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COMSOL CONFERENCE 2014 CAMBRIDGE

MULTIPHYSICAL MODELING OF ELECTRODE-DRIVEN RENAL DENERVATION FOR HYPERTENSION TREATMENT

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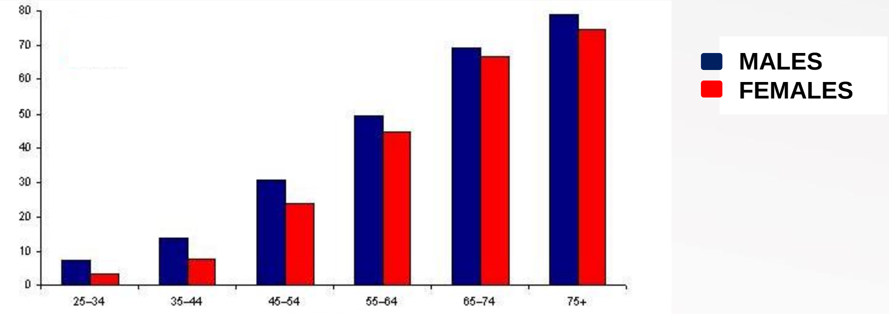
AGENDA

- **Introduction**
  - Renal Denervation (RDN) as a treatment for Hypertension
  - Radio Frequency (RF) catheter-based solution for RDN
- **Methods**
  - *Ex-vivo* bench setup for ablation performance evaluation
  - Schematic view of *ex-vivo* vs *in-vivo* systems and electrical circuit model
  - Numerical modeling of the *ex-vivo* bench setup
    - Geometry reconstruction
    - Governing equations – Model parameters
    - Boundary conditions
    - Domain discretization
- **Results & Discussion**
  - *Ex-vivo* bench setup: ablation patterns and temperature profile
  - Numerical modeling: ablation patterns and temperature profile
  - Comparison between numerical results and experimental data
- **Conclusions & Future Developments**

INTRODUCTION:
Renal Denervation (RDN) as a treatment for Hypertension

Hypertension (HTN): chronic elevated arterial blood pressure (BP) affecting ~ 1.5 billion people worldwide

Population %age with hypertension:
systolic BP > 140 mmHg
diastolic BP > 90 mmHg



Age group [years]

Activation of Renal Sympathetic Nerves: responsible for BP increase via blood vessels vasoconstriction

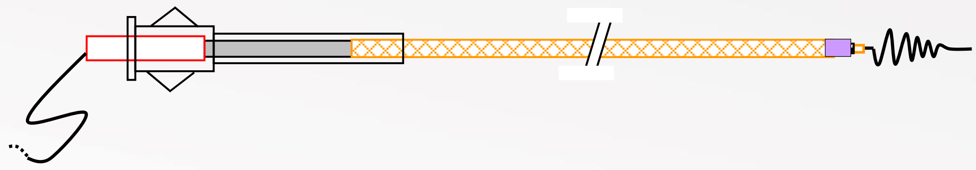
Percutaneous Sympathetic RDN: safe and effective therapy resulting in substantial BP improvement in patients with resistant HTN (2 year follow-up*)

(*) Renal sympathetic denervation in patients with treatment-resistant hypertension (The Symplicity HTN-2 Trial): a randomised controlled trial. The Lancet 4 December 2010 (Volume 376 Issue 9756 Pages 1903-1909)

INTRODUCTION:
Radio Frequency (RF) catheter-based solution for RDN

RF GENERATOR

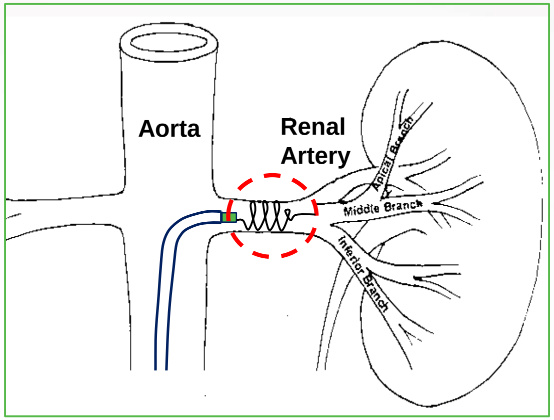
CATHETER BODY



STENT

RF ablation damages tissues via electric energy converted into thermal energy

- NiTi Stent System connected to 460 KHz RF generator
- Stent System delivered and deployed into renal artery
- Nerve Ablation via RF energy



METHODS:
Ex-vivo bench setup for ablation performance evaluation

1. **Test setup**:
   - Saltwater bath
   - Tissue preparation – porcine renal arteries in fixture
   - Sample Setup
2. **Test run**:
   - Place ground plate underwater
   - Submerge tissue & catheter in saltwater bath
   - Run ablation
3. **Inspection**:
   - Visually inspect vessel
   - Identify ablation lesions

METHODS:

Ex-vivo bench setup for ablation performance evaluation

Salt Water Bath

Saline water:

Concentration: 5 g / L

Total water volume: 12.5 L

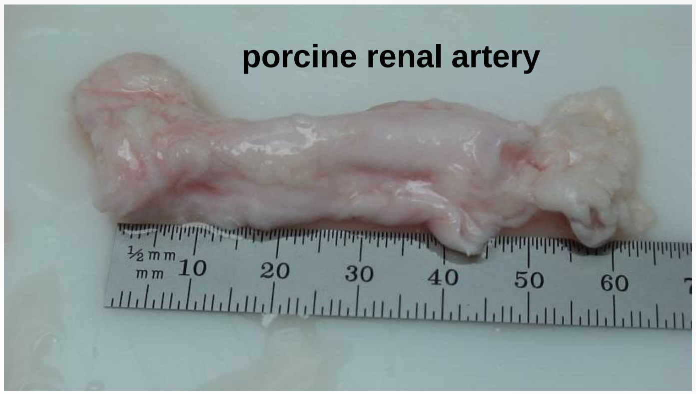
Water pump

300 mL / min

METHODS:

Ex-vivo bench setup for ablation performance evaluation

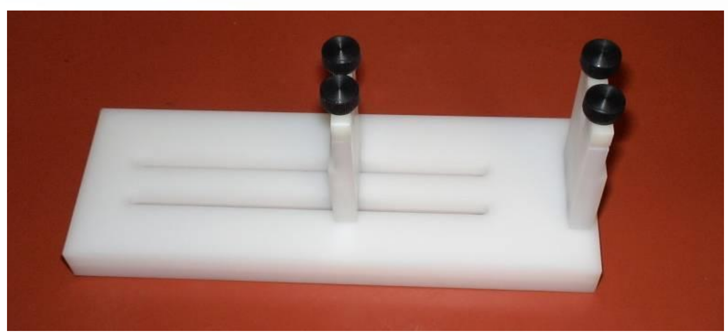
Tissue Preparation: porcine renal artery in fixture



Working Length Measurement

Inner Diameter Measurement

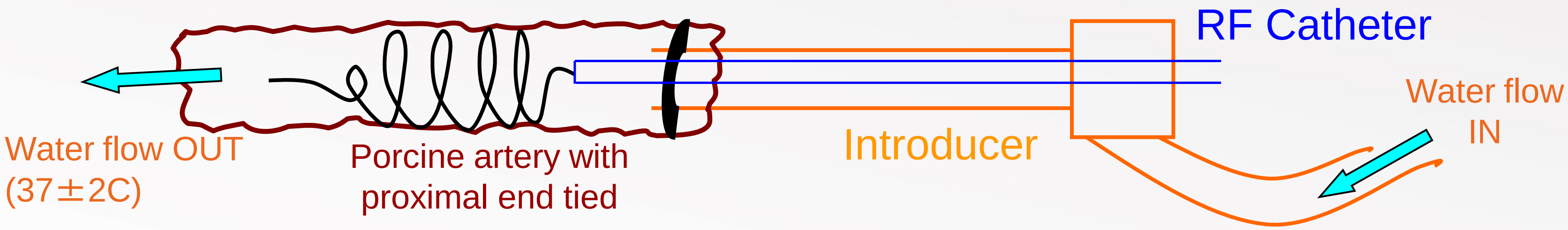
Fixture

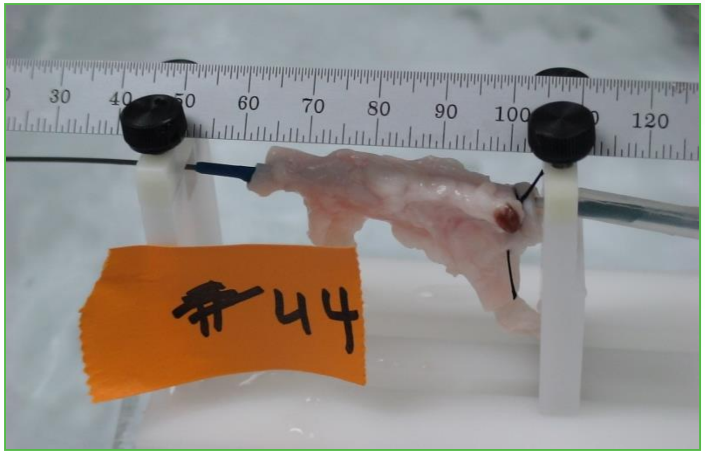


METHODS:

Ex-vivo bench setup for ablation performance evaluation

Sample Setup





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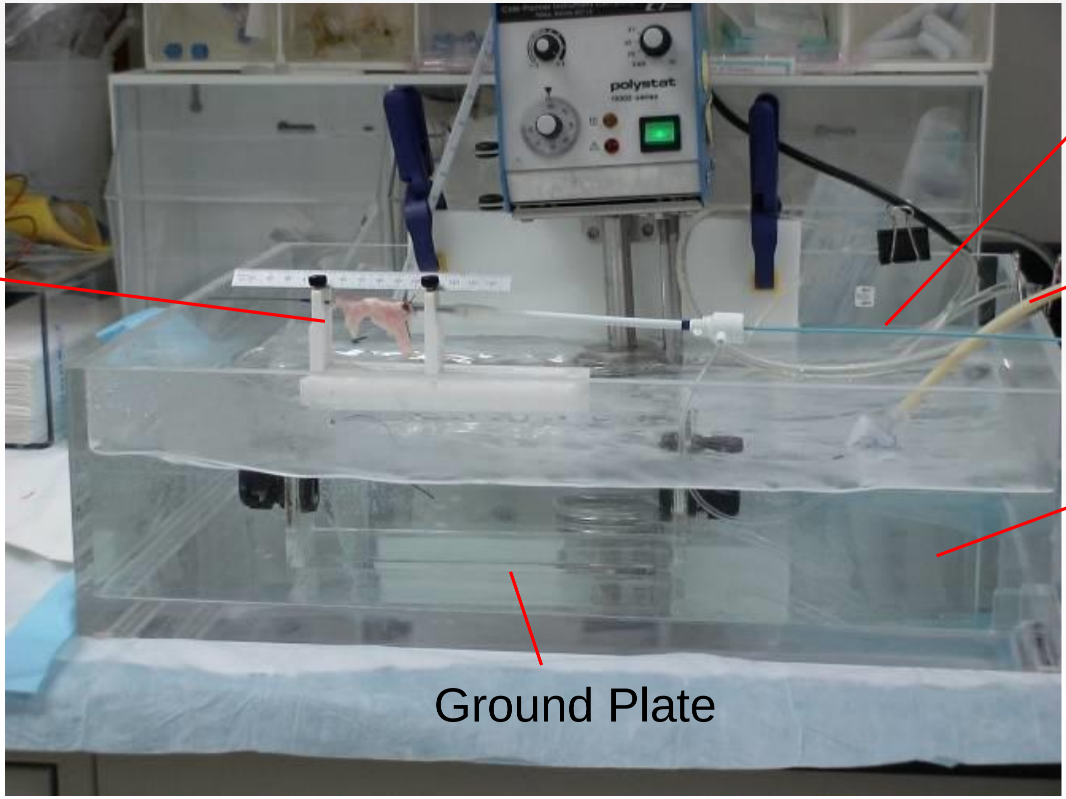
METHODS:

***Ex-vivo* bench setup for ablation performance evaluation**

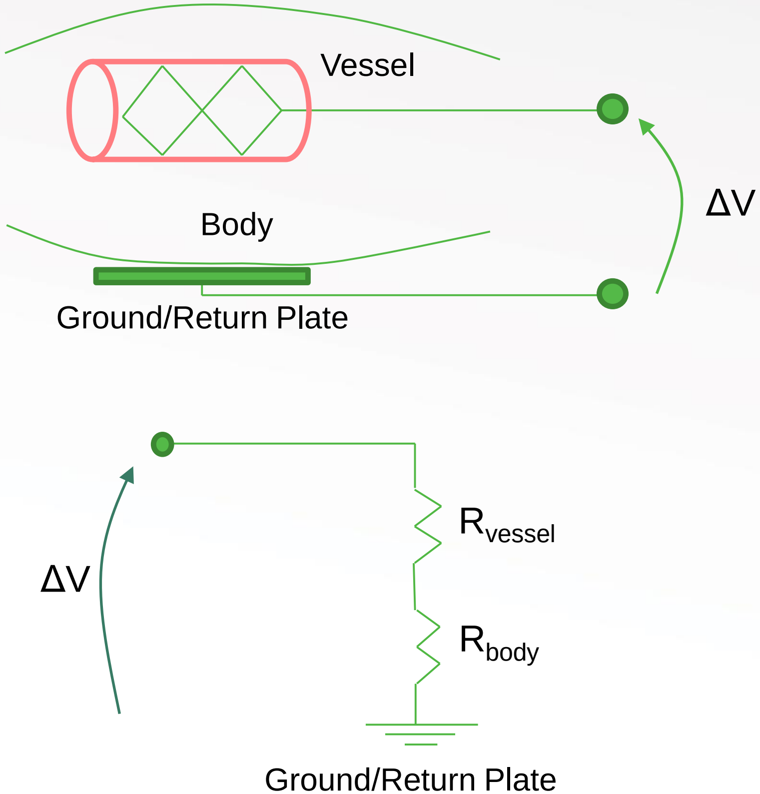
Sample Setup: catheter ready to run



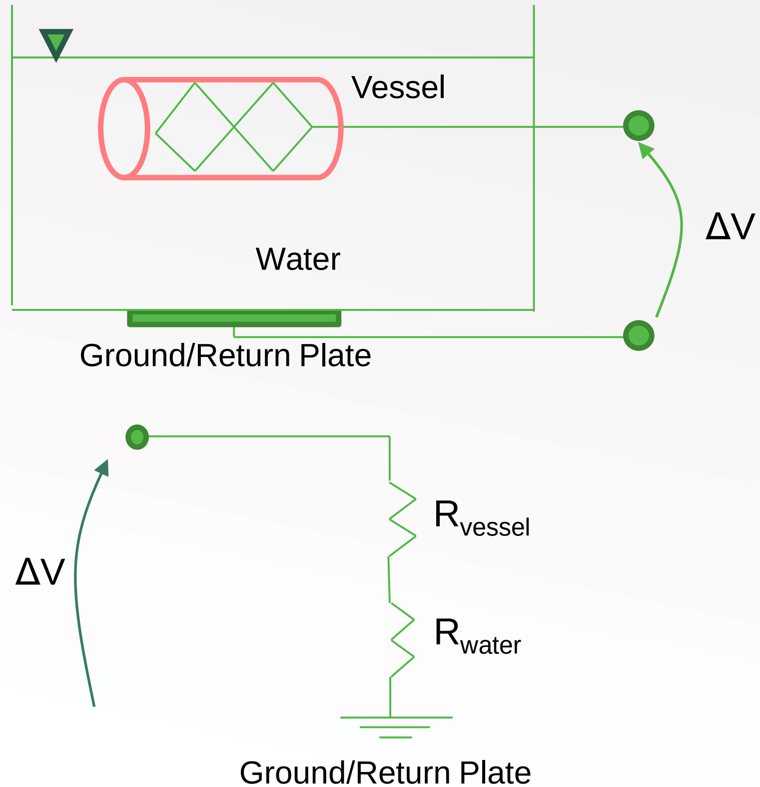
METHODS:

Schematic view of *ex-vivo vs in-vivo* systems and electrical circuit model

In-vivo



Ex-vivo



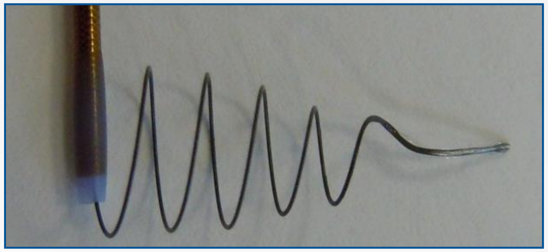
RF generator delivers voltage (ΔV) at constant power setting and measures the overall impedance of the system

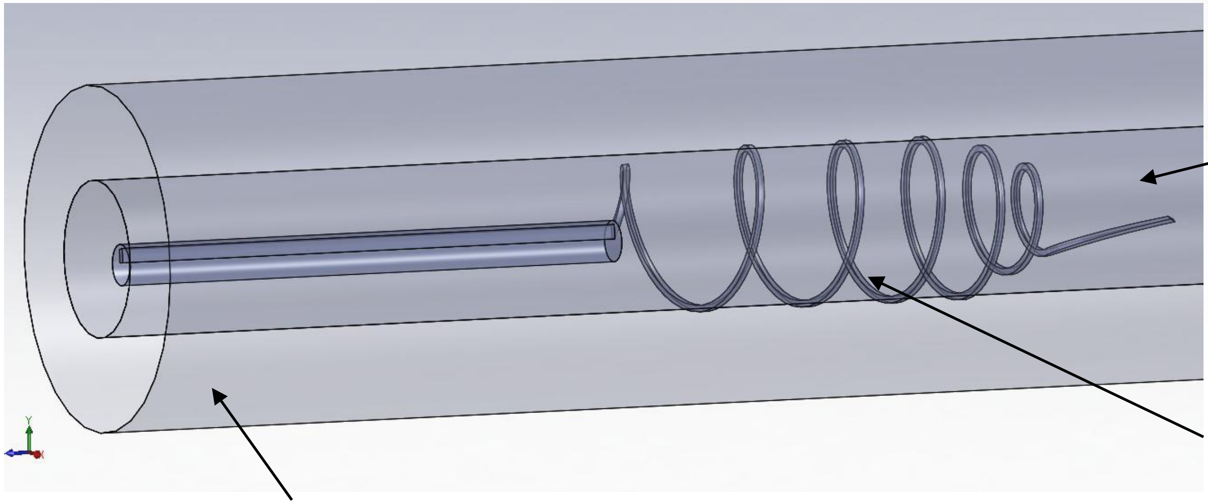
METHODS:
Numerical modeling of the *ex-vivo* bench setup:
→ Geometry reconstruction

CAD reconstruction of the simplified domains:

- **"Monofilament" (MF) stent geometry:** from in-house prototypes
- **Artery domain:** 5 mm inner diameter / 50 mm length

  Arterial wall: 3 mm thickness



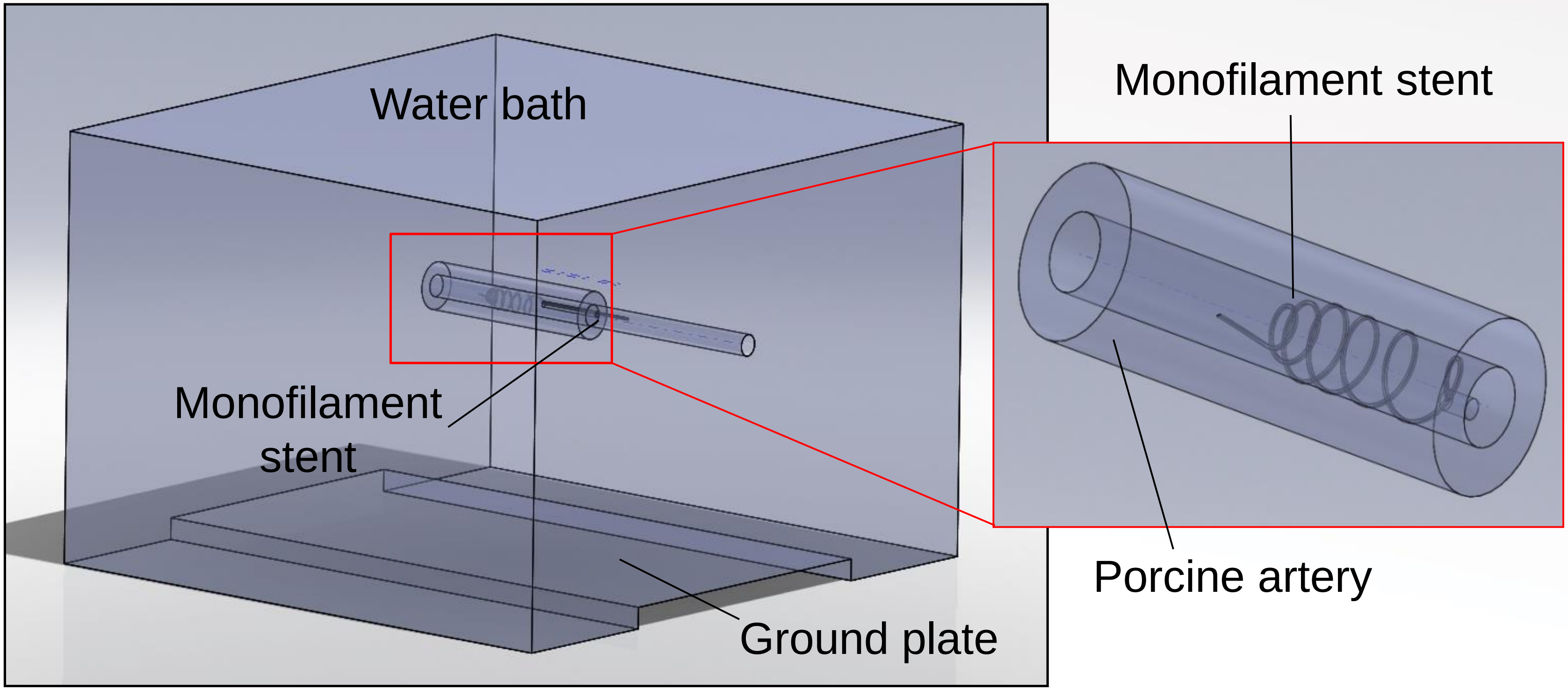


METHODS:

Numerical modeling of the *ex-vivo* bench setup:

→ Geometry reconstruction

- ***Ex-vivo* water bath with ground plate** from Santa Rosa *ex-vivo* bench setup

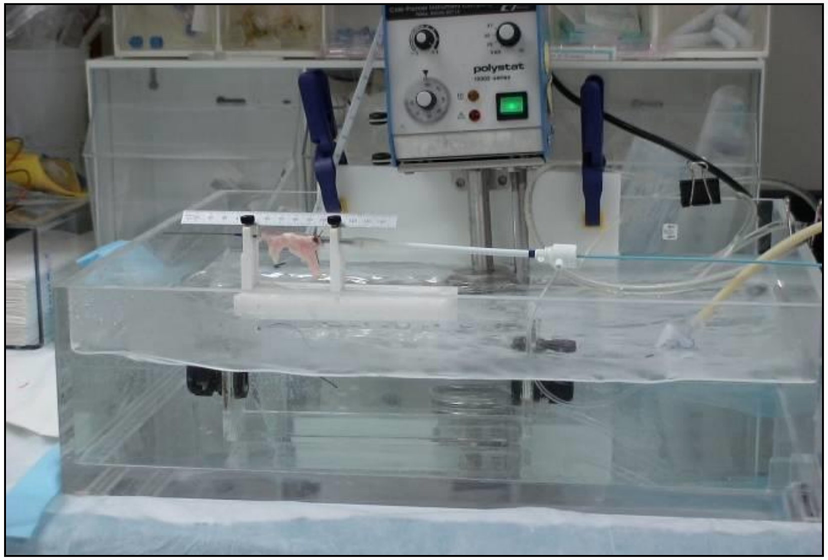


METHODS:

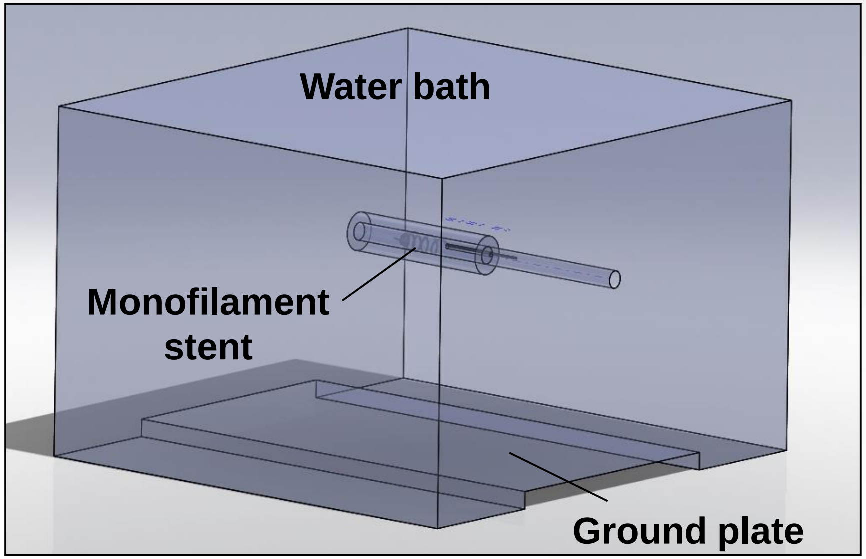
Numerical modeling of the *ex-vivo* bench setup:

→ Geometry reconstruction

BENCH SETUP



CAD RECONSTRUCTION



METHODS:

Numerical modeling of the *ex-vivo* bench setup:

→ Governing equations – Model parameters

Fluid flow (*Transient analysis*):

- Navier Stokes $$\rho\left(\frac{\partial v}{\partial t} + v\nabla v\right) = -\nabla p + \mu\nabla^2 v + f$$
- Mass balance $$\frac{\partial \rho}{\partial t} + \nabla\cdot(\rho v) = 0$$

Hp
- Fluid model: Newtonian, viscosity and density values from literature
- Rigid arterial wall and stent model

Water and Arterial Wall properties [(*)]

Water density, ρ_w	999.7 [Kg/m^3]
Vessel density, ρ_v	1060 [Kg/m^3]
Water dynamic viscosity, μ	6.67 *10^{-4} [Pa*s]

[(*)] *The Biomedical Engineering HandBook, Second Edition.Ed*. J. D. Bronzino *Boca Raton: CRC Press LLC, 2000;*
Distribution of blood viscosity values and biochemical correlates in healthy adults, Clinical Chemistry 42: 1996
Mostafa H.et al., Thermophysical Properties of Seawater: A Review of Existing Correlations and Data, Desalination and Water Treatment, 2010

METHODS:
Numerical modeling of the *ex-vivo* bench setup:
→ Governing equations – Model parameters

Heat Transfer (*Transient analysis*):

$$\rho C_p \frac{\delta T}{\delta t} + \rho C_p u \nabla T = \nabla \cdot (K \nabla T) + JE$$

- $\rho C_p \frac{\delta T}{\delta t}$: Inertial Effects
- $\rho C_p u \nabla T$: In blood Heat Convection
- $\nabla \cdot (K \nabla T)$: In tissue Heat Conduction
- JE: RF related Joule Loss Energy

$$\nabla(\sigma + j\omega\epsilon_r\epsilon_0) \cdot \nabla V = 0$$

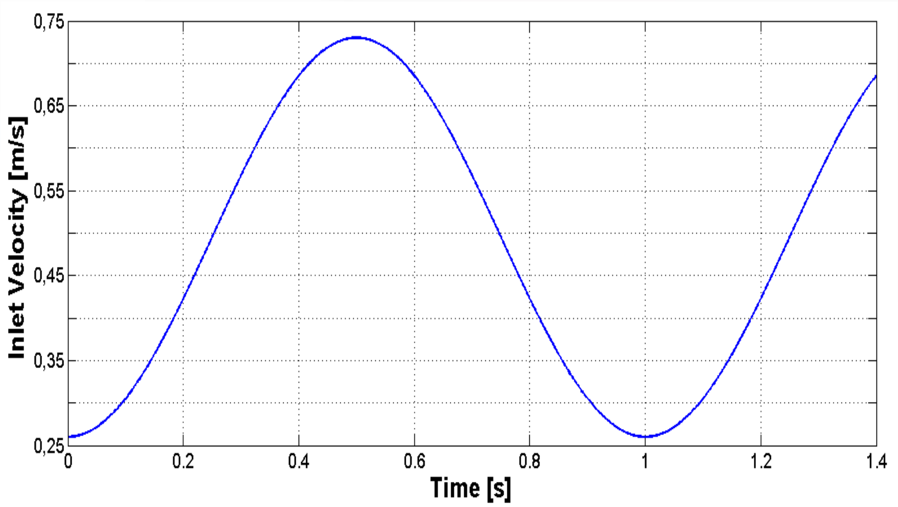
Cp: specific heat [J/kg*K]
K: thermal conductivity [W/m*K]
T: temperature [K]
J: current density [A/m^2]
E: electric field intensity [V/m]
u: water velocity [m/s]
ρ: density [kg/m^3]
$\boldsymbol{\varepsilon_r}$: Relative Permittivity
$\boldsymbol{\varepsilon_0}$: Vacuum Permittivity
σ: Electrical conductivity
ω: Frequency
V: Voltage

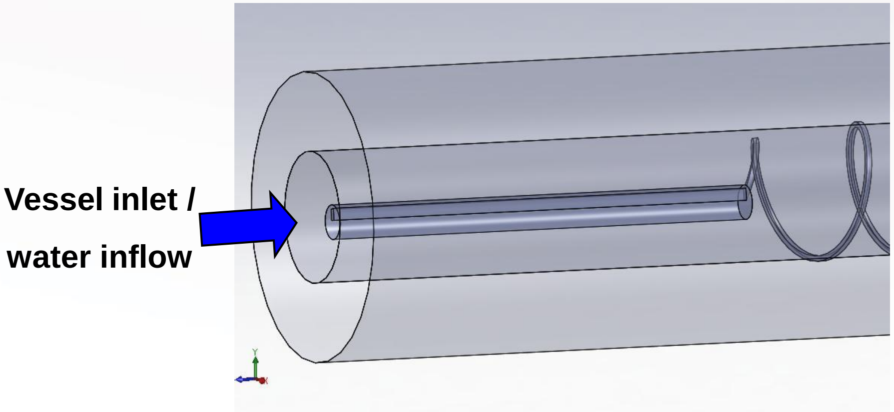
Parameter	Water properties (*)	Arterial wall properties (*)
Specific Heat, cp	4129 [J/kg*K]	3600 [J/kg*K]
Thermal Conductivity, K	0.63 [W/m*K]	0.512 [W/m*K]
Electrical conductivity, σ	0.83 [S/m]	0.25 [S/m]
Relative Permittivity, εr	81	$1*10^7$

METHODS:
Numerical modeling of the *ex-vivo* bench setup:
→ Boundary conditions

Re_{max} = 1070 → **Laminar fluid flow** (90 seconds transient analysis)

- Pulsatile (60 bpm) diastolic-systolic velocity prescribed at *vessel inlet* (water inflow)
- Renal diastolic and systolic blood velocity values taken from litterature (*)





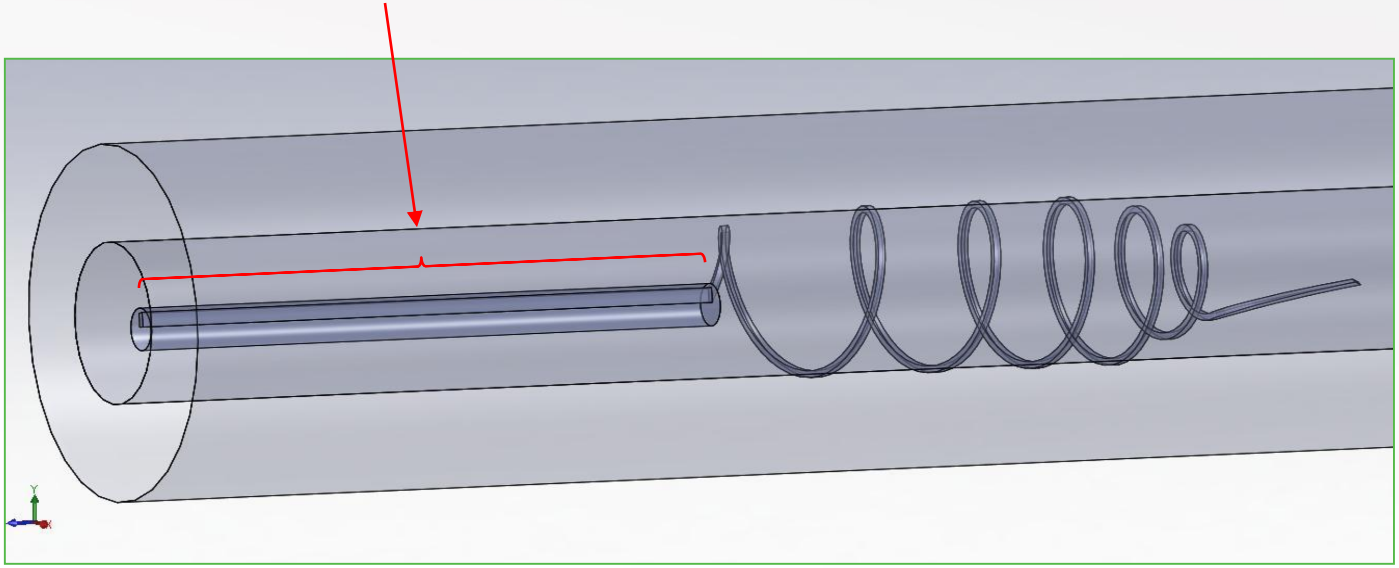
(*) *The Biomedical Engineering HandBook, Second Edition.Ed*. J. D. Bronzino *Boca Raton: CRC Press LLC, 2000; Distribution of blood viscosity values and biochemical correlates in healthy adults, Clinical Chemistry 42: 1996*

METHODS:

Numerical modeling of the *ex-vivo* bench setup:

→ Boundary conditions

- Catheter body equivalent electrical resistance (approx. 30 Ω):



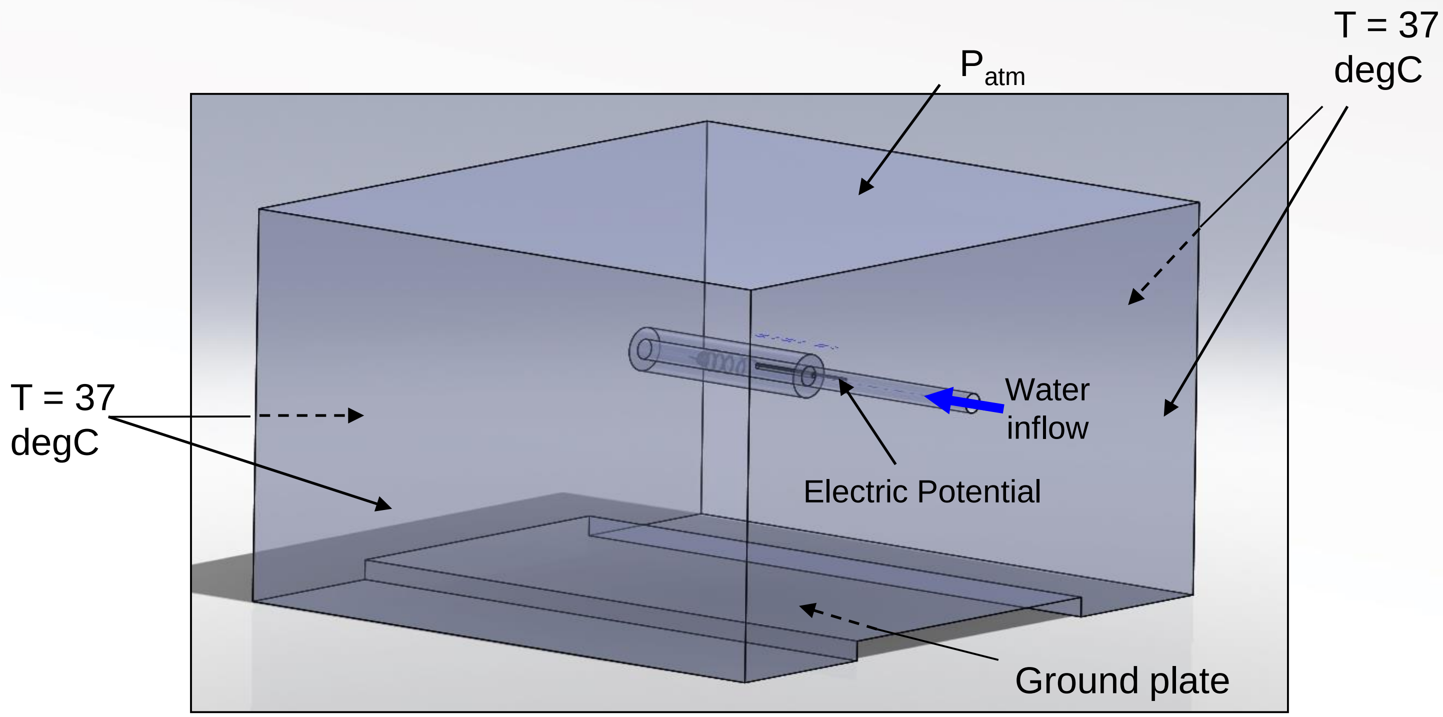
$$Electrical\ Resistance = \frac{conductor\ length}{(conductor\ cross\ section) * (electrical\ conductivity)}$$

METHODS:

Numerical modeling of the *ex-vivo* bench setup:

→ Boundary conditions

- Constant pressure (P_{atm}, no viscous stress) at *vessel outlet*
- No slip at *vessel* and *stent walls*
- 40W RF Generator power setting delivered via electric potential



CFD & Heat Transfer coupled simulations

Methods: Boundary Conditions

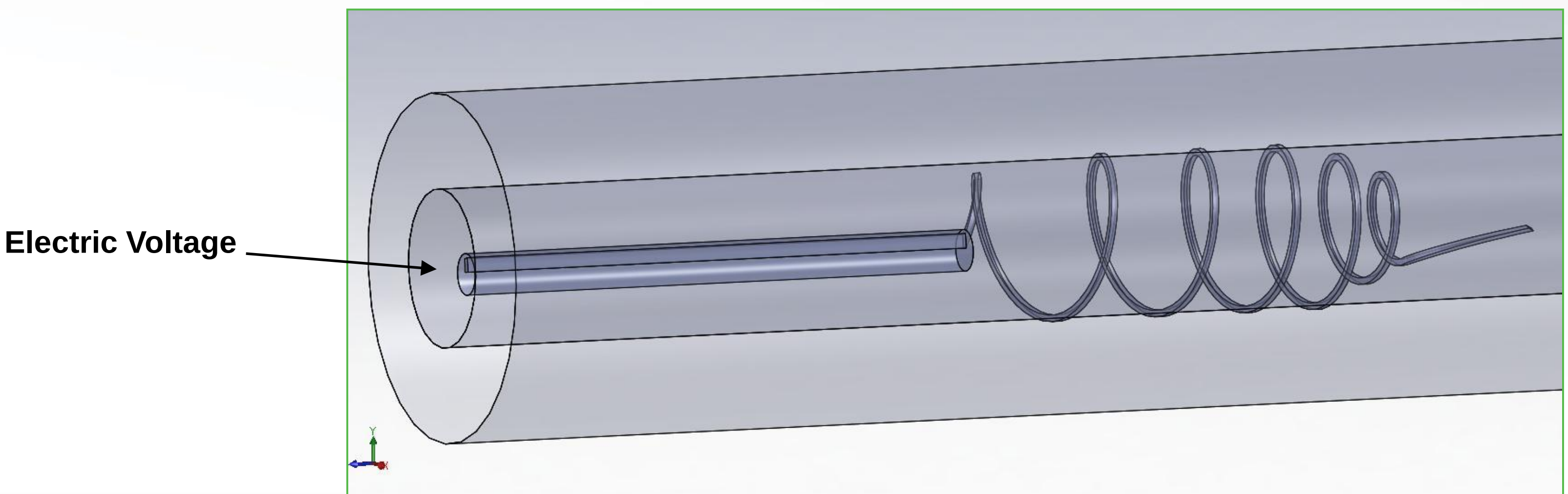
- ***Electric Voltage*** applied to *stent inlet surface* so that:

Power Loss $_{\text{3D domain}}$ + Power Loss $_{\text{Catheter body}}$ = RF Generator Wattage

Global Equations

$f(u,u_t,u_{tt},t) = 0,\ u(t_0) = u_0,\ u_t(t_0) = u_{t0}$

Name	f(u,ut,utt,t) (1)	Initial value (u	Initial value (u	Description
W	(intop1(jh.Qrh)-Power)[1/W]	1	0	



METHODS:

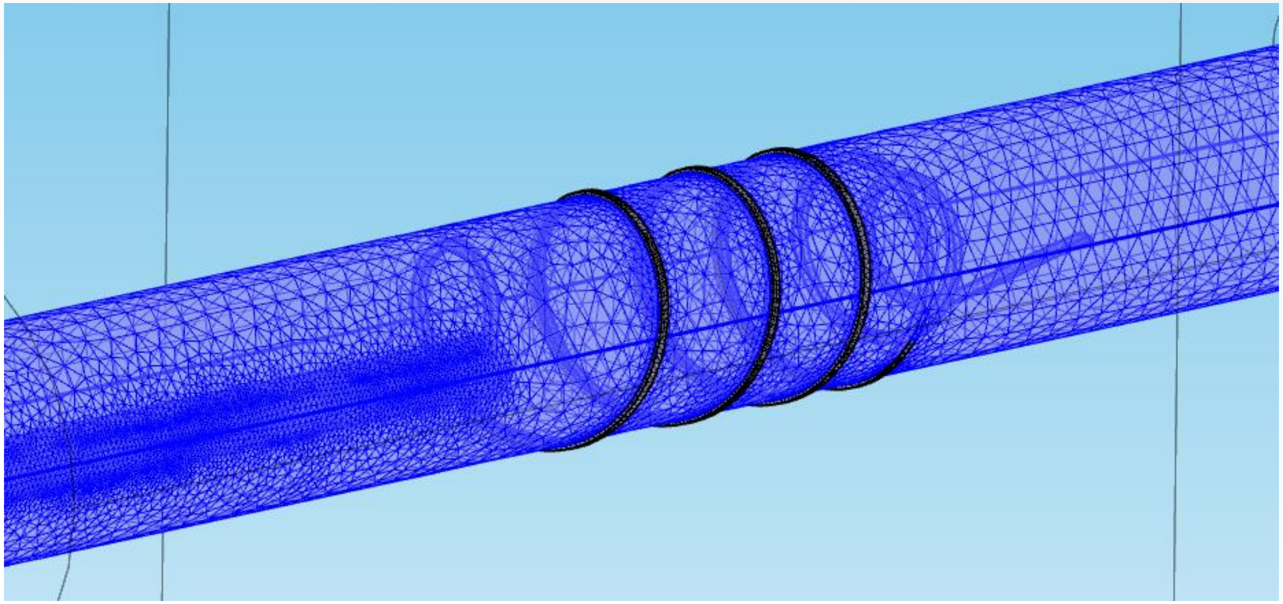
Numerical modeling of the *ex-vivo* bench setup:

→ Domain discretization

Mesh → 599655 tetrahedral elements

Average element quality *q* [(*)] = 0,81

User-controlled mesh refinement in sharp regions



(*) $q = \frac{72\sqrt{3}V}{\left(\sum_1^6 h^2{}_i\right)^{3/2}}$; where *V* denotes element volume and *h* denotes side lengths.

RESULTS & DISCUSSION:

Ex-vivo bench setup: ablation patterns and temperature profile

RF Ablation Test					Ablation Results			
Test #	PWR [W]	Time [sec]	Proximal Ø [mm]	Distal Ø [mm]	Score 1 = none / light 5 = heaviest	Lesion length [mm]	Temp [C]	Comments
101025-01	60	60	3,683	2,794	4,5	15		Very heavy, well-done lesion. Brown color, 2 deep wire grooves. "Pop" heard & seen during ablation.
101025-02	50	90	4,6736	3,683	1		43	
101025-03	50	120	4,9276	4,7752	1		51	Temp increased 36-51C for first 60sec; Avg 51C for last 60sec
101025-04a	50	120	6,35	6,223	1		41	
101025-04b	50	120	6,35	6,223	1		43	
101025-05a	60	120	6,35	5,08	1,5		48	
101025-05b	60	120	6,35	5,08	2,5	8	50	
101025-06	70	60	3,302	2,1336	4,5	10	40-75	Imp: increases 98-105, Avg 101Ω; Temp: increased 40-75C
101025-07	70	70	3,302	2,2352	5,5	15	49-84 range	Generator spontaneously stopped at 1:10min. Imp: 104Ω avg; increase to 200 in last 15 sec. Temp: Variable - see profile. Range = 49-84C
101025-08	60	90	3,302	1,5748	2	10	49	
101025-09	65	60	4,3434	2,794	3	15	50	
101025-10	65	120	5,08	4,4196	1		43	Temp increased 40-46; Avg 43C.
101025-11	65	120	4,3688	2,032	1		45	
101025-12	65	90	4,9276	2,2352	2	7	47	
101025-13	80	90	3,6322	2,794	4	13	57	Temp: increased 40-62C w/in first ~30sec; Avg 57C from 30-90 sec.
101025-14	80	62	3,6322	1,7272	3	15	43-70 ↓70-63	Temp: increased 43-70C from 1-45sec; Decreased 70-63C from 45-60sec.
101025-15	70	60	3,6322	2,794	3	20	49 & 65	Temp: Avg 49C for first 35 sec; Avg 65C from 40-60 sec.

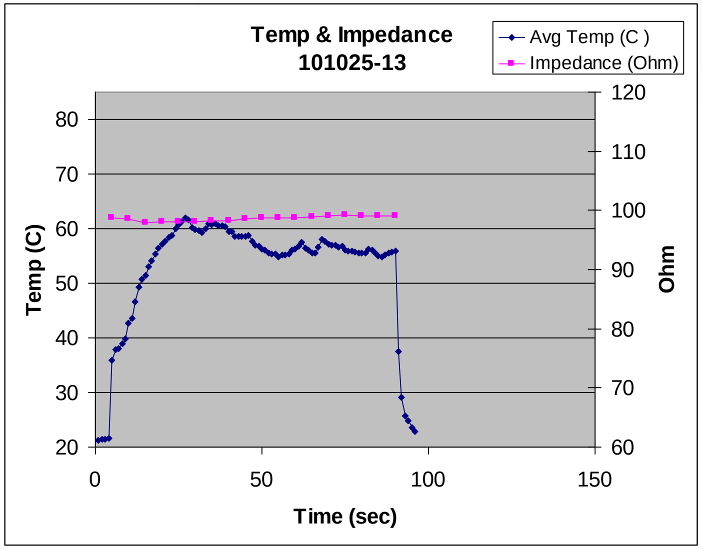
- Variable ablation score (from 1 to 5) with a few heavy lesions.
- Total impedance measured between 90-100 Ω in most cases.

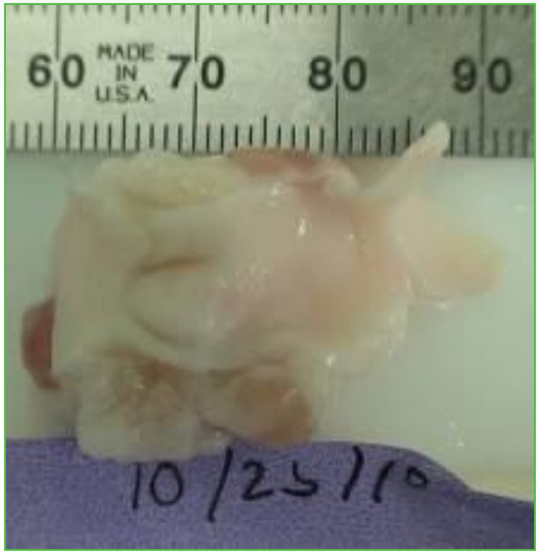
RESULTS & DISCUSSION:

Ex-vivo bench setup: ablation patterns and temperature profile

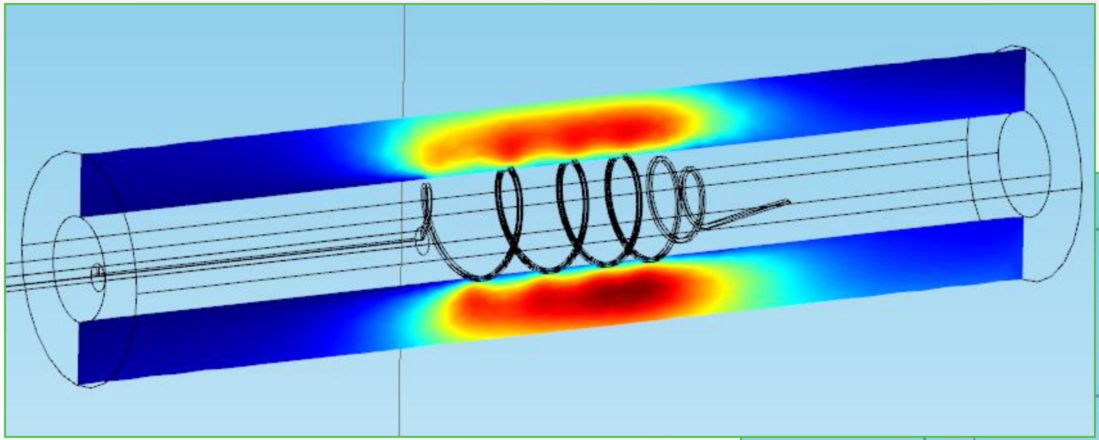
Test # 13 chosen as reference for validation of numerical simulations

Power: 40W
Time: 90 seconds
Impedance: ~ 100 Ω
Rating: 4
Average Temperature: ~ 57 degC from 30 to 90 seconds → measure taken with "in situ" thermo-couple

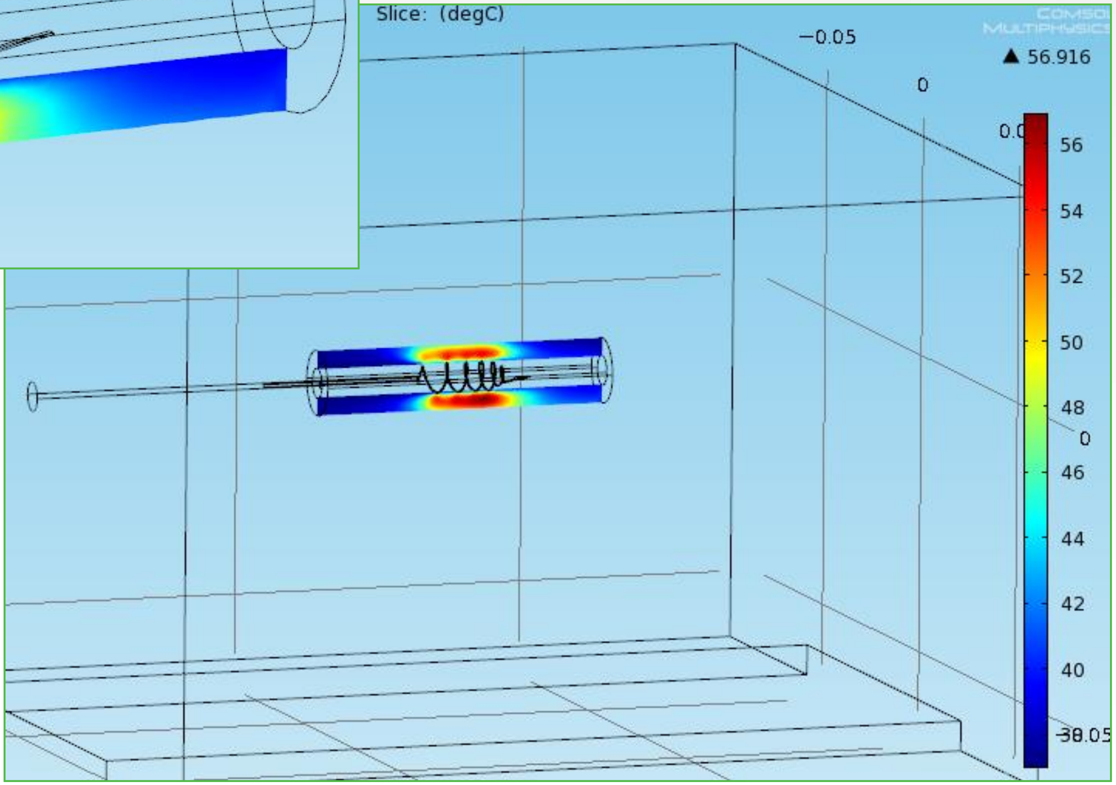




RESULTS & DISCUSSION:
Numerical modeling: ablation patterns and temperature profile



TEMPERATURE SURFACE PLOT [degC]
(vessel longitudinal cross-section)

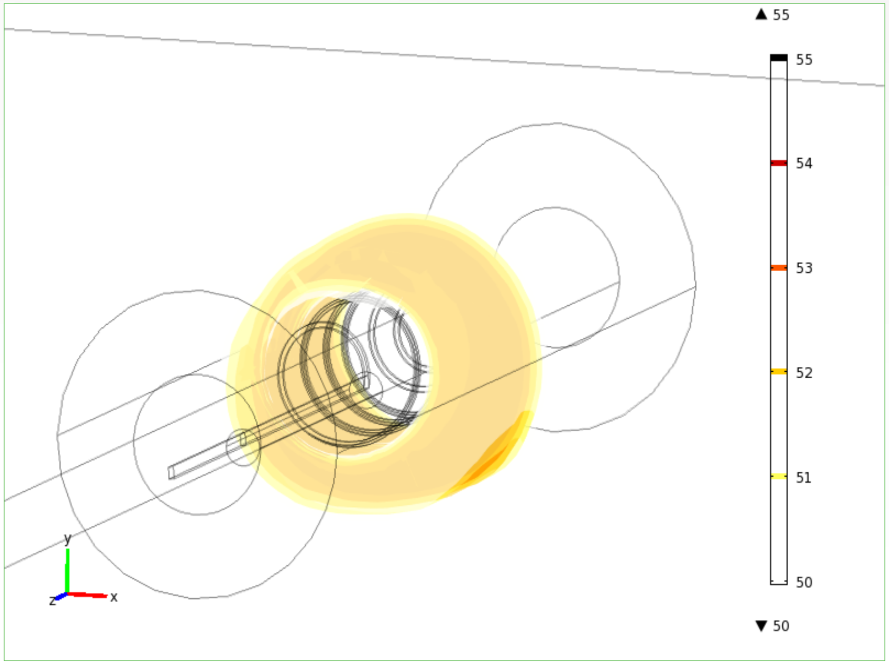


- Symmetrical ablation pattern on vessel wall circumference
- Lower temperature values close to water flow, due to convective cooling effect of water flow

RESULTS & DISCUSSION:
Numerical modeling: ablation patterns and temperature profile

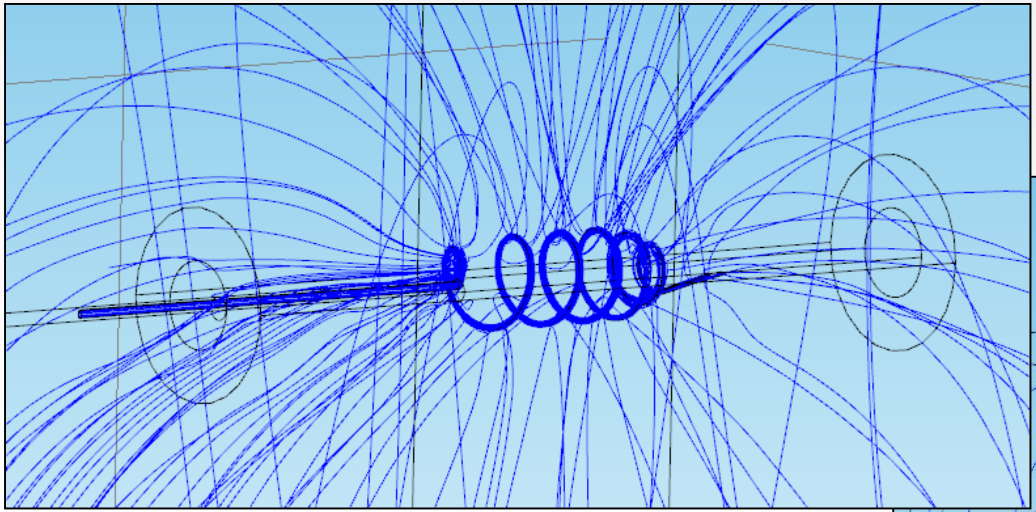
50 degC isotherm surfaces → used for approximation of ablation zone boundaries(*)

TEMPERATURE ISOSURFACE PLOT [degC]
(vessel wall)

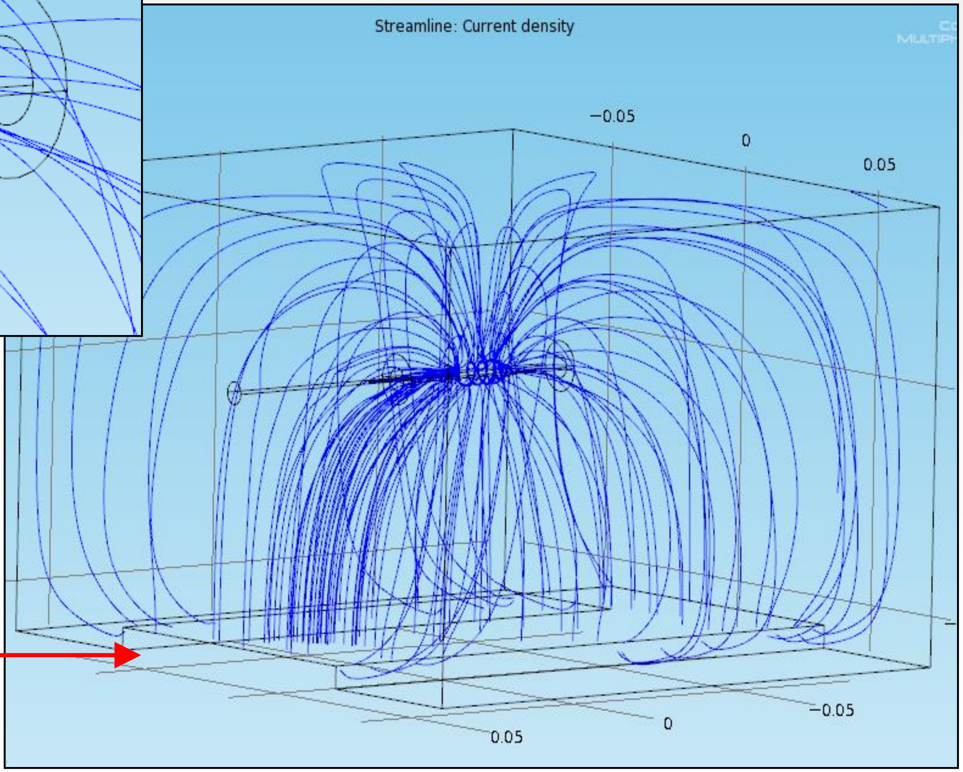


(*) Haemmerich D. "Biophysics of Radiofrequency Ablation", Crit Rev Biomed Eng, in press, 2010

RESULTS & DISCUSSION:
Numerical modeling: ablation patterns and temperature profile



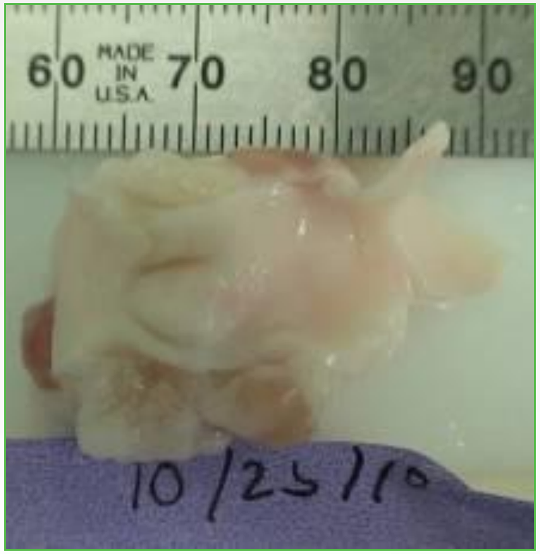
CURRENT DENSITY STREAMLINES PLOT

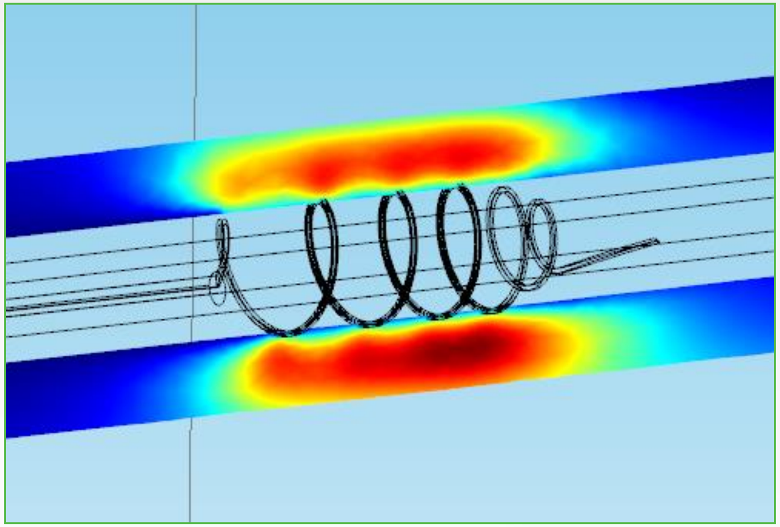


Electric current flows through the artery wall and the water, reaching the ground plate on the bottom of the water bath.

RESULTS & DISCUSSION:
Comparison between numerical results and experimental data

- SIMILAR ABLATION PATTERN IN ARTERIAL VESSEL WALL





- SIMILAR ABLATION TEMPERATURE IN ARTERIAL VESSEL WALL

	Temperature [degC]	
Time [s]	Test # 13	Simulations(*)
60	~56	~57
90	~56	~59

(*) Maximum temperature value in vessel wall domain

CONCLUSIONS & FUTURE DEVELOPMENTS:

CONCLUSIONS → COMPARISON BETWEEN *EX-VIVO* BENCH TESTING AND SIMULATION RESULTS PROVES THE FEASIBILITY OF VALIDATION OF TISSUE ABLATION NUMERICAL MODEL

→ VERSATILE MEANS TO REPRODUCE SEVERAL DESIGNS AND OPERATING CONDITIONS

FUTURE DEVELOPMENTS

- Specific tissue parameter fine tuning

  (e.g., Temperature dependent tissue properties, better-defined NiTi properties)
- Refinement of RF generator modeling
- Better interaction with experimental bench setup

  (e.g., *ex vivo* temperature recording refinement)

THANK YOU FOR YOUR ATTENTION

Backup Slides

Marco Miliani
R&D Sr. Project Engineer

Finite Element Analysis of an RDN stent

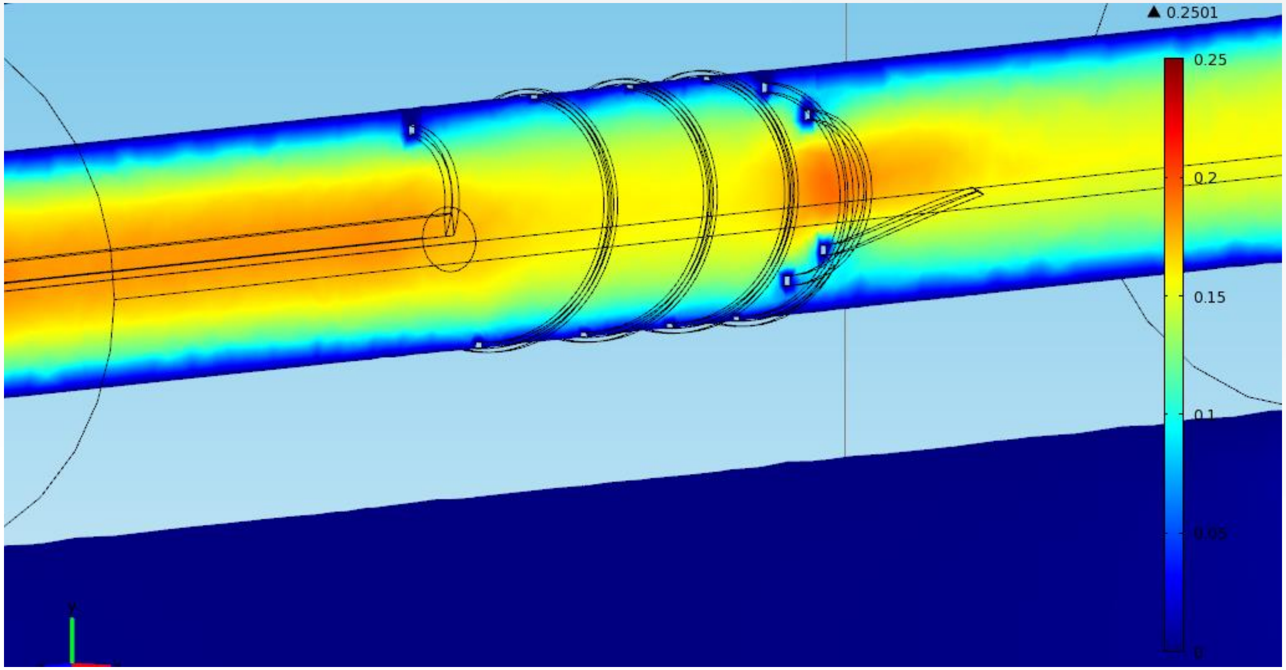
Model limitations

- Model geometries are simplified
- Temperature-dependent changes in tissue and blood properties are neglected (i.e. thermal and electrical properties)
- The model does not account for changes in tissue conductivity by assessing tissue damage
- Not considered the impact of other blood vessels close to the ablation site

CFD & Heat Transfer coupled simulations

Methods: Boundary Conditions

VELOCITY SURFACE PLOT IN PORCINE ARTERY



Innovating for life.