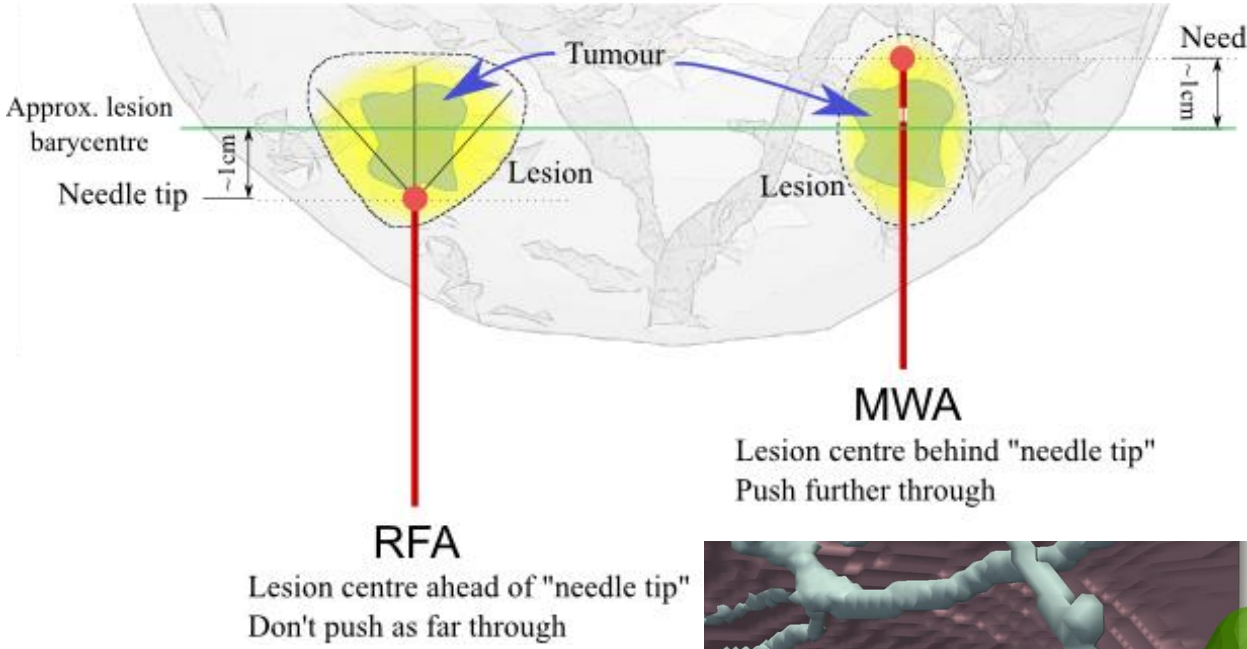
http://www.gomsart-project.eu

http://smart-mict.eu

Rs.~28 Crores

Microwave Ablation

Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

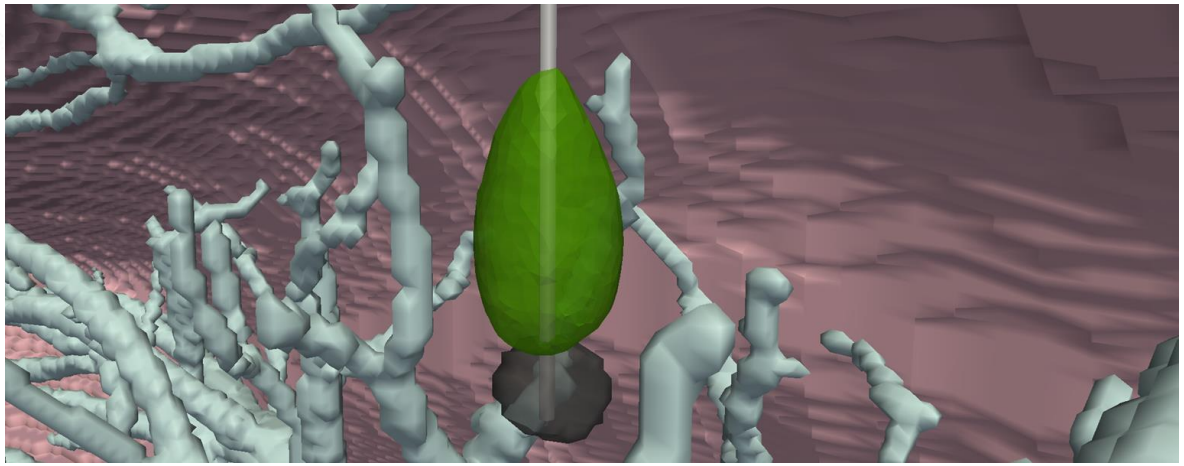


$$\nabla \times \left[\left(\varepsilon_r - \mathrm{i}\frac{\sigma}{\omega \varepsilon_0} \right)^{-1} \nabla \times \mathbf{H} \right] - \mu_r k_0^2 \mathbf{H} = 0$$

Importance of aligning offsetting needle tip according to tumour location.

The MWA lesion shown below is generated at low power (~10W) and demonstrates effect of separate tumour tissue values at these ratings

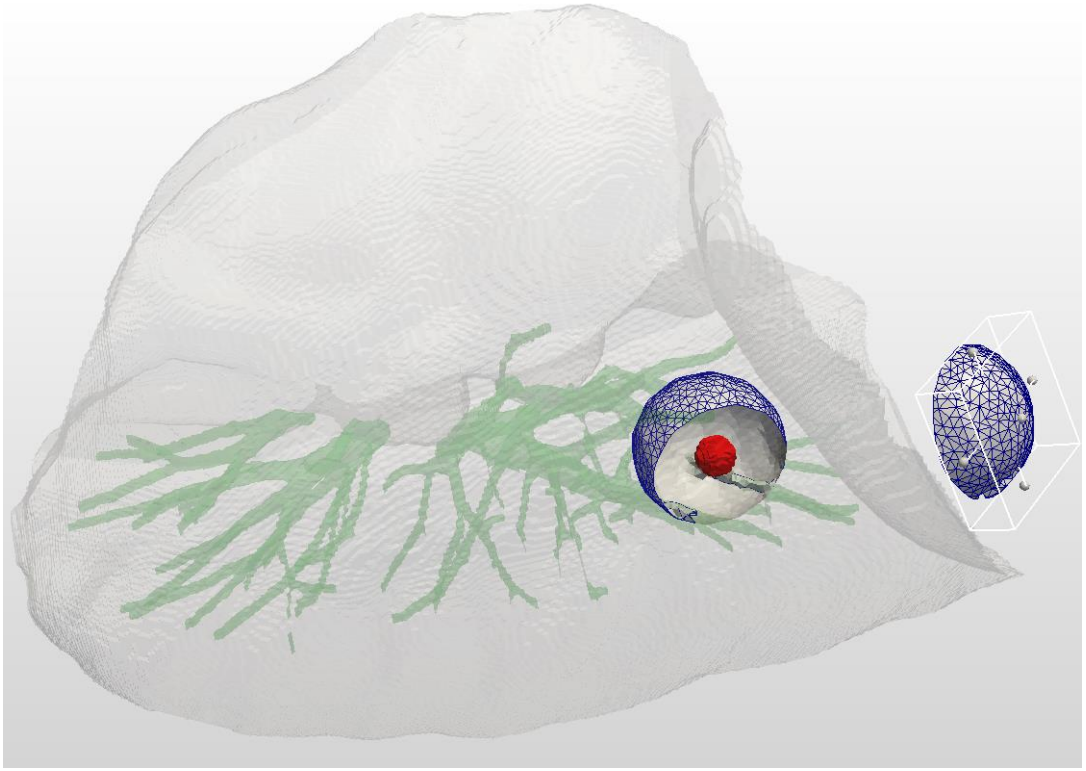
However, at higher power levels, the coupling of temperature and tissue electric properties in the **MWA** simulation are important to represent the physical processes in Go-Smart clinical settings

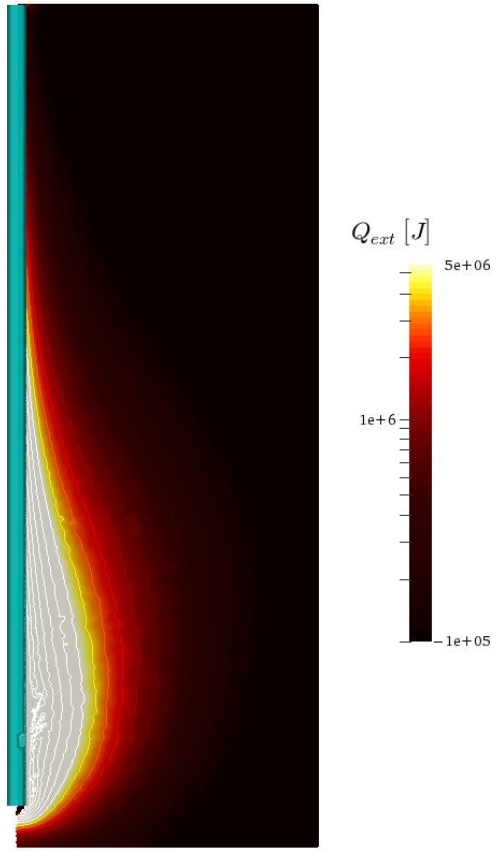


Tumour (black); Vessels (blue); Lesion (green) Lung wall (pink); Needle (grey)

Microwave Ablation

Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

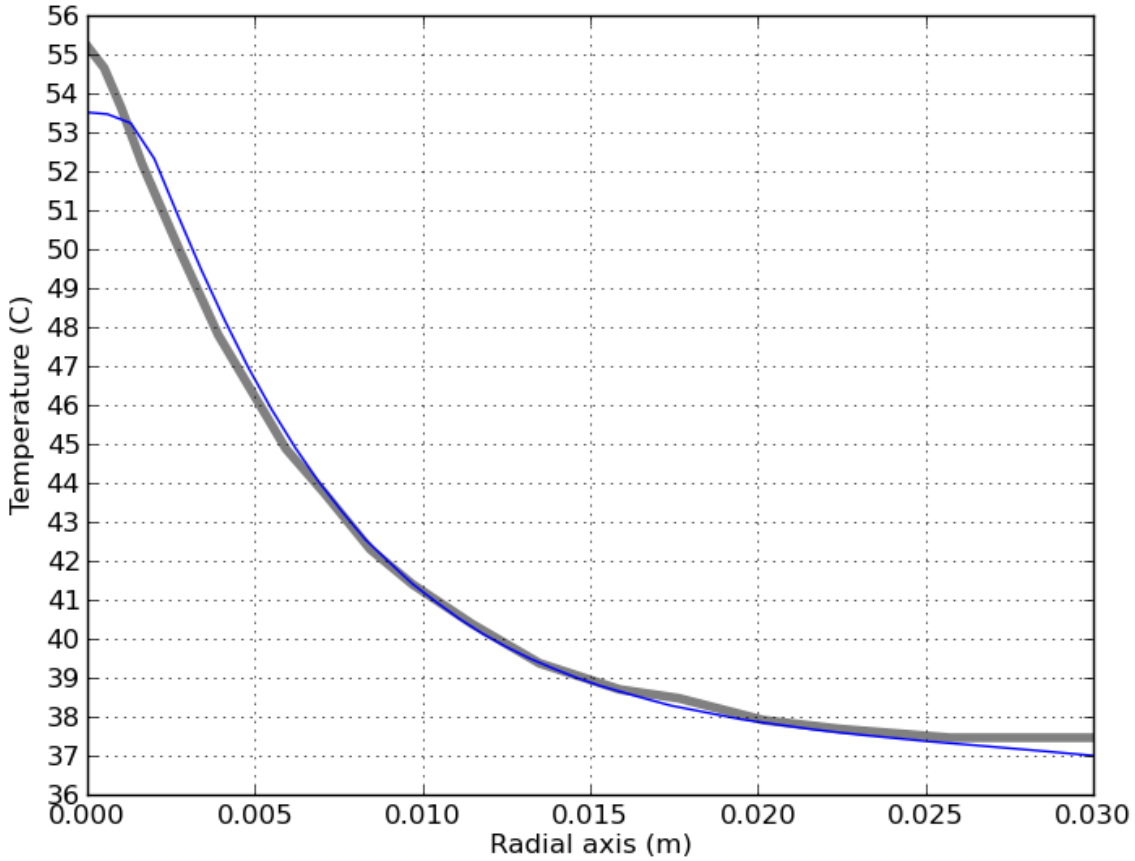




Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

Microwave Ablation

- *Validation within Go-Smart Simulation Framework*
  - ❑ *Gas, 2012*
  - ❑ *COMSOL-based*
  - ❑ *3W steady-state*
  - ❑ *No vessels*



Gas, 2012 – Grey; *Go-Smart Simulation - Blue*

Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

CGAL Meshing

- *Generates a large number of random points within the computational domain*
- *Determines a characteristic element length (Lc) at each of these points*
- *If point is sufficiently close to a previous point, it will be assigned the same Lc value*
- Lc between input values: FarField (FF), ZoneField (ZF) and NearField (NF)
- Exact Lc determined based on a points' distances to important bodies

- Implicit_domain_function computes point's distance from
  - Domain extent
  - Vasculature
  - User-defined centre
  - Tumour edge (zone field)

- Labeled_domain_function adapted to incorporate Implicit_domain_function and to align tetrahedra along subvolume boundaries (such as tumours)
- Minimum of these distances used to interpolate between NF or ZF and FF for Lc

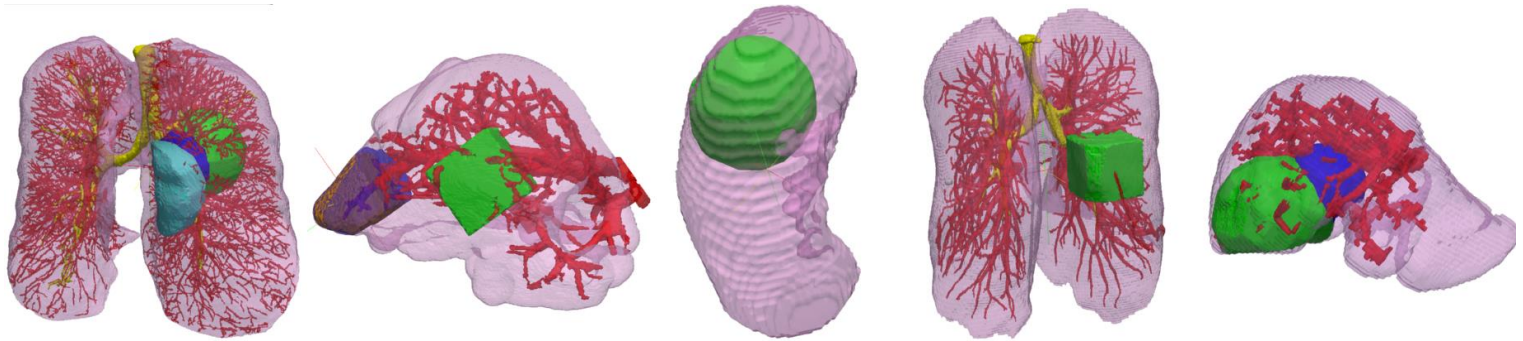
Meshing

Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

CGAL Meshing

- The mesher has been tested extensively – 15 meshes generated from various geometry:
- Capable of consistently generating usable meshes for any geometrical input
- User can control mesh location, density and shape using xml input file

Typical number of elements in mesh ~ 250,000 but can vary widely depending on input parameters
User can choose if needle is removed from mesh
Mesh density controlled by varying Nearfield, Farfield and Zonefield parameters
Tumours can be set as zones distinct from the rest of the mesh
Occasionally there are errors in the mesh
Zero volume or even negative volume elements
Numerical issues in calculating the minimum dihedral angle



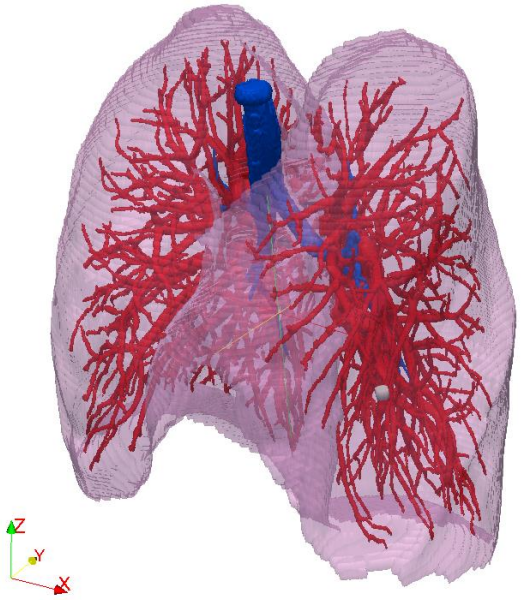
Microwave Ablation

Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

MWA

- ❑ Patient data used along with segmented lesion geometrical data
- ❑ Computational domain centred around tumour location
- ❑ Volumes of predicted lesion and segmented one similar

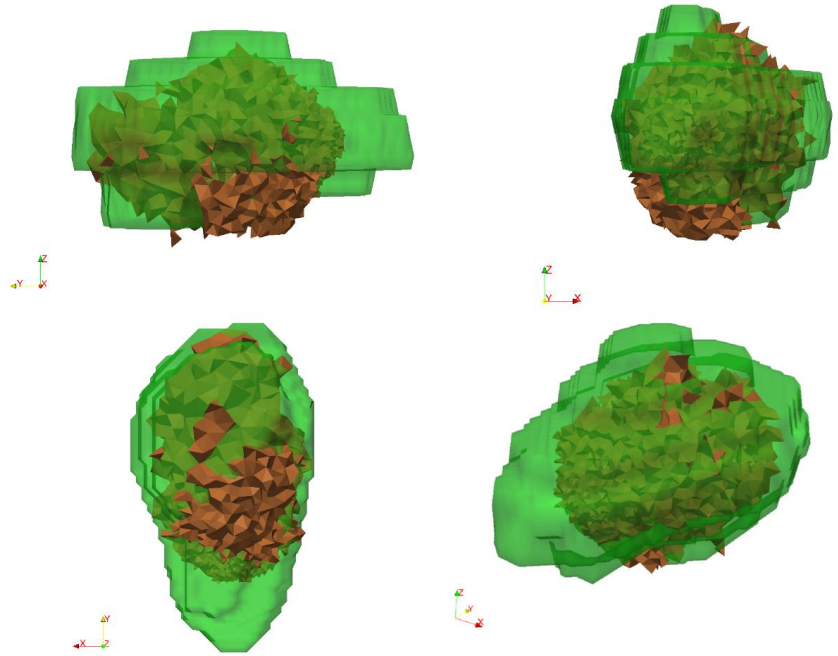
- ✓ Spherical domain centred at tumour of 40mm radius used
- ✓ Input power = 10 Watts
- ✓ Nearfield = 0.4 Farfield = 3.0
- ✓ Simulation conducted for 1000 timesteps, 2 seconds each
- ✓ Tissue electrical properties exhibit strong non-linearity with elevated temperatures - work under way to account for this
- ✓ Water content very influential which becomes an issue at temperatures close to 100^{o}C



Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

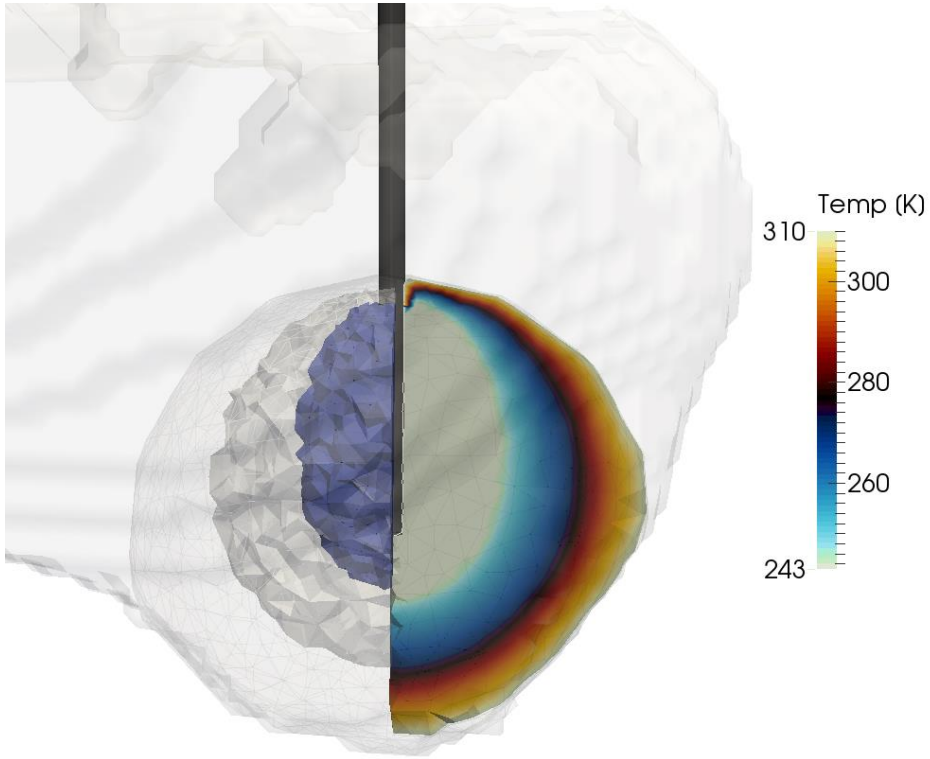
MWA

- Power tailored for desired temperature, temperature issues since solved
- Positioning of needle for comparable lesion requires experience with simulation
- Cells with Dead >= 0.8 taken to be in lesion
- Predicted lesion (orange) of comparable volume to segmented one (green):



Cryoablation

Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment



- *White surface – ice ball*
- *Purple surface – lesion extent*

Cryoablation

- *Fluid flowing through a cryogenic needle*
  - ❑ *Presently, fixed needle surface temperature*
  - ❑ *Lesion given by -50C isotherm*
  - ❑ *Computes and accounts for*
  - ❑ *change of physical properties with phase*

Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

Cryoablation

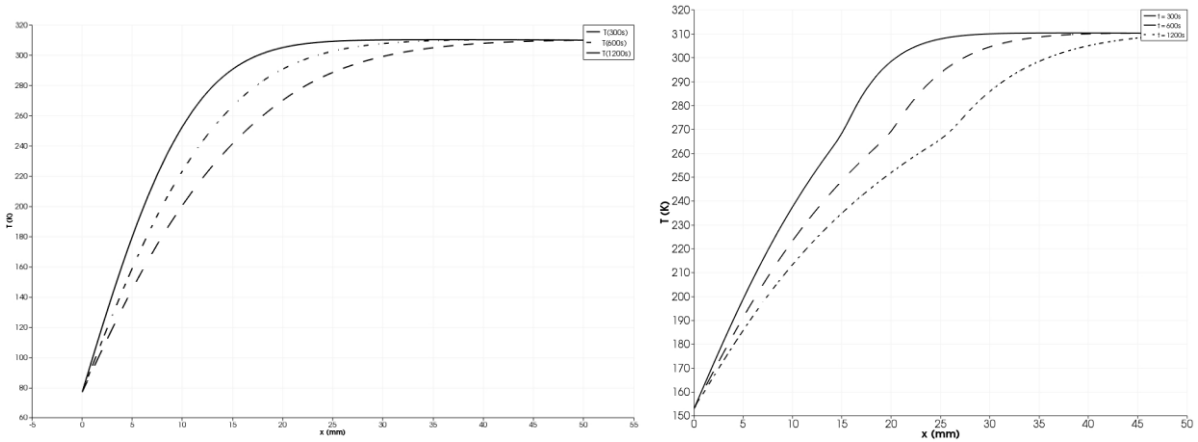
- *Front-tracking*
- *More stable, efficient*
- *Physical properties change in ice-ball and surrounding mushy* zone
  - ✓ e.g. heat capacity, conductivity, enthalpy, perfusion
- *Temporal phase change model*
- *Incorporates latent heat of phase change by defining an effective heat capacity that varies appropriately around solidus and liquidus temperatures*

$$k_{eff}(T) = \begin{cases} k_s & T < T_s \\ k_s + \dfrac{1}{2(T_l - T_s)}(k_l - k_s)(T - T_s) & T_s \le T \le T_l \\ k_l & T > T_l \end{cases}$$

$$c_{\text{eff}}(T) = \begin{cases} c_f, & T < T_s, \\ \frac{c_f + c_u}{2} + \frac{h_{sf}}{2(T_l - T_s)}, & T_s \le T \le T_l, \\ c_u, & T > T_l, \end{cases}$$

Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

Cryoablation



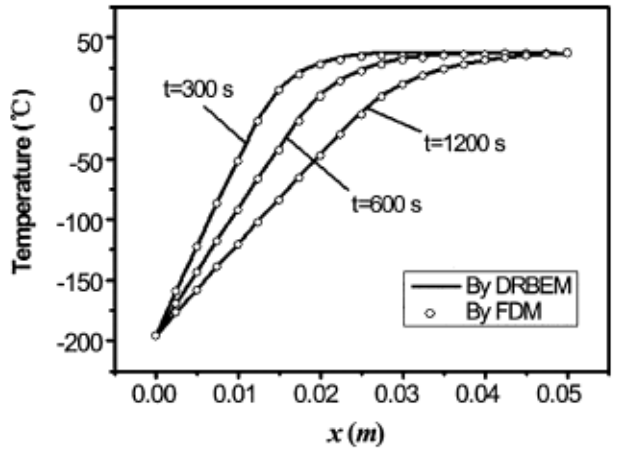


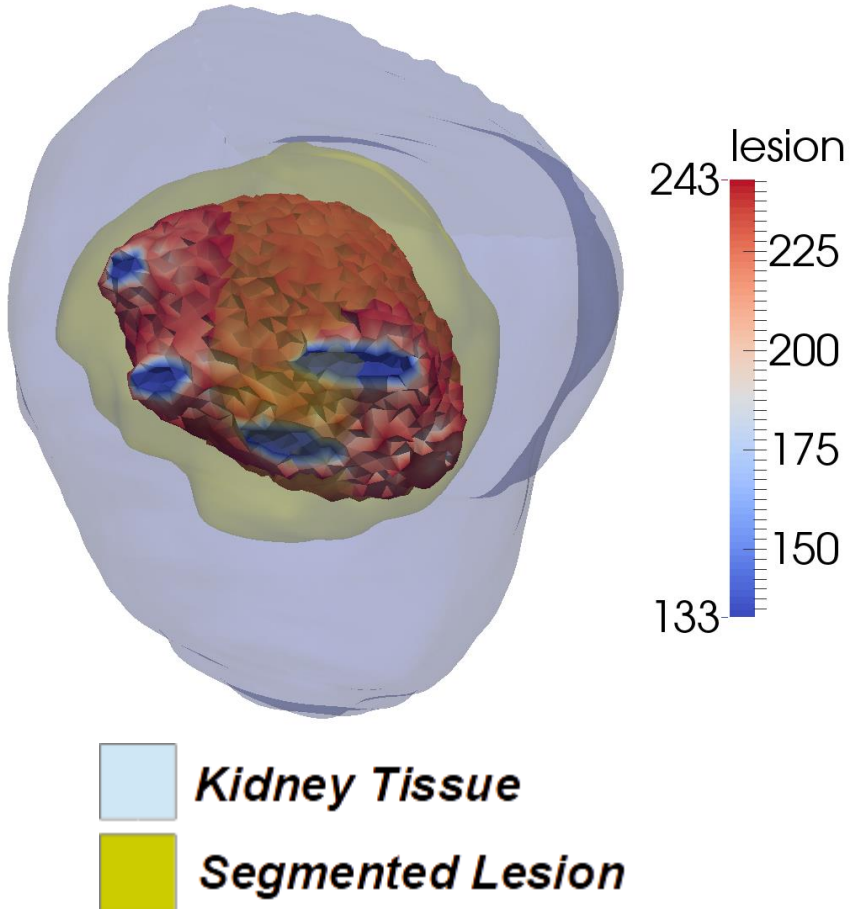
Fig. 4. Temperature distribution at different times for Problem 1.

Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

Cryoablation

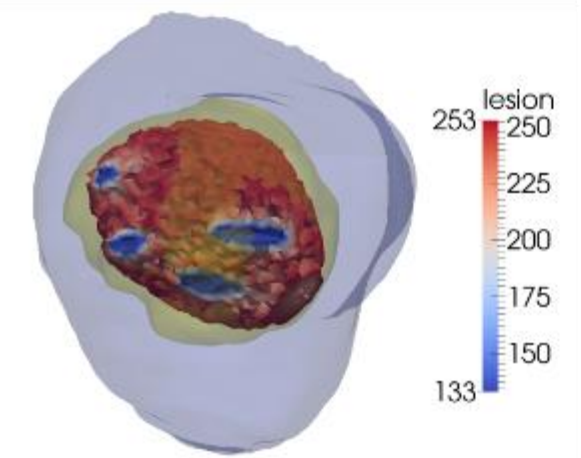
- Freeze-Thaw Cycle
  - *10 min. freezing*
  - *1 min. passive thawing*
  - *2 min. active thawing*
  - *(repeat)*

  - Cells considered dead where tissue temperature below -40°C
  - GSSF restart functionality undergoing testing

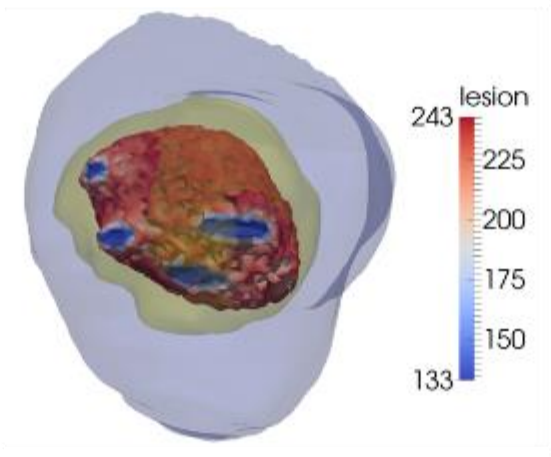


Cryoablation

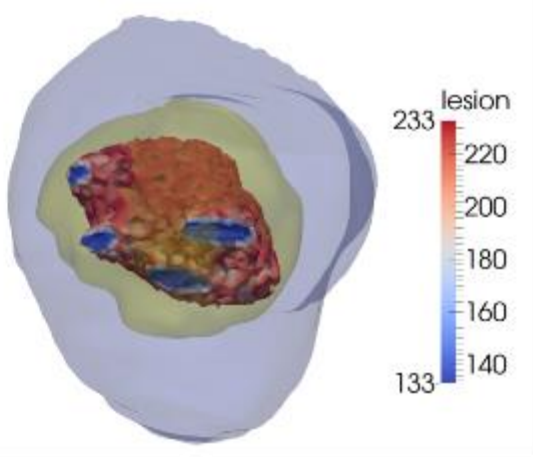
Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment



-20°C isotherm



-30°C isotherm



-40°C isotherm

Simulated Time: 26 minutes
Elements: 232,954

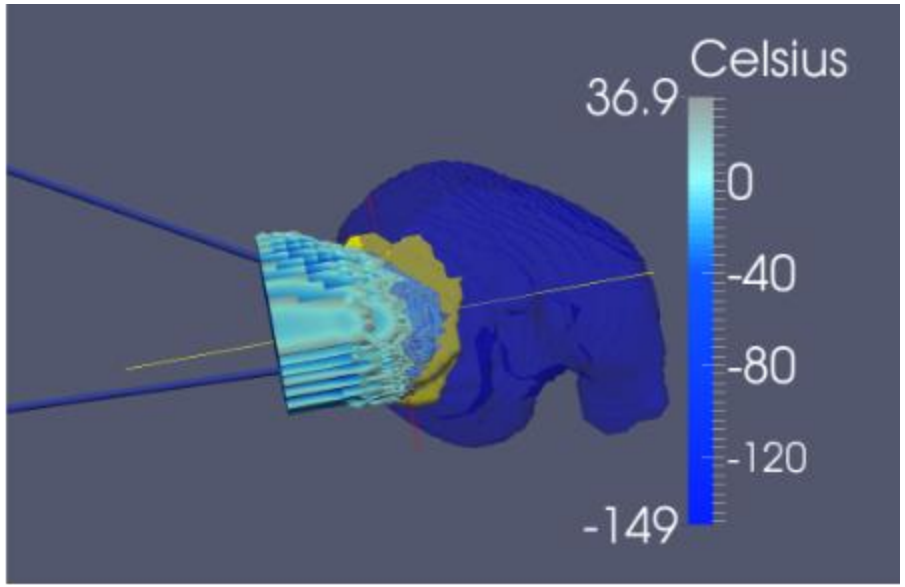
Kidney Tissue

Segmented Lesion

Cryoablation

Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

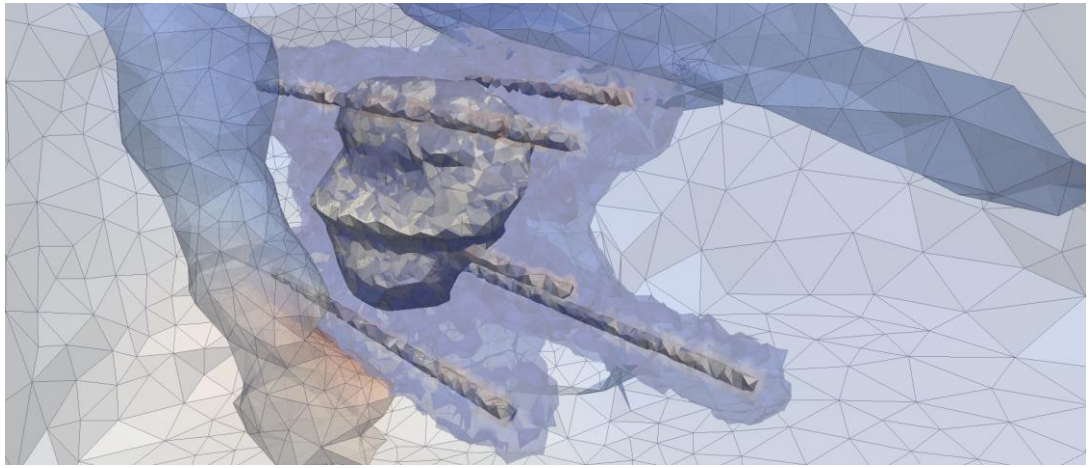
Needles	2
Simulation	26 min
Elements	2,079,334
Runtime	6 min
Processors	8



Irreversible Electroporation

Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

IRE



- *Modeled using simple electric potential solver*
  - Current test - 6 needles
  - Anodes and cathodes; 9 consecutive pairs
  - Calculate cumulative coverage

$$\nabla.(\sigma\nabla\phi) = 0$$
$$\left.\frac{\partial\phi}{\partial n}\right|_{A_i} = V_i$$
$$\left.\frac{\partial\phi}{\partial n}\right|_{C_i} = 0$$

Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

IRE

Electric potential:

$$\nabla \cdot (\sigma \nabla \phi) = 0 \qquad E = \frac{1}{2}(\nabla \phi)^2 \qquad \sigma = \begin{cases} \sigma_u & E > E_u \\ \text{lin.int.} & E_l \leq E \leq E_u \\ \sigma_l & E < E_l \end{cases}$$

Active needle pairs:

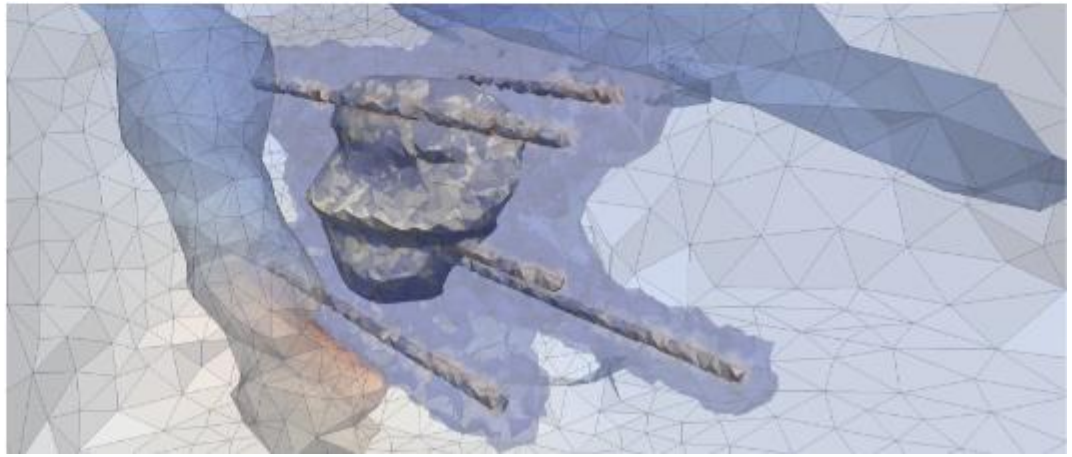
$\phi = V$ on anode

$\phi = 0$ on cathode

$(\nabla \phi) \cdot n = 0$ remaining boundaries

Investigating efficient, representative 2D quick simulations for instant feedback.

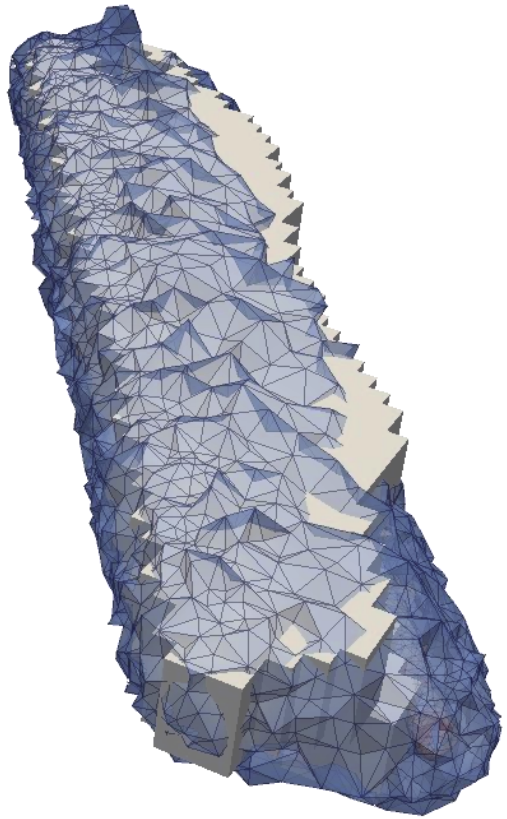
FE Engines:
Elmer FEM / FEniCS



Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

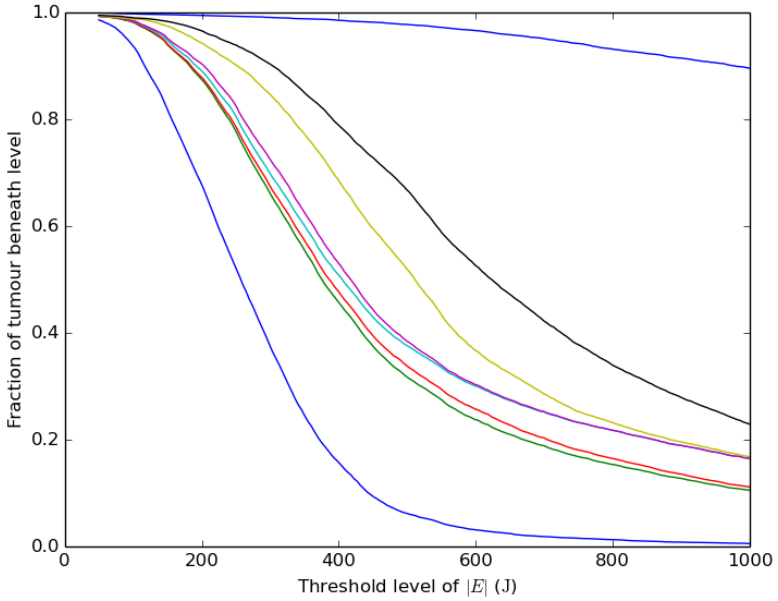
IRE

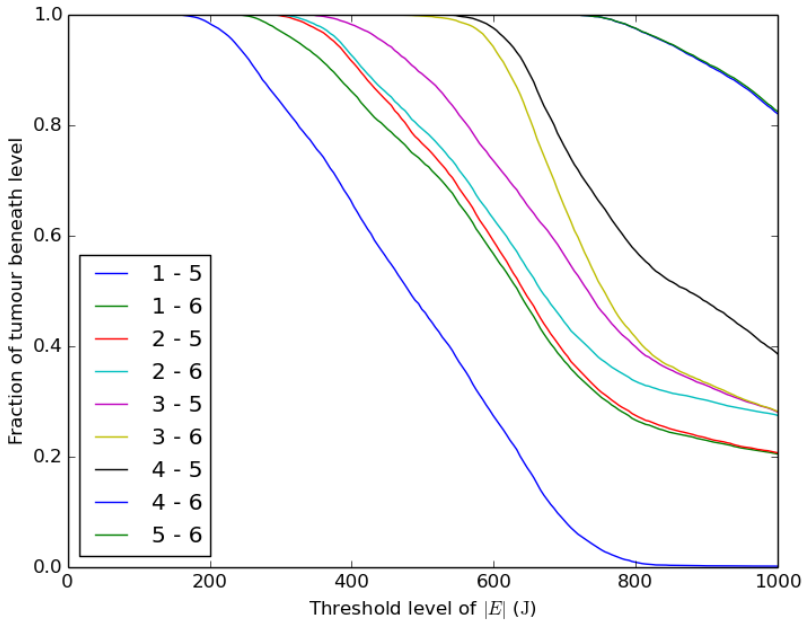
- *Electrical properties change based on the deposited energy*
- *Final lesion is defined as an isovolume based on a chosen threshold of the local energy maximum over the whole protocol sequence*



Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

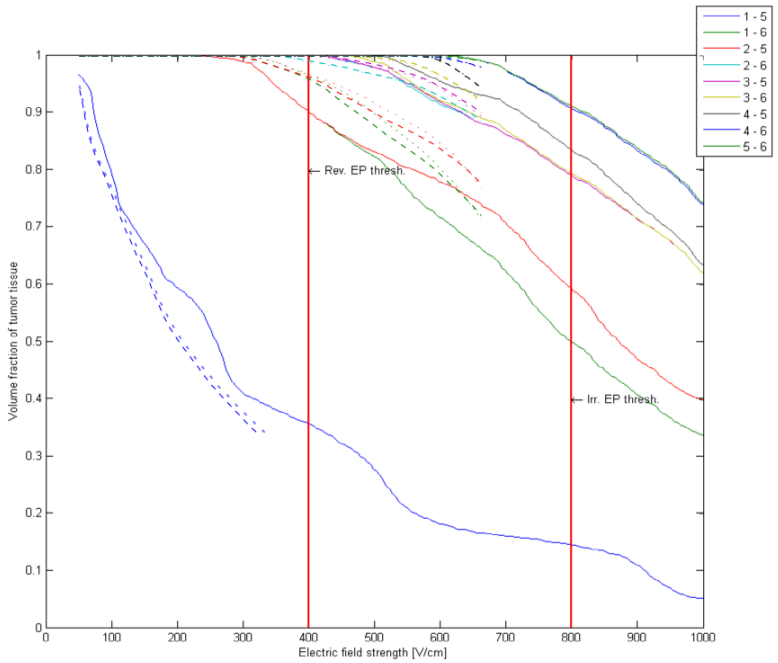
IRE

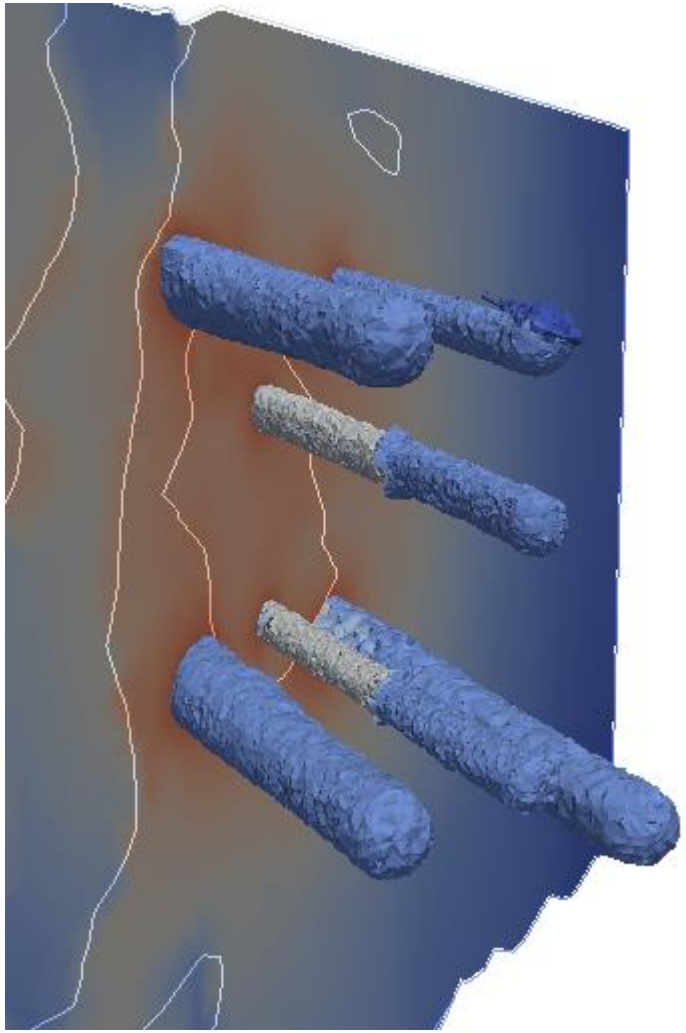




Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

IRE

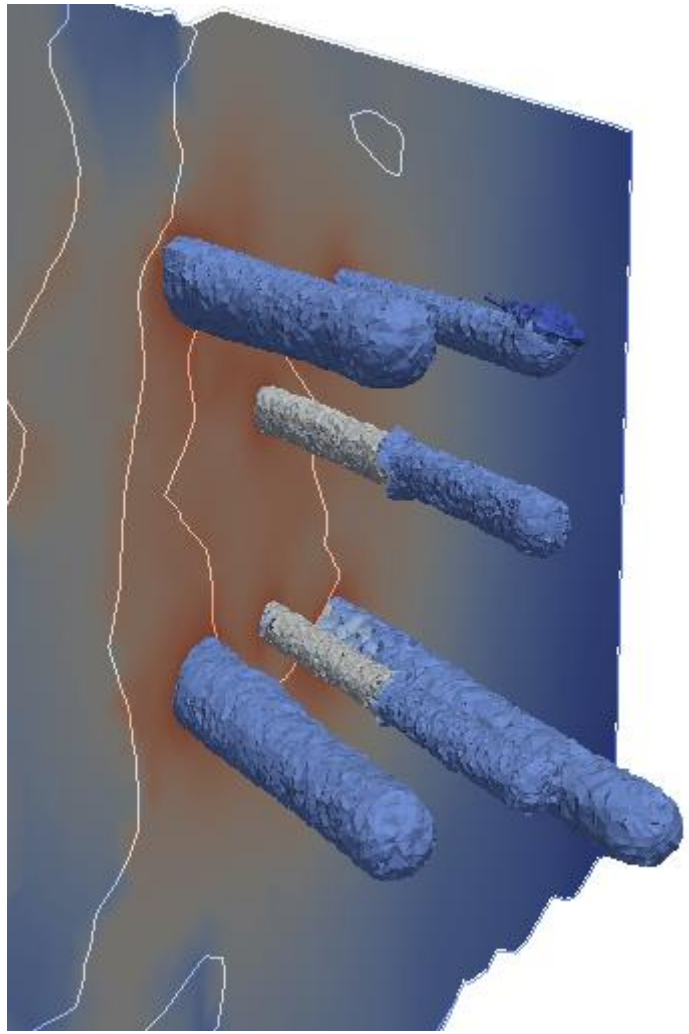




Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

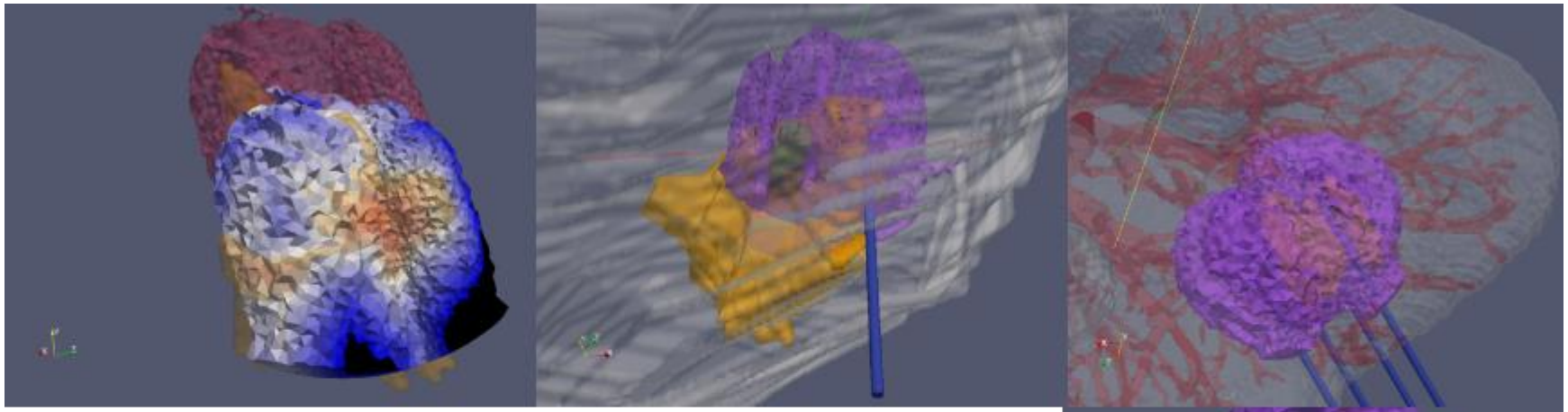
IRE

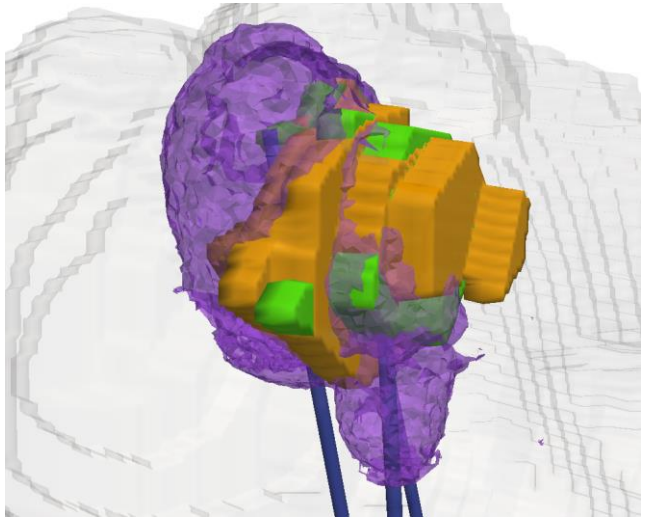
- Location of varying tissue types
  - Based on existing models,
  - observable effect of tumour
- Effects of almost-parallel placement
  - under/over-treatment at ends
  - rounding off at mismatching tips
  - selecting representative axis
- Accurately modelling effects of altering pulse duration, pulse length and capturing active length of needle

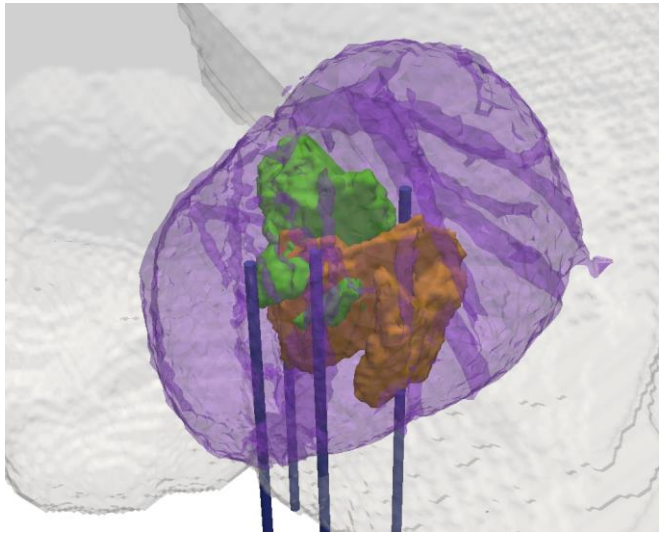


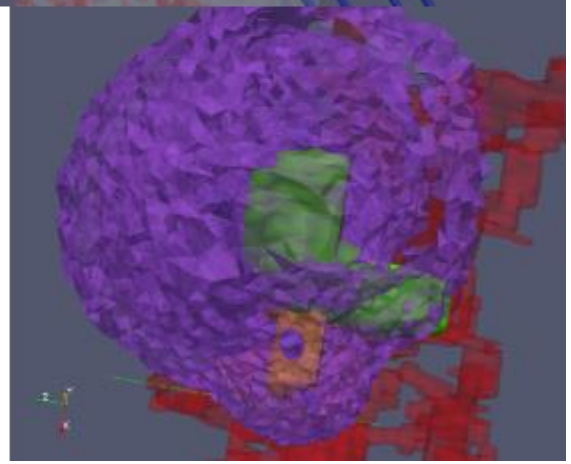
Generic Open-end Simulation, Environment for Minimally Invasive Cancer Treatment

IRE



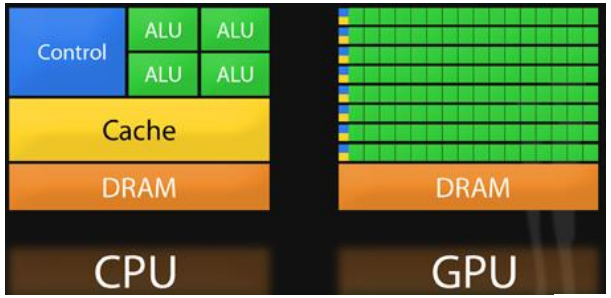






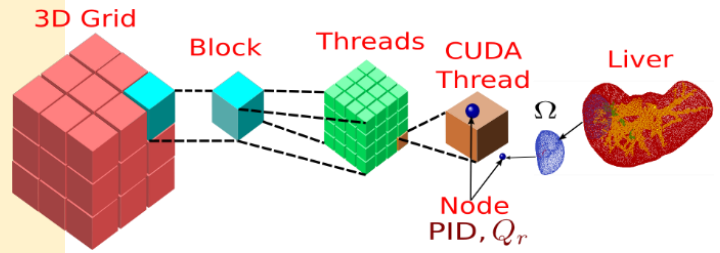
Summary

Computations in GPU



- CPU does
  - Mesh generation
  - Receives mesh
  - Generates neighbours
  - Constructs the initial CSR matrix

- Each node requires
  - PID controlled power input
  - Source term (Q_r)
- Each thread of GPU computes Each Node's
  - PID controlled power input
  - Source term

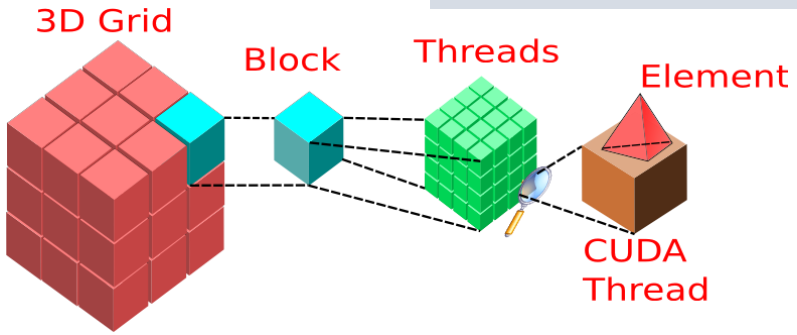


- Each element requires
  - 4 x 4 matrix inversion
  - Stiffness matrix construction
  - Mass matrix construction
  - Volume computation

- Each thread of GPU computes each Element's
  - 4 x 4 matrix inversion
  - Stiffness matrix
  - Mass matrix
  - Volume

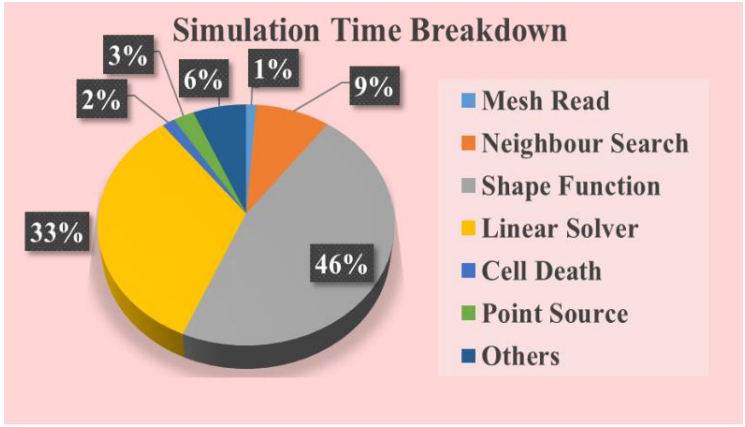
	0	1	2	3	4
0	2.0		3.5		6.7
1		8.2		9.2	
2		1.1	2.8		
3	3.0		1.5	4.5	
4		2.5		8.9	

	0	1	2	3	4	5	6	7	8	9	10	11
rowptr	0	3	5	7	10	12						
colind	0	2	4	1	3	1	2	0	2	3	1	3
values	2.0	3.5	6.7	8.2	9.2	1.1	2.8	3.0	1.5	4.5	2.5	8.9



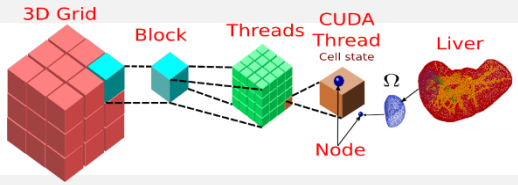
Linear Solver and Assembly

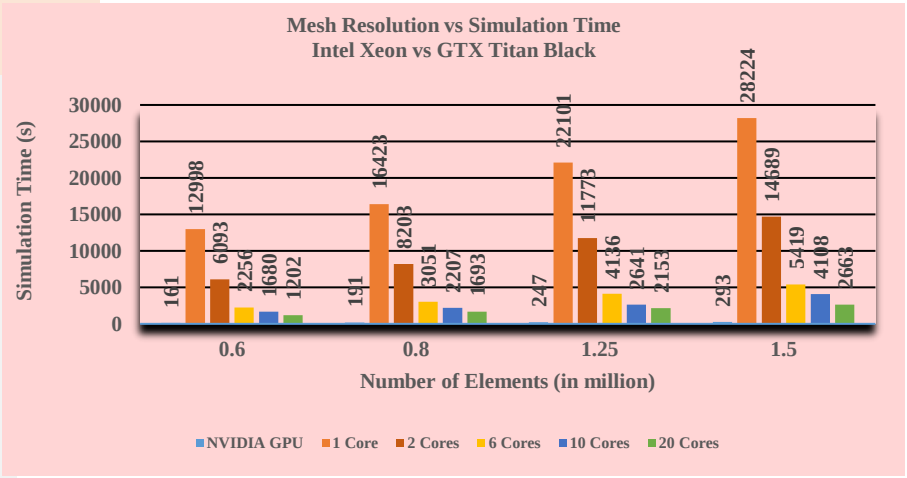
- Assembly
  - Stiffness matrix assembled directly to CSR matrix
  - Neighbour map algorithm between stiffness matrix and CSR matrix
- ILU Precondition BICGSTAB
- CUDA Libraries
- ILU Computation using CUSPARE[1] library
- Each solver operation uses CUBLAS[1] and CUSPARSE[1] libraries



- Each node requires
  - Dead state
  - Alive state
  - Blood Perfusion value
  - Specific heat capacity valu

- Each thread of GPU computes each node's
  - Dead state
  - Alive state
  - Blood Perfusion value
  - Specific heat capacity value





[1]NVIDIA Corporation (2015), CUDA C Programming guide, Version 7.5

Simulation Speedup

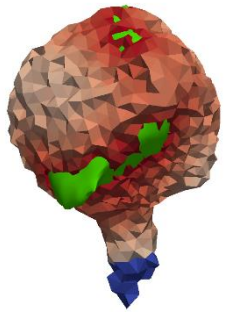
Pat.	# Abl.	RFA Real duration (minutes)	Perfusion $\frac{ml/100ml}{min}$	Sim. Time (sec)
4	1	18	21.6, 21.6	104
5	2	28	0, 0	103
6	2	11	36, 21.6	73
7	2	19	21.6, 36	115
8	2	29	105.6, 36	188
9	1	12	36, 21.6	64

$$DICE = \frac{2|V_{se} \cap V_{si}|}{|V_{se}| + |V_{si}|}$$

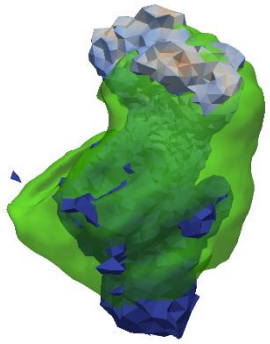
$$RVD = \left|\frac{|V_{se}|}{|V_{si}|} - 1\right|$$

$$Volume\ \ overlap = \frac{|V_{si} \cap V_{se}|}{|V_{si} \cup V_{se}|}$$

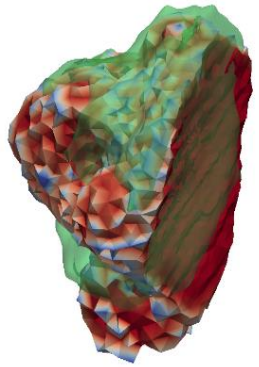
Accepted:
Surface deviation < 3.5mm
RVD < 20 %



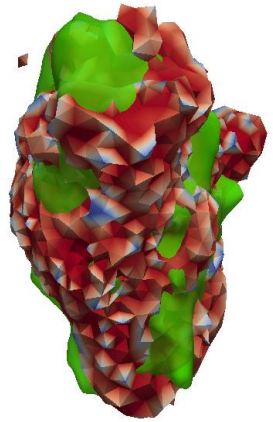
RVD: 18
Surf Dev: 2.28



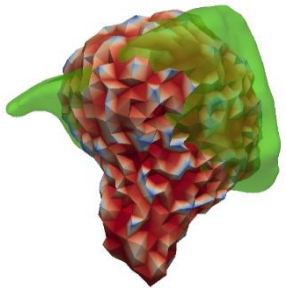
RVD: 74
Surf Dev: 3.09



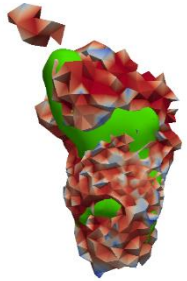
RVD: 6.67
Surf Dev: 2.88



RVD: 0.003
Surf Dev: 4.57



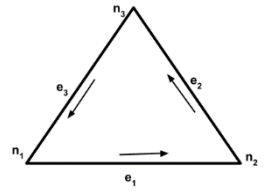
RVD: 0.61
Surf Dev: 2.74

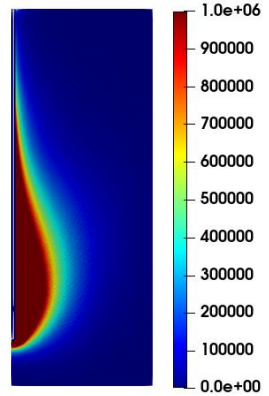


RVD: 55.71
Surf Dev: 1.88

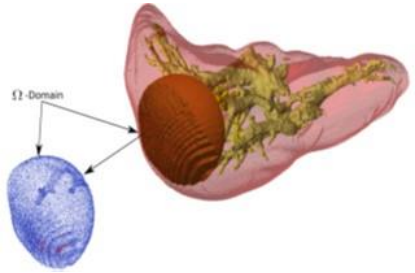
Pat.	# Abl.	RFA Real duration (minutes)	Perfusion $\frac{ml/100ml}{min}$	Sim. Time (sec)
10	1	13	125, 125	70
11	2	32	110, 40	137
12	3	62	68.9, 70	322
13	1	9	85, 25	44
14	2	15	95, 60	95
15	3	14	135, 0	92
16	3	53	140, 45	313
17	3	62	60, 0	323
18	2	26	132, 36	150
19	1	11	57,36	83
20	1	8	47, 36	34
21	1	12	40, 36	53

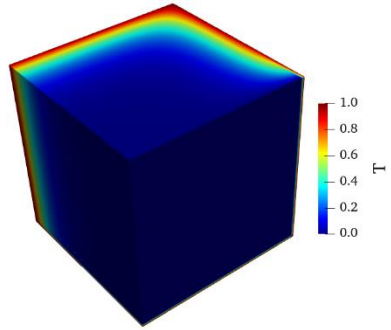
Advanced Research





- GPU accelerated MWA Solver for online computing
- Vector Finite Element Method for Microwave Ablation
- Finite Pointset based simulation of FSI problems of RFA Treatment





Summary

- A maximum of 6 minutes computation time for an hour protocol
- If machines are available with 4GPUs on a PC with super cooling fan, it is possible to run 4 simulations at the same time by changing parameters such as GPU and port numbers
  - 20-20-20: 20 simulations for a 20 minutes protocol could be done in 20 minutes
- Provides good accuracy with less than 2.5mm surface deviation error
- RVD average: 17.99%

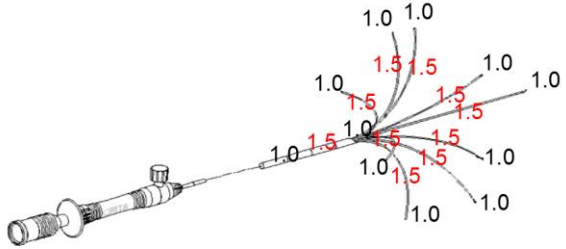
This presentation: based on the following articles:

Panchatcharam Mariappan, P. Weir, R. Flanagan, et al, ***GPU-based RFA Simulation for minimally invasive cancer treatment of liver tumours***, International Journal of Computer Assisted Radiology and Surgery, 12(1): 59-68, 2017

Panchatcharam M, Phil W and Ronan F, GPU accelerated finite element method for radiofrequency ablated cancer treatment, *PRACE DAYS 2015*, May 2015: **Best Poster Presentation Award**

References

1. Gangadhara B, **Panchatcharam M**, A Vector Finite Element Approach to Temperature Dependent Parameters of Microwave Ablation for Liver Cancer, International Journal for Numerical Methods in Biomedical Engineering, 2023
2. **Panchatcharam M,** Gangadhara B, Ronan F, A Point Source Model to Represent Heat Distribution Without Calculating the Joule Heat during Radiofrequency Ablation, Frontiers in Thermal Engineering, 2022
3. Cindric H, **Panchatcharam M**, Beyer L, Wiggermann P and Moche M, Miklavcic D and Kos B, Retrospective study for validation and improvement of numerical treatment planning of irreversible electroporation ablation for treatment of liver tumors, *IEEE Transactions on Biomedical Engineering*, 2021.
4. Martin J.A, **Panchatcharam M**, Philip V, Ronan F, Sjoerd F. M. J, Mika P, Marina K, Michael M and Jurgen F, Software-based planning of ultrasound and CT-guided percutaneous radiofrequency ablation in hepatic tumors, *International Journal of Computer Assisted Radiology and Surgery*, 16, pp. 1051-1057, 2021
5. Tim Van O, Jan H, Michael M, Phil W, **Panchatcharam M,** Ronan Flanagan, Mika P, Stephen P, Marina K, Sjoerd, F. M. J and Jurgen F, Validation of a web-based planning tool for percutaneous cryoablation of renal tumors, *CardioVascular and Interventional Radiology*, September 2020 (IF: 0.67)
6. Michael M, Harald B, Jurgen F, Camila A H, Daniel S, Philipp B, Marina K, Sjoerd J, Roberto B S, Gaber K, Mika P, Martin E, Horst R P, Philip V, Ronan F, **Panchatcharam M** and Martin R, *Clinical evaluation in silico planning and real-time simulation of hepatic radiofrequency ablation (ClinicIMPPACT Trial)*, European Radiology, 30, 934-942, 2020. (IF: 4.101)
7. Philip V, **Panchatcharam M,** Mika P, Ronan F, Roberto B s, Rupert H P, Jurgen F, Dieter S, Marina K and Michael M, *RFA Guardian: Comprehensive simulation of radiofrequency ablation treatment of liver tumors*, Nature Scientific Reports,8(1), 2018. (IF: 4.529)
8. Martin R, Philip B, Daniel S, Marina K, Sjoerd J, Roberto B. S, Martin E, Philip V, Ronan F, **Panchatcharam M,** Harald B and Micahel M, *A prospective development study of software-guided radio-frequency ablation of primary and secondary liver tumors: Clinical intervention modeling, planning and proof for ablation cancer treatment (ClinicIMPPACT)*, Contemporary Clinical Trials Communications, 8, 25-32, 2017. (IF: 1.935)
9. **Panchatcharam M,** Phil W, Ronan F, Philip V, Tuomas A, Mika P, Michael M, Harald B, Jurgen F, Horst R P, Roberto B S and Marina K, *GPU-based RFA simulation for minimally invasive cancer treatment of liver tumours*, International Journal of Computer Assisted Radiology and Surgery, 12(1): 59-68, 2017 (IF: 1.707)



End of Lecture