POLITECNICO MILANO 1863

LASER optima

GA 759159

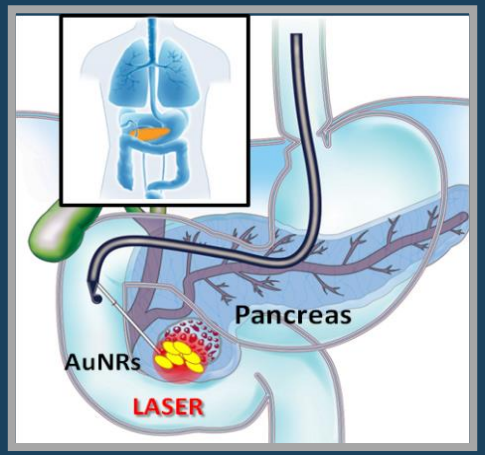
European Research Council
Established by the European Commission

Laser *su misura* per il trattamento dei tumori

Seminari di Cultura Matematica

Paola Saccomandi, PhD

Politecnico di Milano
Department of Mechanical Engineering
Italy

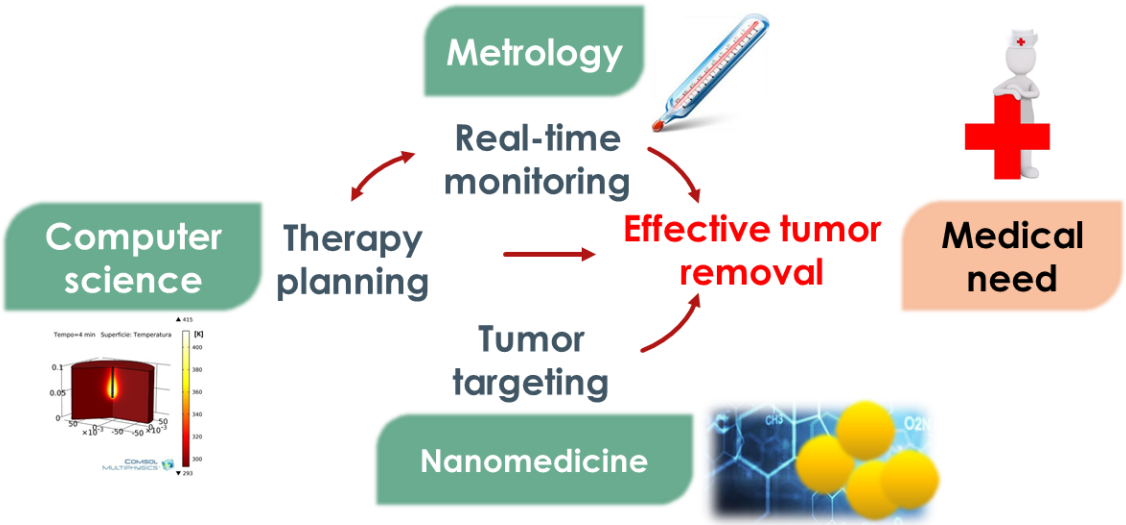


27/03/2019, Milano

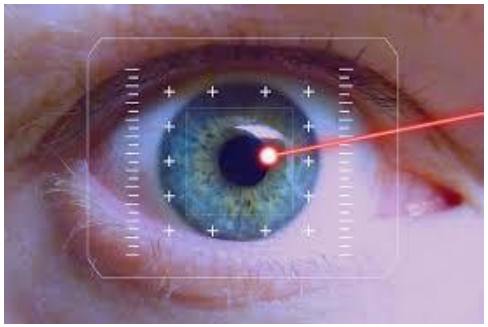
ERC Starting Grant 2017

LASER OPTIMAL

Laser Ablation: SElectivity and monitoRing for OPTImal tuMor removAL



This project has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (GA n. 759159)



Ophthalmology

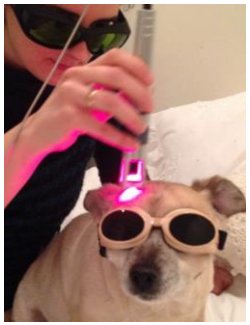
Pain relief

Surgery

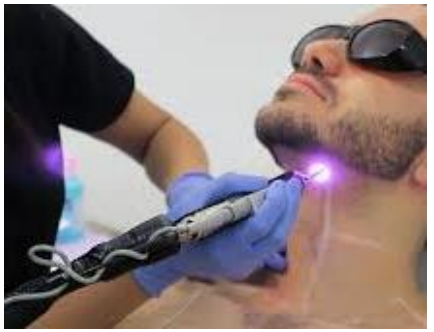
Laser in medical applications

Dentistry

Veterinary



Cosmetics

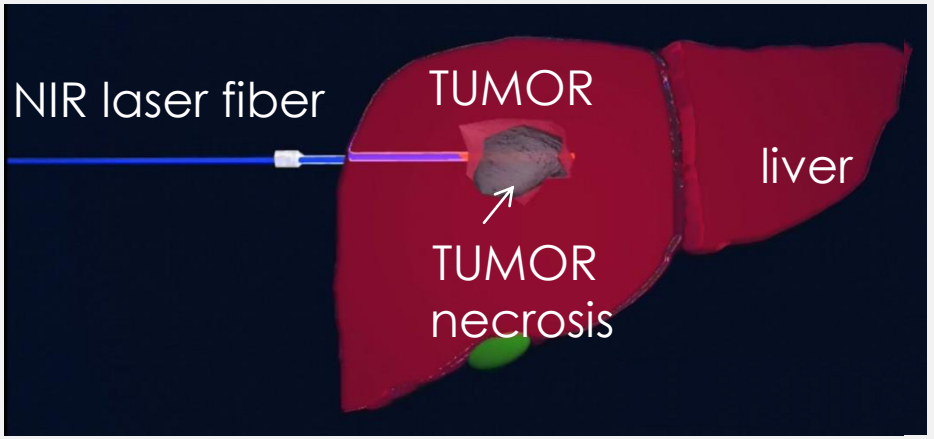


Laser Ablation

increases **tissue temperature**

(>50 °C)

to induce coagulative tumor necrosis



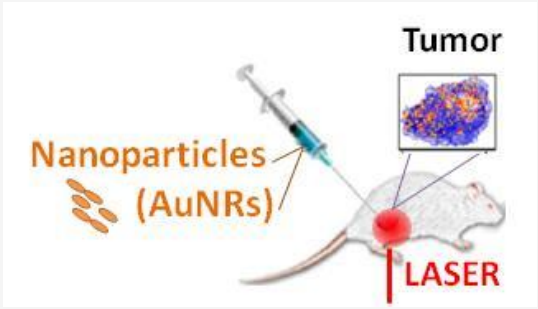
Final aims of optimal thermal ablation

- ✓ **Necrosis** of the whole tumor (+ safety margins)
- ✓ **Minimize** the thermal damage to the surrounding healthy tissue

1. Nanoparticles
Tumor targeting and selectivity

Inoculation of gold nanorods in tumor

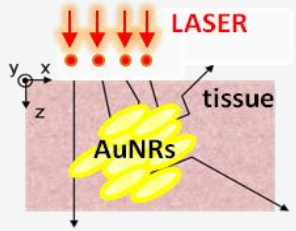
(surface plasmon resonance)



Mooney, .., Saccomandi ***Int J Hyperthermia*** 2017

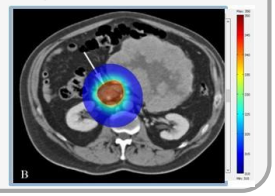
2. Therapy planning
Defining optimal LASER settings

- Numerical model of temperature map in tumor during NIR LASER ABLATION
- Simulation NIR laser-AuNRs-tissue interaction



Saccomandi, ***Las Med Scie*** 2016

- Analysis of pre-operative patient images



Saccomandi ***IEEE Trans Biomed Eng*** 2012

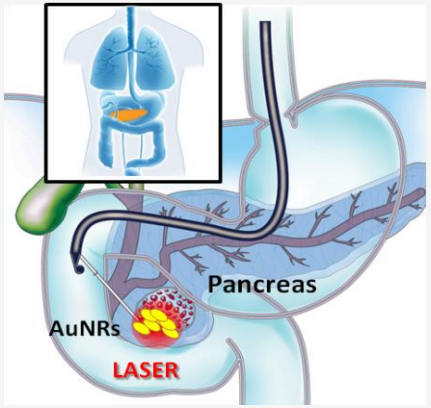
Goal

TUMOR REMOVAL

Safe & Selective

3. Laser ablation
Tumor treatment

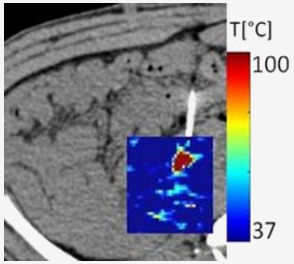
Endoscopic/ percutaneous guidance of laser fiber in tumor



Di Matteo, Saccomandi ***Gastrointest Endoscopy*** 2014,2016

4. Thermometry
Real-time feedback

- Real-time measurement of **tumor temperature gradient: index of therapy efficacy**
- Accuracy/sensitivity assay of various approaches *optical sensors, CT, MR images*



Saccomandi ***Int J Hyperthermia*** 2013,***Phys Med Biol*** 2013, ***Med Eng Phys*** 2015

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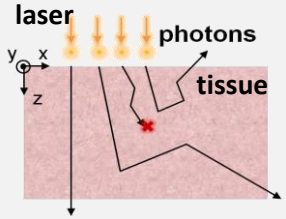
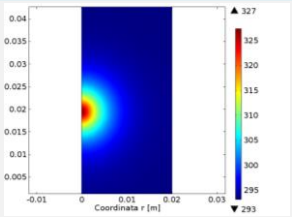
•Laser tissue-interaction: from mathematical model to clinical practice

Laser energy

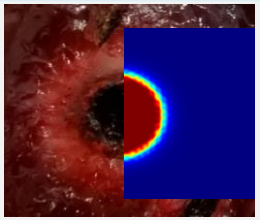
Absorption



Temperature increase



Thermal damage



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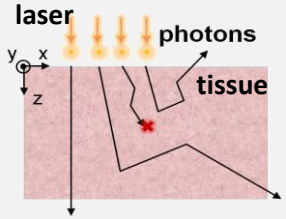

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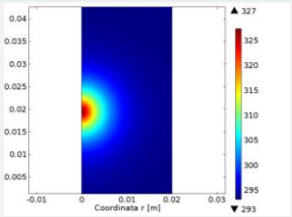
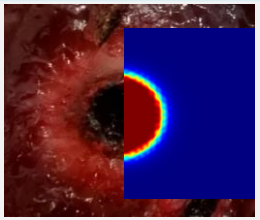
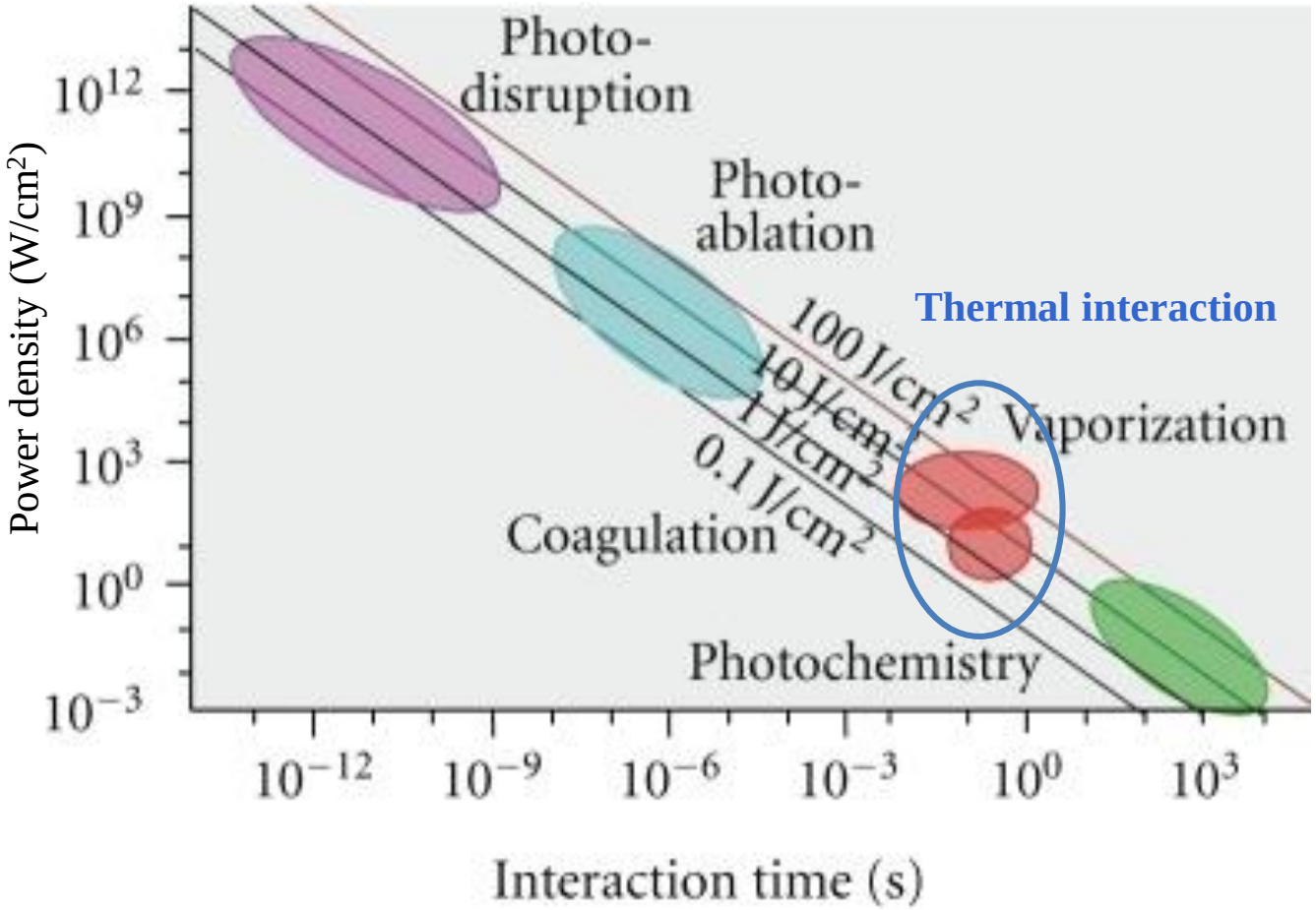


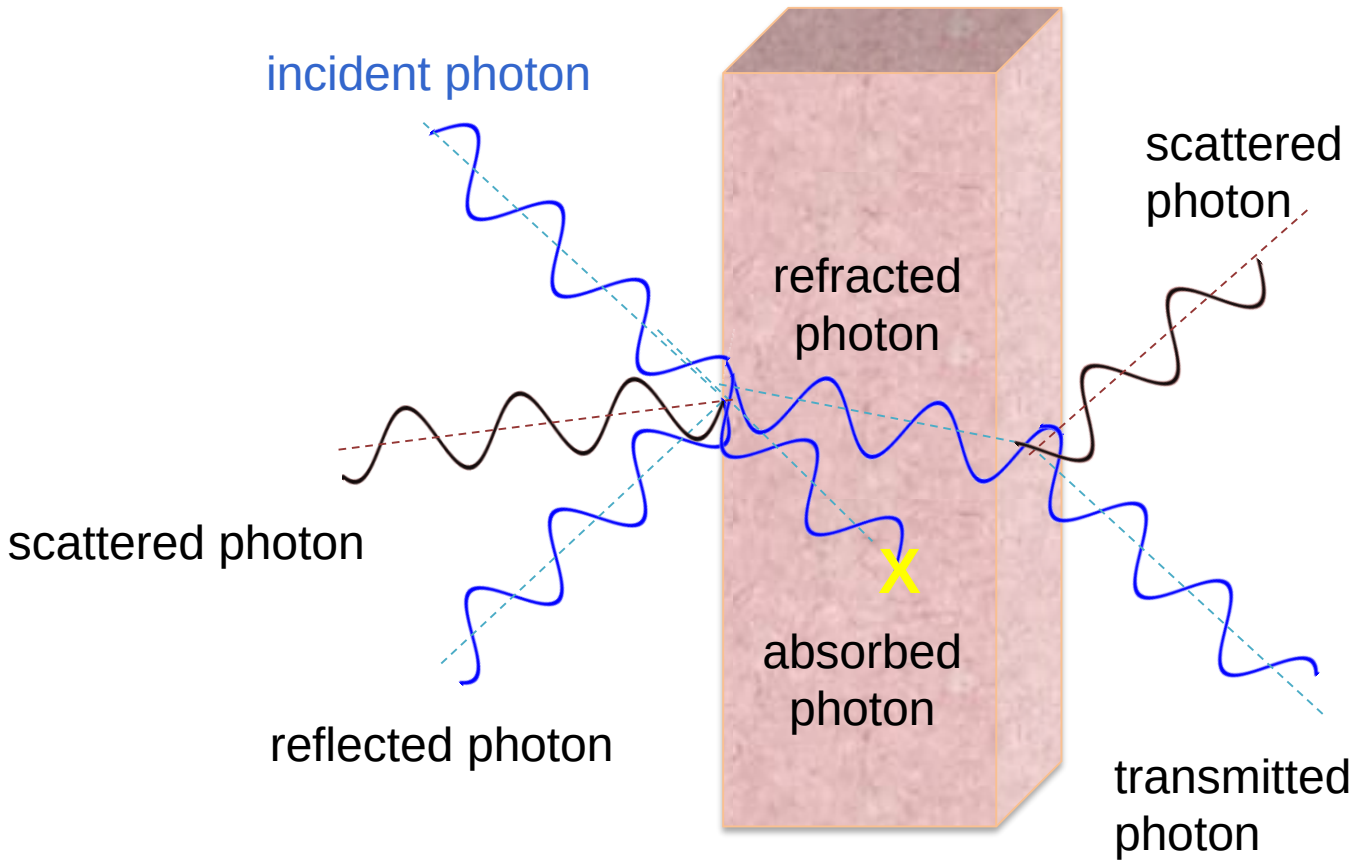
Thermal damage



Mechanisms of laser-tissue interaction



Biomedical Optics: fundamentals

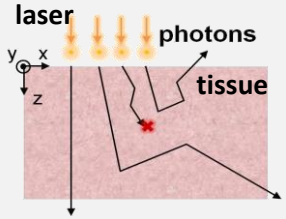


Biomaterials are complex structures, so any combination of interaction with light is possible.

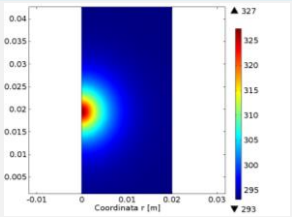
•Laser tissue-interaction: from mathematical model to clinical practice

Laser energy

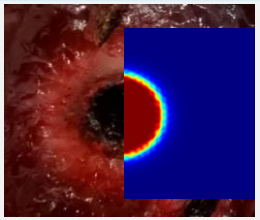
Absorption



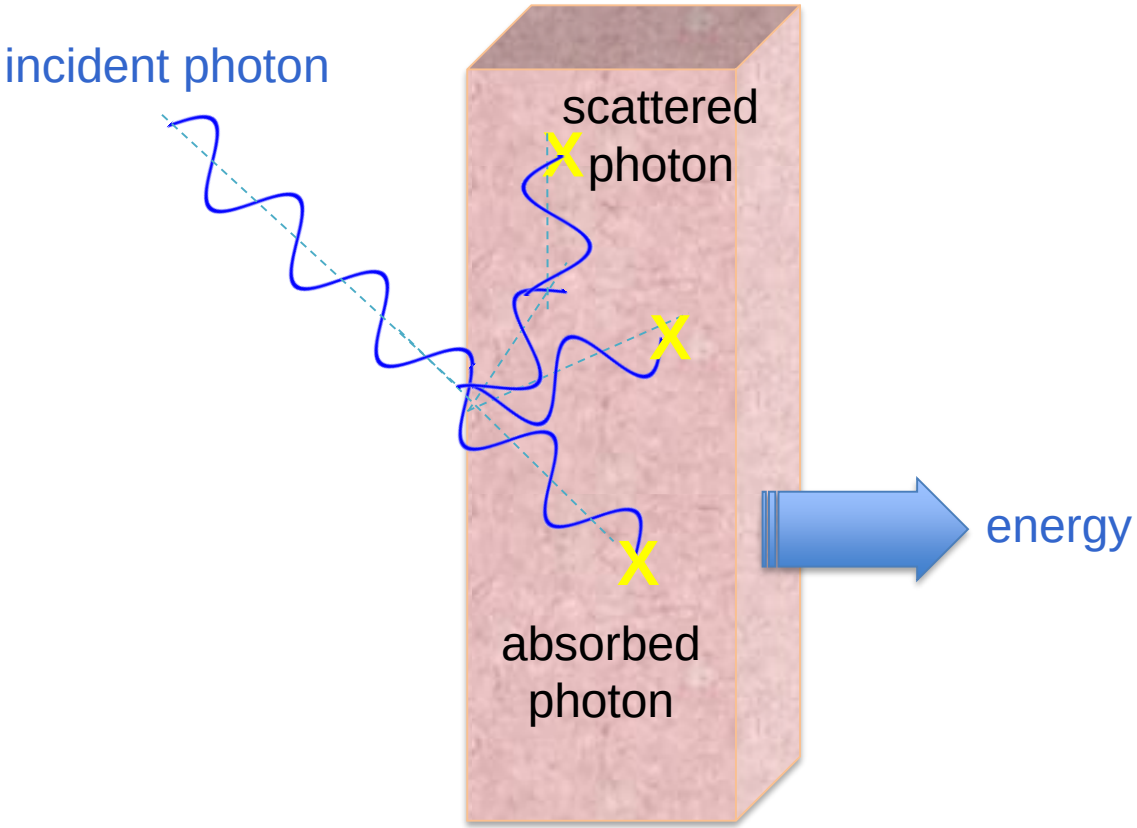
Temperature increase



Thermal damage



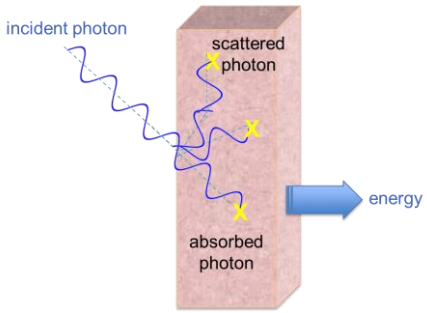
Biomedical Optics: fundamentals



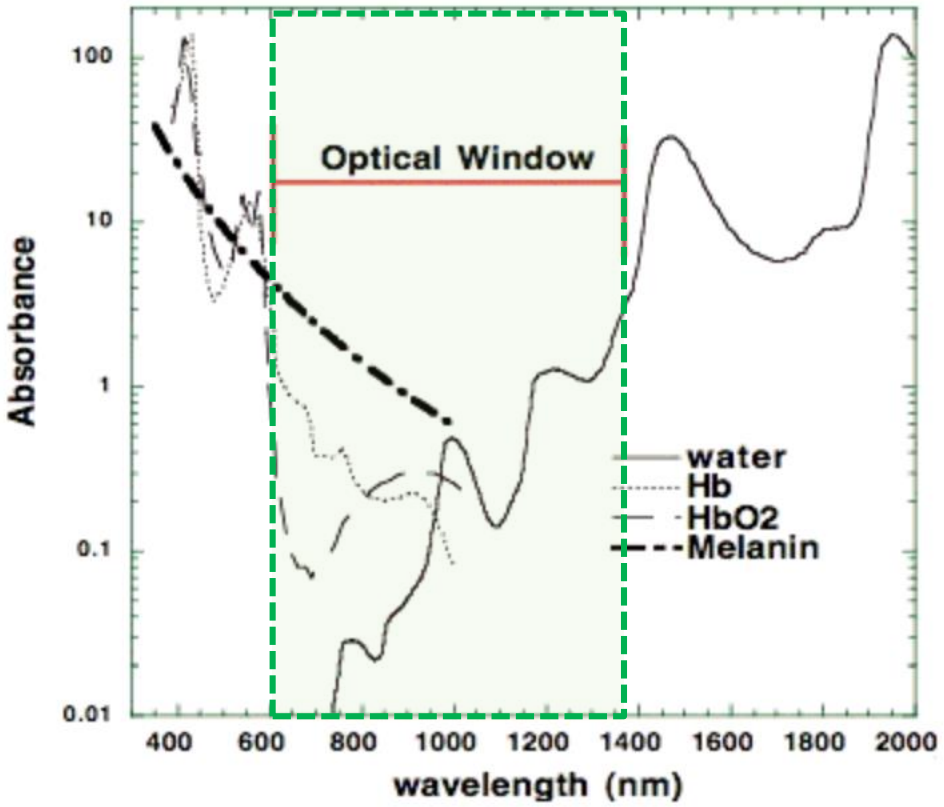
Scattering:
change in the direction of motion of a particle after collision with another particle

Absorption:
the loss of light as it passes through the tissue, and it is converted into another energy form

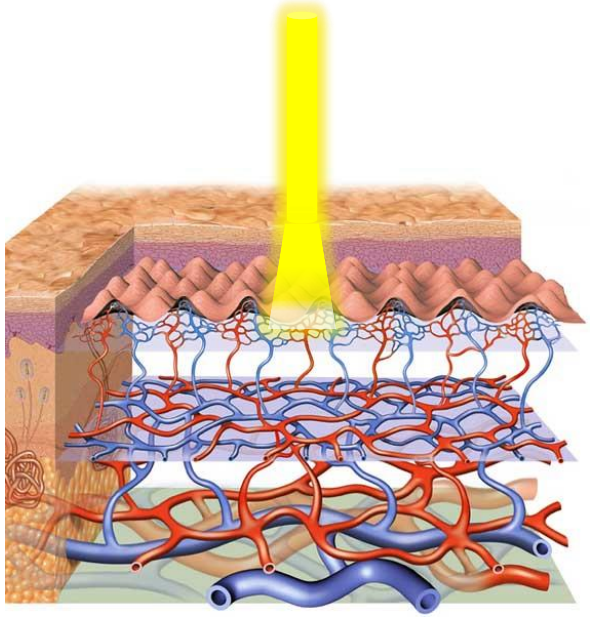
Biomedical Optics: fundamentals



The ability of light to penetrate a tissue
and deposit energy in tissues is key to therapeutic applications



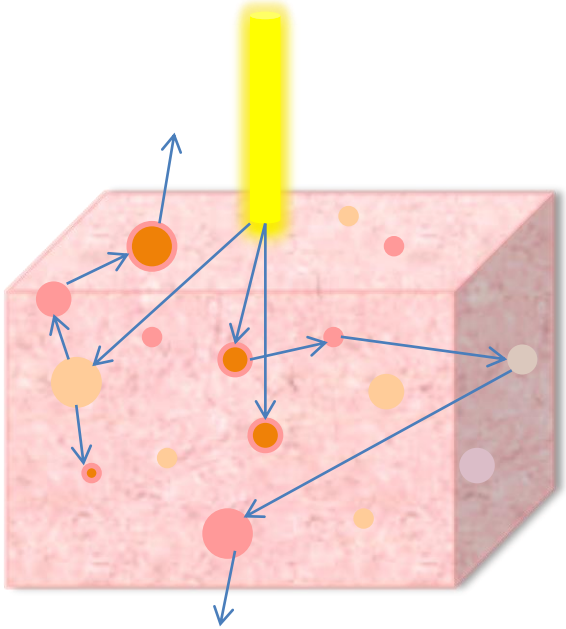
advantages of reduced absorption and scattering
→ deeper penetration of light inside tissues



Turbid medium

the scattering phenomenon is *strong*

An exact modelling of the inhomogeneous and **turbid** tissue is not available.
The tissue is represented as an **absorbing bulk material with scattering particles** randomly distributed over the volume.



Lambert-Beer law – Phase function

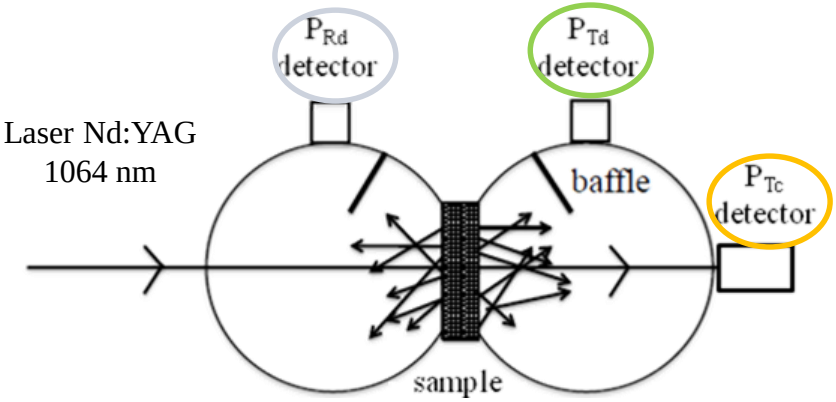
attenuation (scattering and absorption)

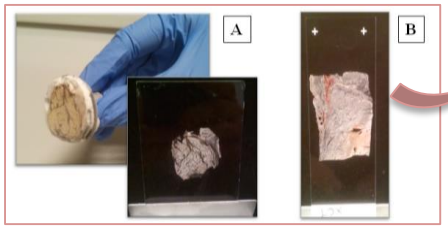
"The Deeper the Glass, the Darker the Brew, the Less of the Incident Light that Gets Through"

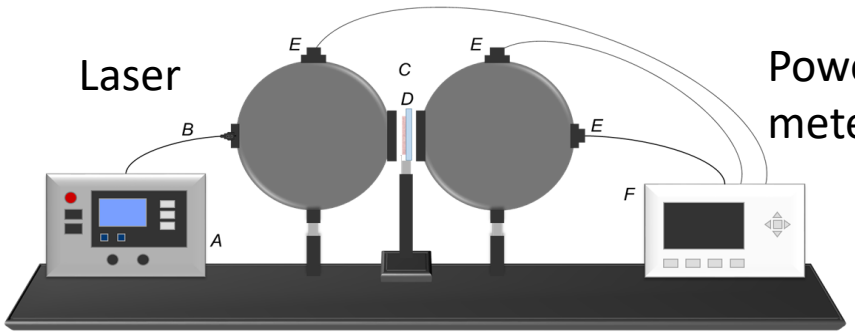
$$I(z) = I_0 \cdot e^{-\mu_{eff} \cdot z}$$

$$\mu_{eff} = \sqrt{3\mu_\alpha[\mu_\alpha + \mu_s(1-g)]}$$

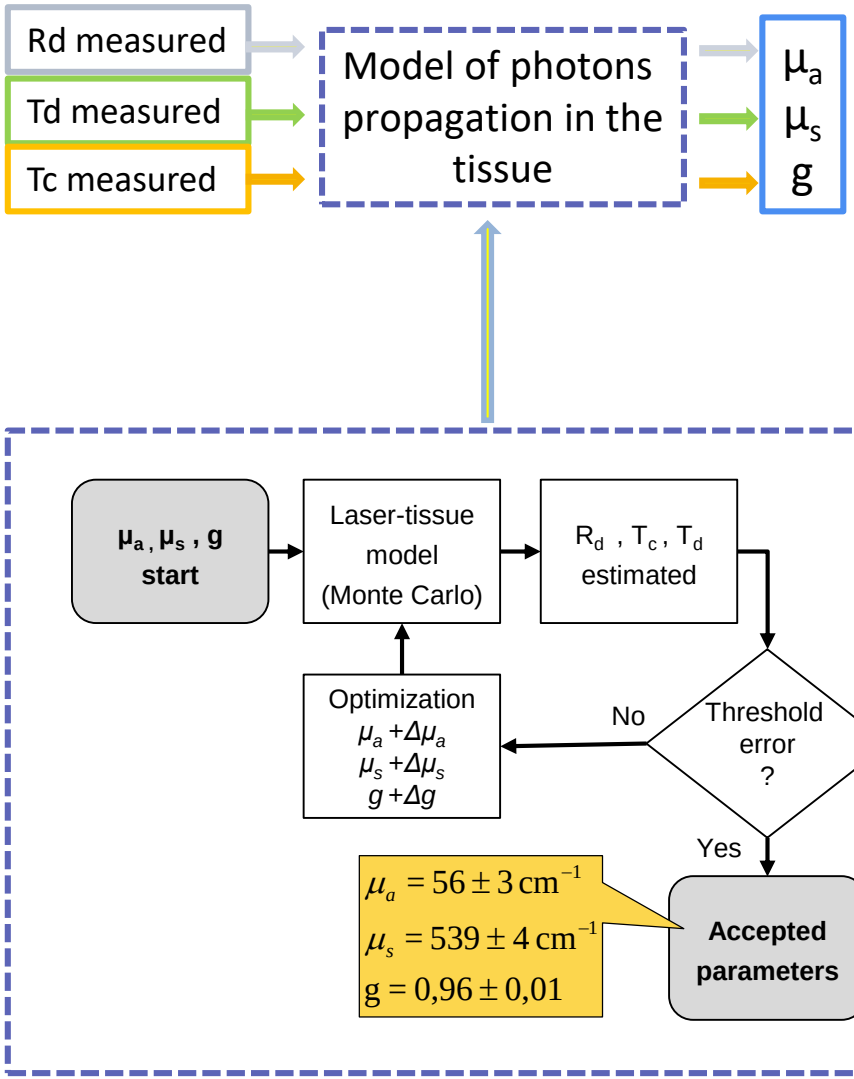
Absorption coefficient	Scattering coefficient	Anisotropy coefficient
μ_a [cm^{-1}]	μ_s [cm^{-1}]	g
~0.1 cm^{-1}	~100 cm^{-1}	~0.95

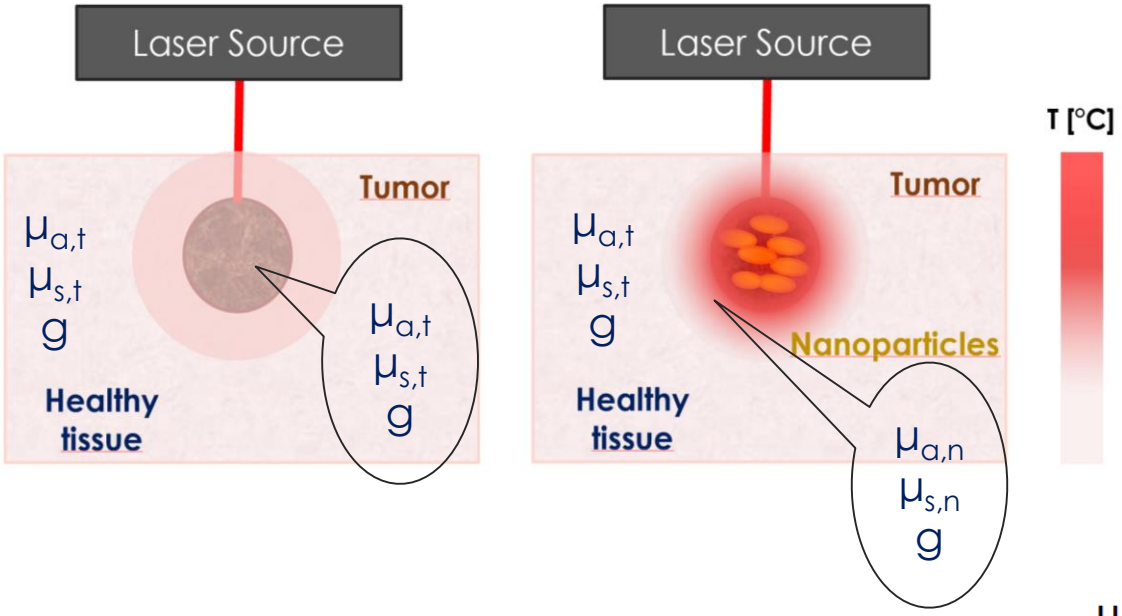


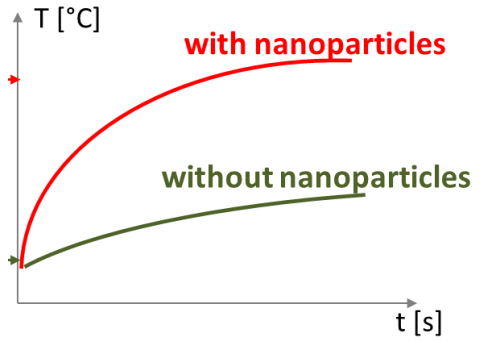




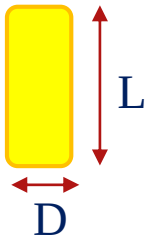
Optical properties estimation







Quantity	Value	Unit
ρ	1050	$kg \cdot m^{-3}$
c	3700	$J \cdot kg^{-1} \cdot K^{-1}$
k	0.5	$W \cdot m^{-1} K^{-1}$
ρ_b	1060	$kg \cdot m^{-3}$
c_b	3640	$J \cdot kg^{-1} \cdot K^{-1}$
w_b	0.02	s^{-1}
μ_{at}	5.7	cm^{-1}
μ_{st}	97	cm^{-1}
μ_{an}	40.6	cm^{-1}
μ_{sn}	0.0028	cm^{-1}
g	0.94	cm^{-1}
D	10	nm
L	41	nm
λ	800	nm



$$\mu_{eff} = \sqrt{3\mu_a[\mu_a + \mu_s(1-g)]}$$

$$\mu_a = \mu_{at} + \mu_{an}$$

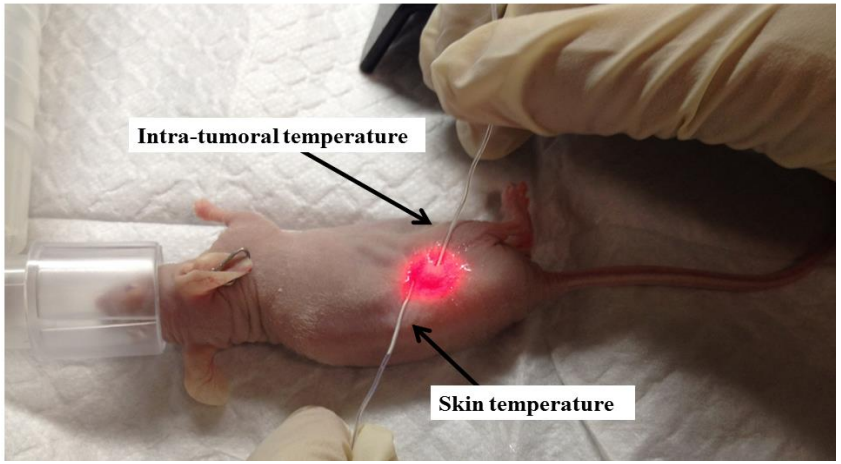
$$\mu_s = \mu_{st} + \mu_{sn}$$

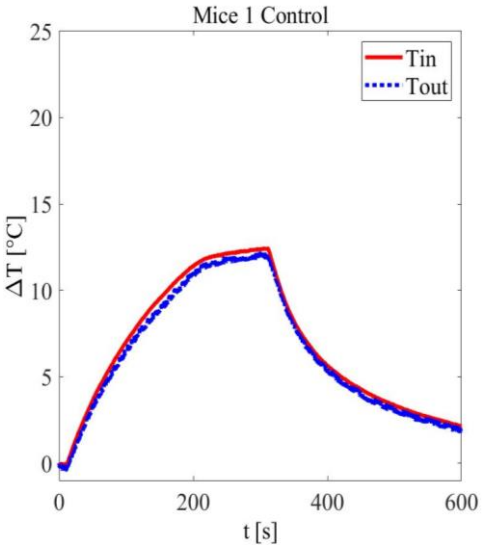
$$\mu_{an} = \frac{2\pi f_v}{\lambda V_{np}} imag\left(\frac{a_1}{3} + \frac{a_2}{3} + \frac{a_3}{3}\right),$$

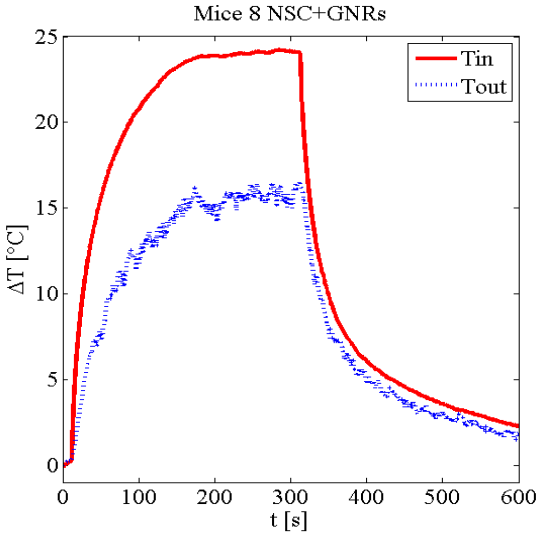
$$\mu_{sn} = \frac{16\pi^3 f_v}{18\lambda^4 V_{np}}\left(|a_1|^2 + |a_2|^2 + |a_3|^2\right)$$

$$a_i = f(D/L)$$

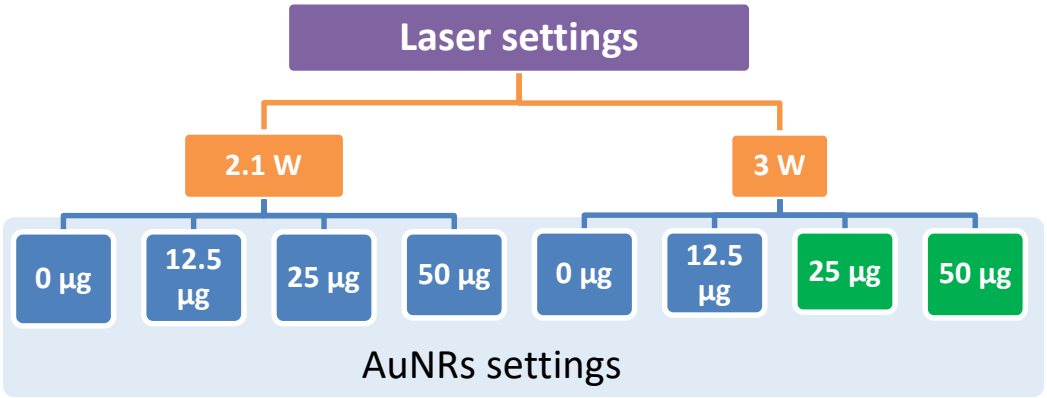
•Laser tissue-interaction: from mathematical model to clinical practice

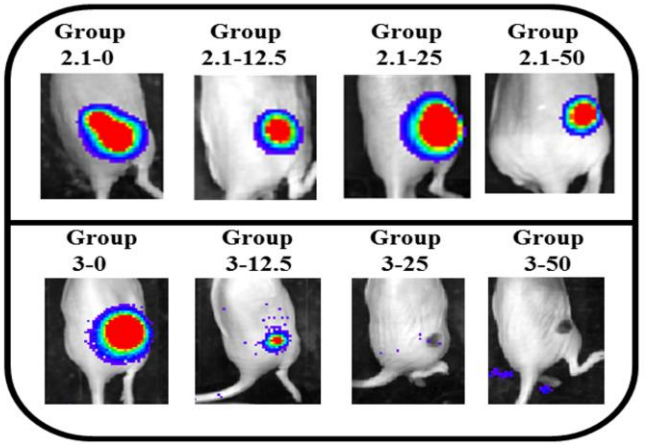






Representative xenogen images 2 days after AuNRs-mediated LA LA.





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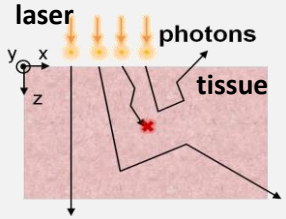
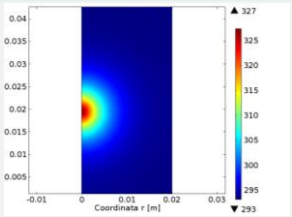
Laser energy

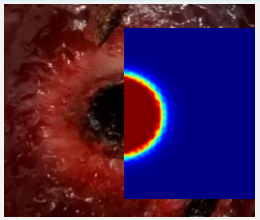
Absorption



Temperature increase



Thermal damage



Thermal outcome in living tissues

Nat Rev Cancer. 2014 Mar;14(3):199-208. doi: 10.1038/nrc3672.

Thermal ablation of tumours: biological mechanisms and advances in therapy.

Chu KF[1], Dupuy DE[1].

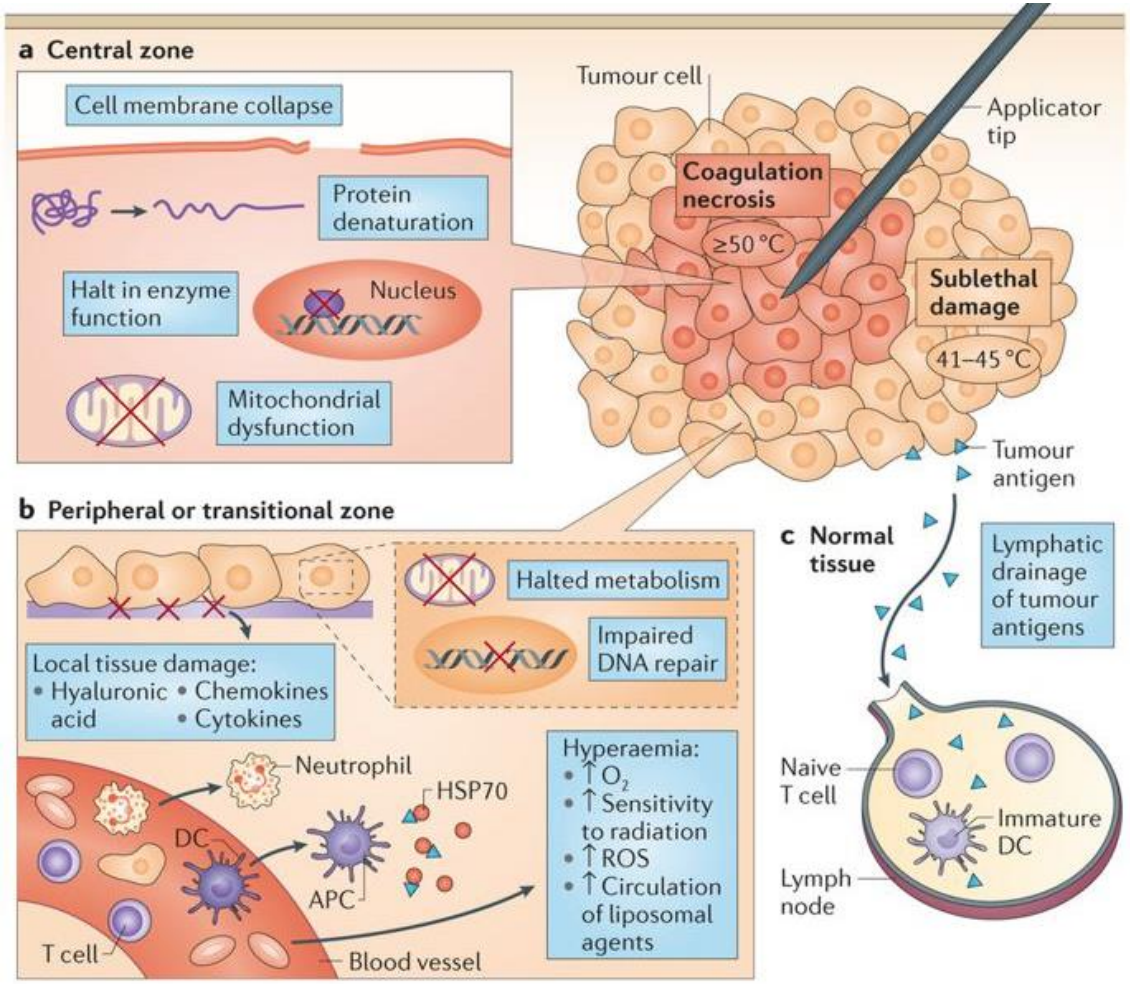
Author information

Abstract

Minimally invasive thermal ablation of tumours has become common since the advent of modern imaging. From the ablation of small, unresectable tumours to experimental therapies, percutaneous radiofrequency ablation, microwave ablation, cryoablation and irreversible electroporation have an increasing role in the treatment of solid neoplasms. This Opinion article examines the mechanisms of tumour cell death that are induced by the most common thermoablative techniques and discusses the rapidly developing areas of research in the field, including combinatorial ablation and immunotherapy, synergy with conventional chemotherapy and radiation, and the development of a new ablation modality in irreversible electroporation.

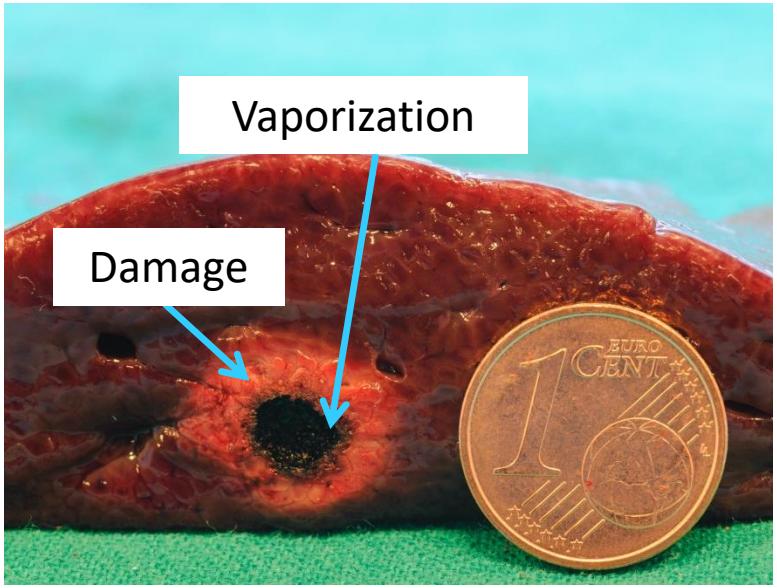
PMID: 24561446 DOI: 10.1038/nrc3672

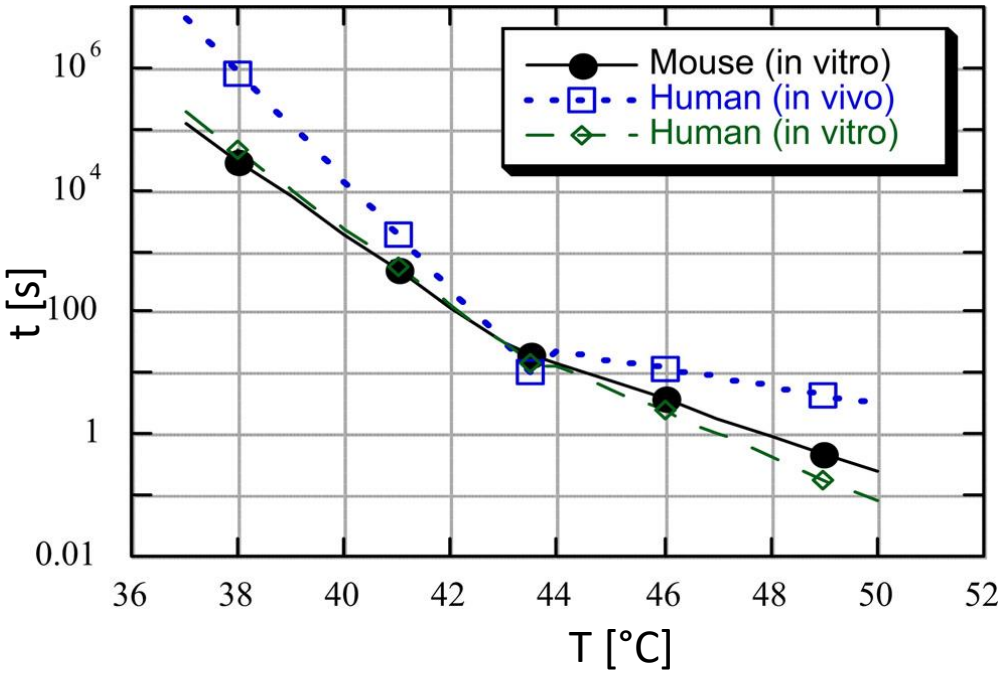
[Indexed for MEDLINE]



Nature Reviews | Cancer

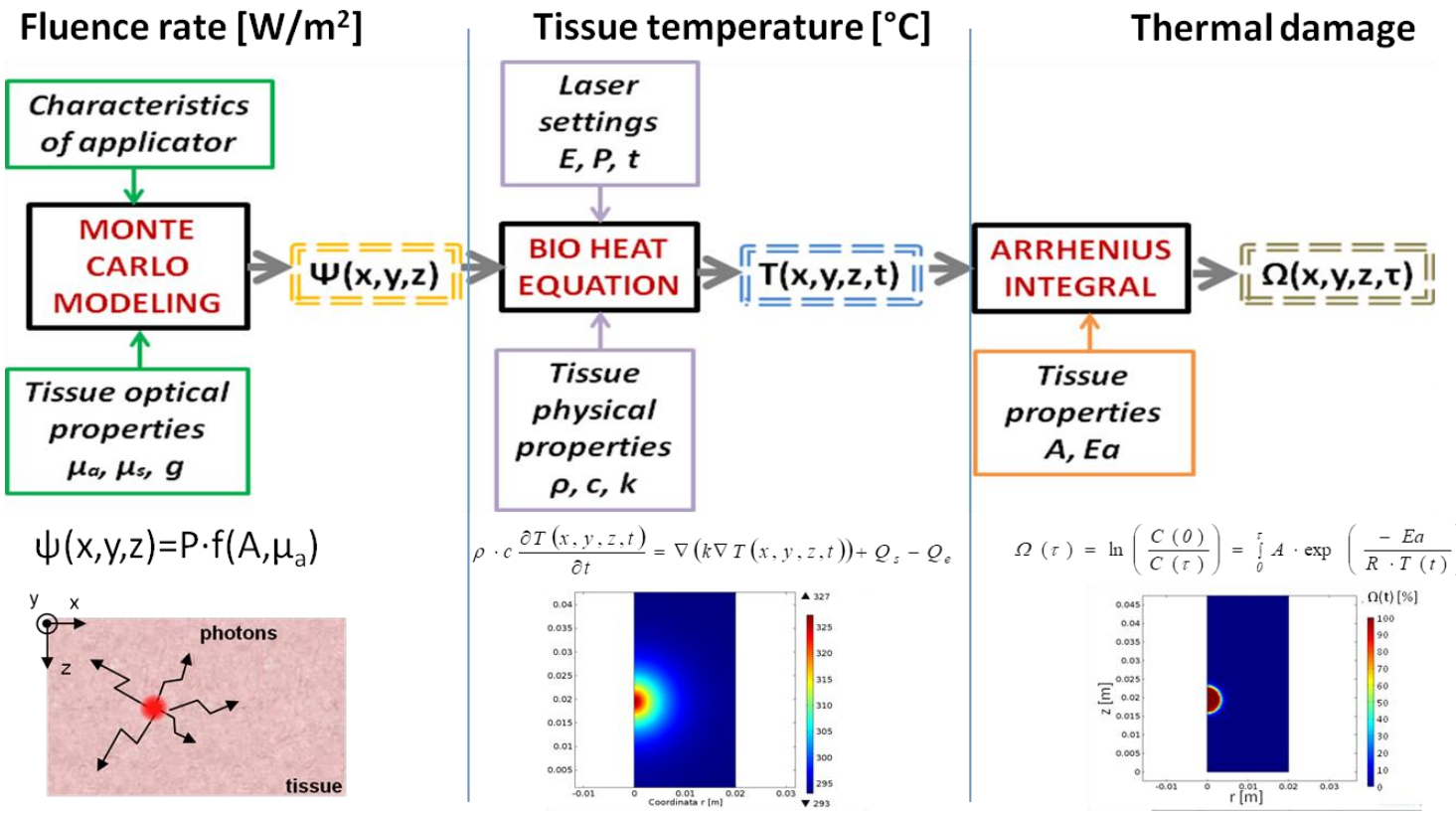
Thermal outcome in living tissues





Dewhrist, 2003 Proc SPIE Int Soc Opt Eng.

•Laser tissue-interaction: from mathematical model to clinical practice



Numerical Model approach to:

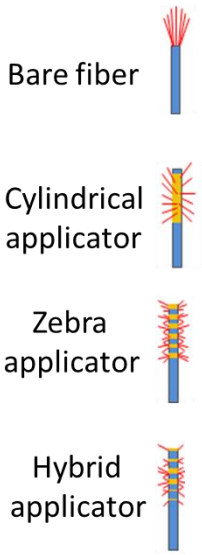
- plan the therapy (optimal settings) ⟶ Control ?
- predict the outcome

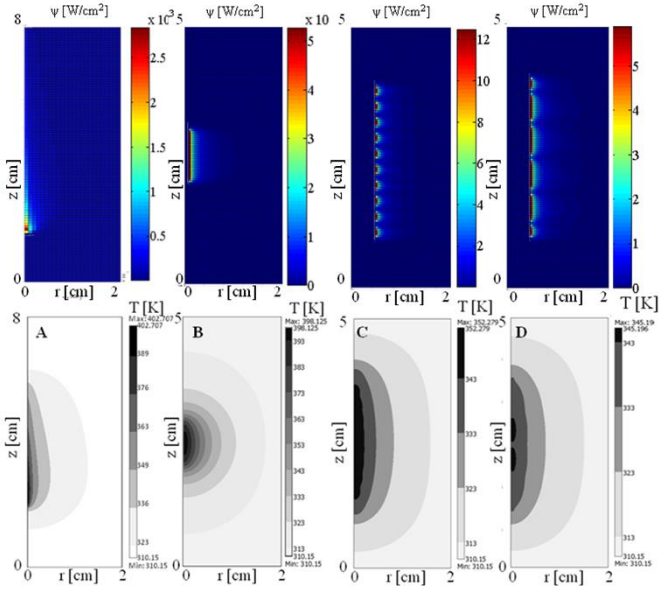
Heat transfer modeling

$$\rho \cdot c \frac{\partial T(x,y,z,t)}{\partial t} = \nabla \cdot \left(k \cdot \nabla T(x,y,z,t)\right) + Q_b + Q_m + Q_l - Q_e$$

Model inputs:

- mechanical tissue properties
- thermal tissue properties
- optical properties
- temperature dependent properties
- defined geometry of the tissue domain and of the laser fiber applicator





Models should account for:
influence of the soft tissue properties,
presence of blood vessels, ..

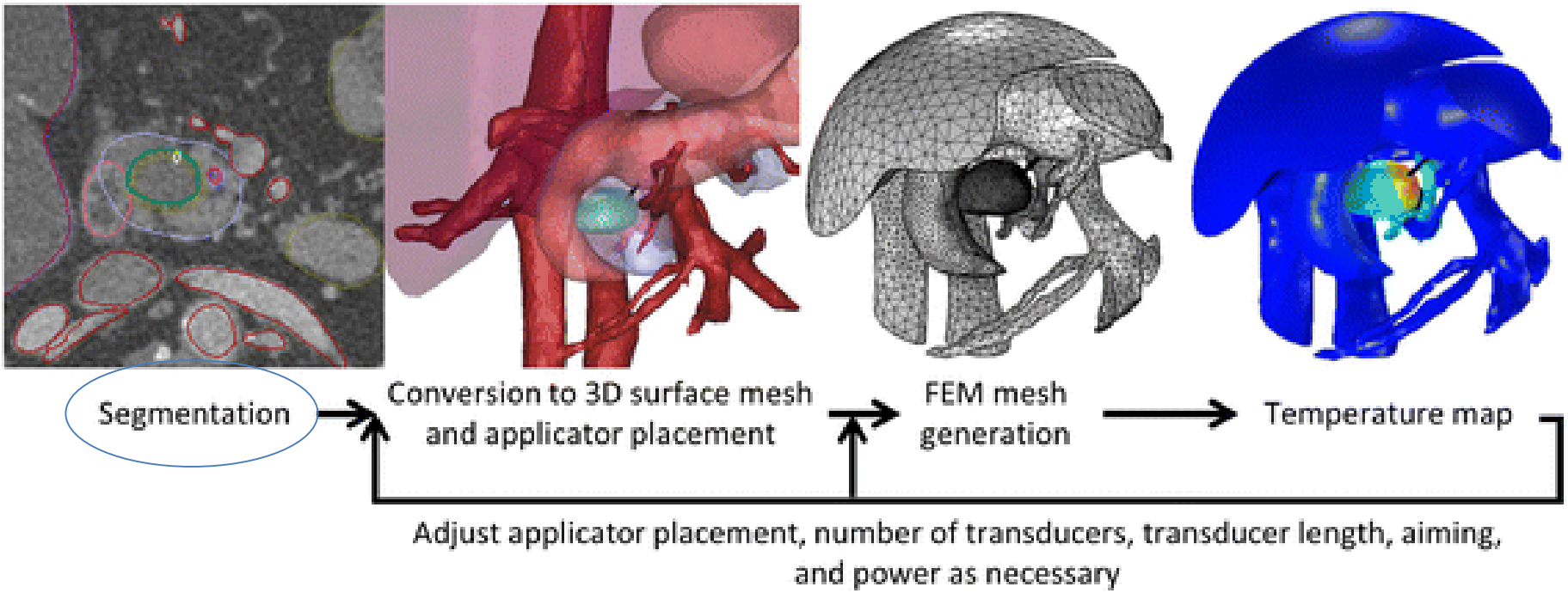
Saccomandi P, Schena E, Caponero MA, Di Matteo FM, Martino M, Pandolfi M, Silvestri S. Theoretical analysis and experimental evaluation of laser induced interstitial thermotherapy in ex vivo porcine pancreas. IEEE TRANSACTION OF BIOMEDICAL ENGINEERING, Vol. 59, n. 10, pp. 2958-2964, Ott 2012.

Hyperthermal treatment planning (HTP) systems

1. Generation of the patient model

2. Finite element analysis based on individual patient anatomies

3. Calculation of temperature distributed into the tissue



Scott, S.J., Adams, M.S., Salgaonkar, V. et al. J Ther Ultrasound (2017) 5: 10. https://doi.org/10.1186/s40349-017-0090-2. Open Access

Hyperthermal treatment planning (HTP) systems

1. Generation of the patient model

2. Finite element analysis based on individual patient anatomies (mesh generation)

3. Calculation of temperature distributed into the tissue

- no segmentation
→short computation time (30 s)
→real time use

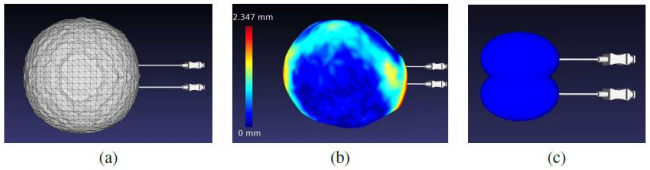
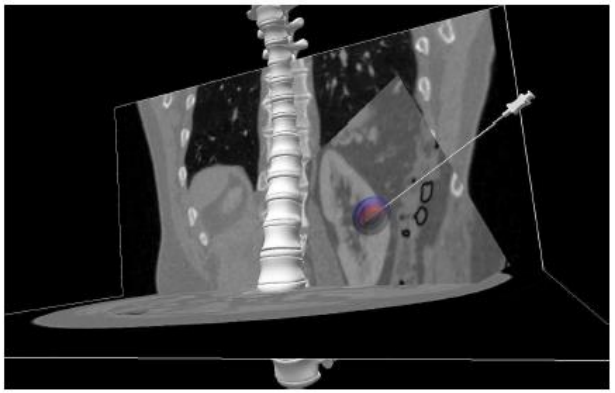


Figure 5. Iso-surface obtained from: (a) simulation, (b) patient-specific data (with Hausdorff distance) and (c) manufacturer.


(a)

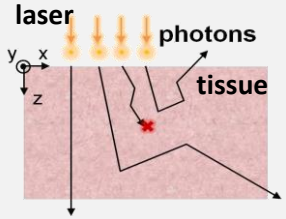

(b)

COTIN, Stephane. "Interactive planning of cryotherapy using physics-based simulation." Medicine Meets Virtual Reality 21: NextMed/MMVR21 196 (2014): 423

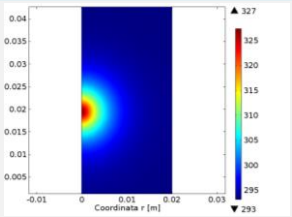
•Laser tissue-interaction: from mathematical model to clinical practice

Laser energy

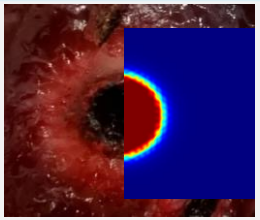
Absorption



Temperature increase

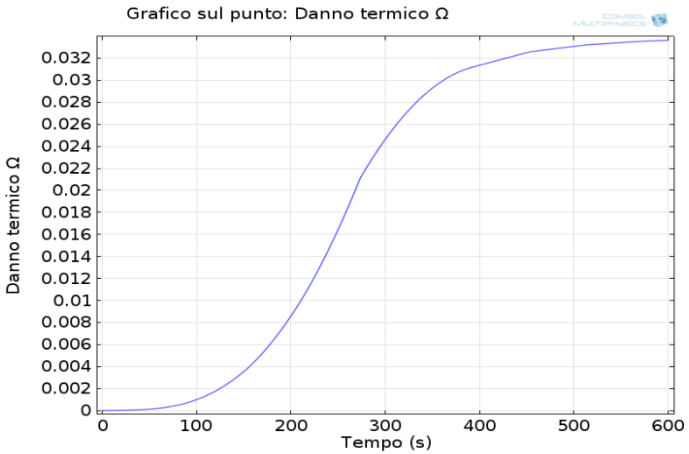


Thermal damage



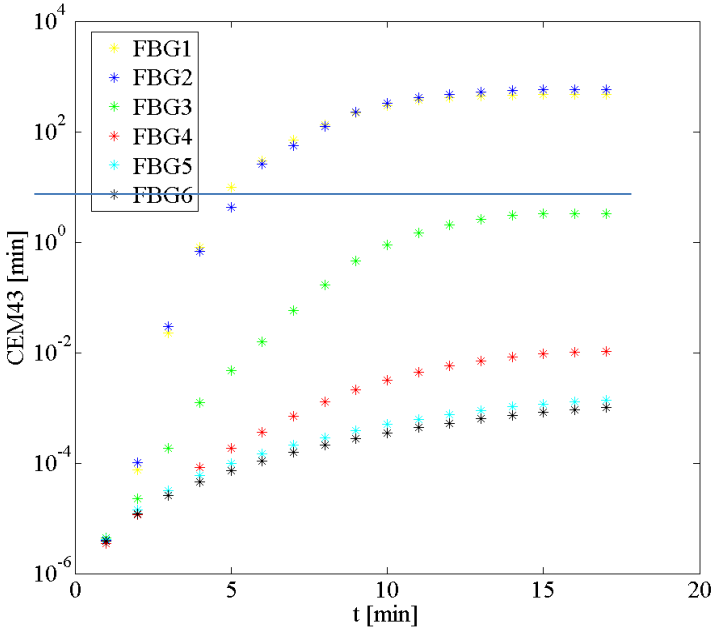
Thermal damage

$$\Omega(\tau) = \ln\left\{\frac{C(0)}{C(\tau)}\right\} = \int_0^{\tau} Ae^{\left[\frac{-E_a}{RT(t)}\right]}dt$$



Arrhenius calculations in numerical models can be used to predict the probability of irreversible thermal damage

$$CEM\,43 = \sum_{i=1}^{n} t_i \cdot R^{(43-T_i)}$$

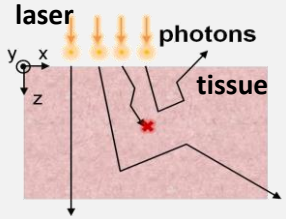


Cumulative Equivalent Minute: Conversion of any time–temperature history to an equivalent number of minutes of heating at 43 °C

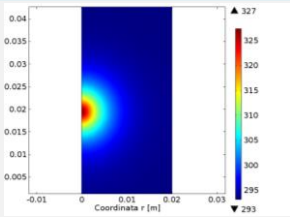
•Laser tissue-interaction: from mathematical model to clinical practice

Laser energy

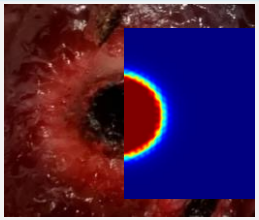
Absorption



Temperature increase



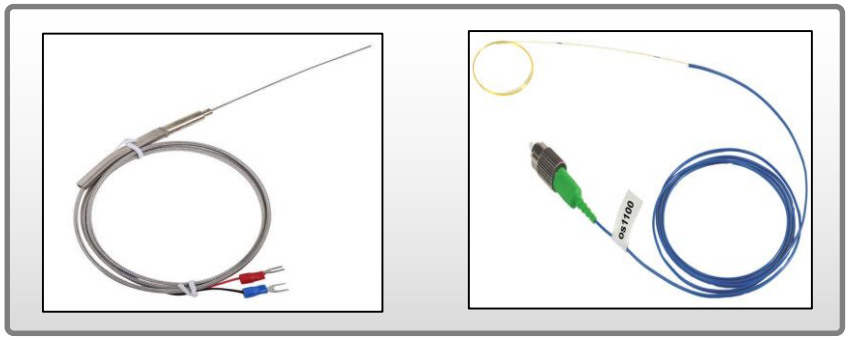
Thermal damage

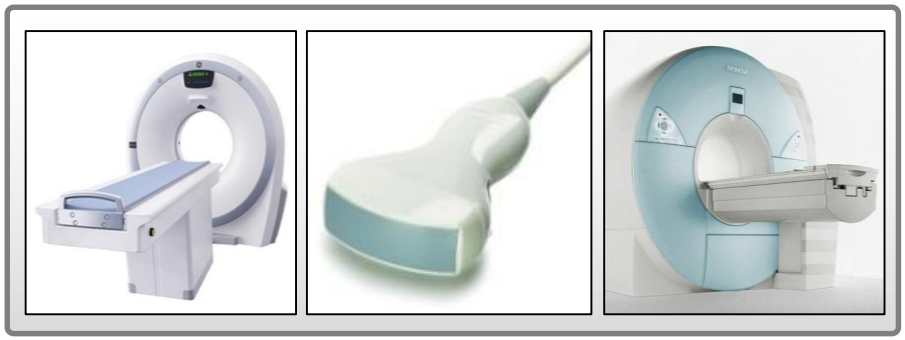


Measurement of thermal effects!

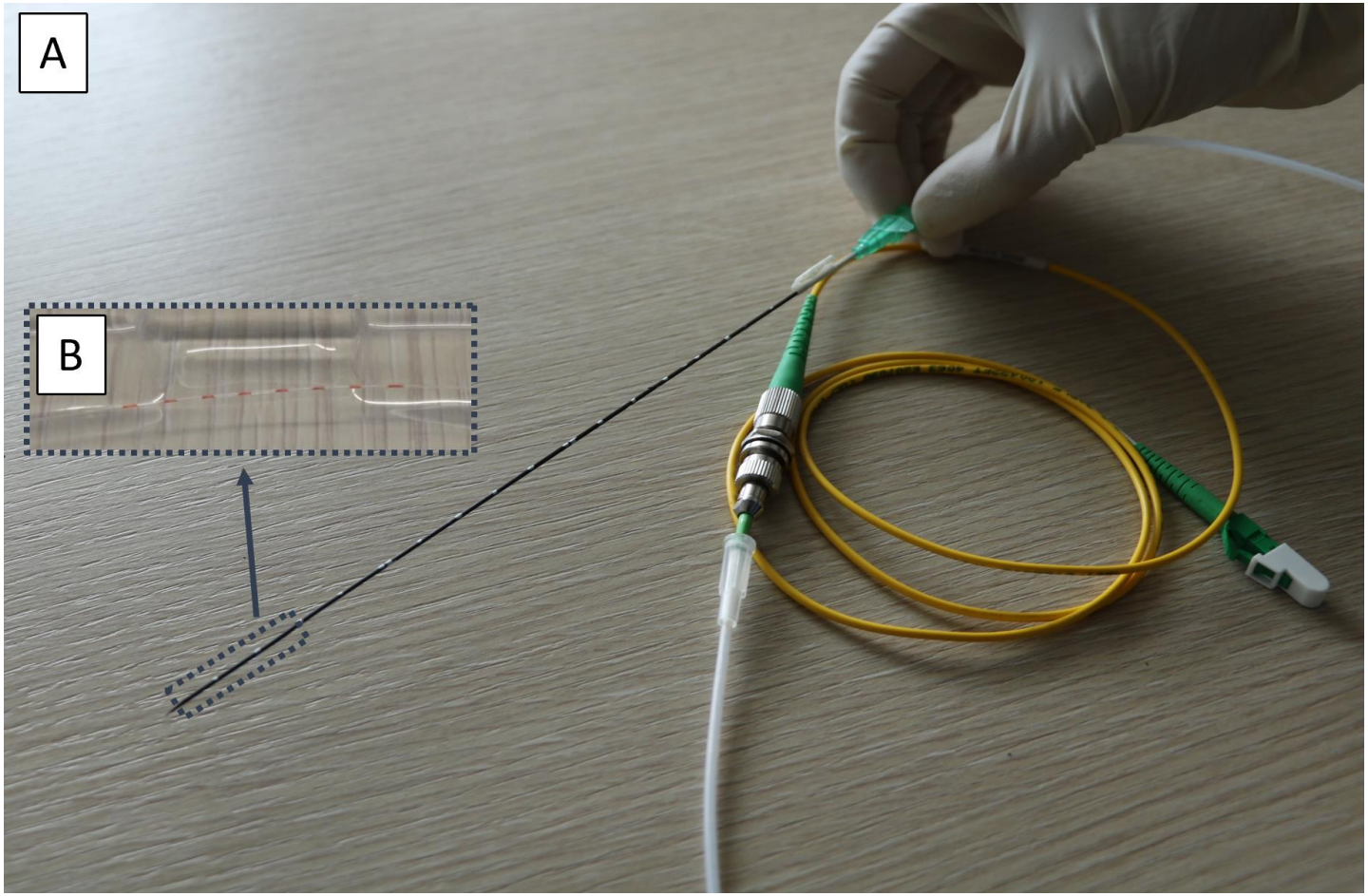
Thermometry during thermal therapies

- CONTACT *(invasive)* techniques
  - Thermocouples
  - Fiber Optic Sensors
- CONTACTLESS *(non-invasive)* techniques
  - Computed Tomography
  - Ultrasound
  - Magnetic Resonance Imaging

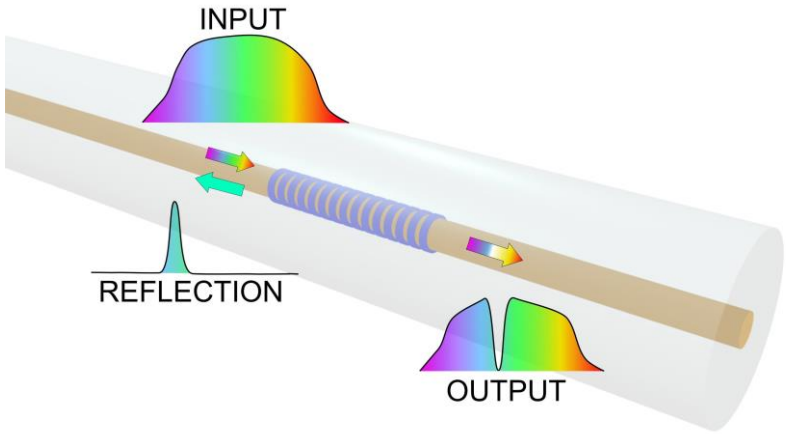


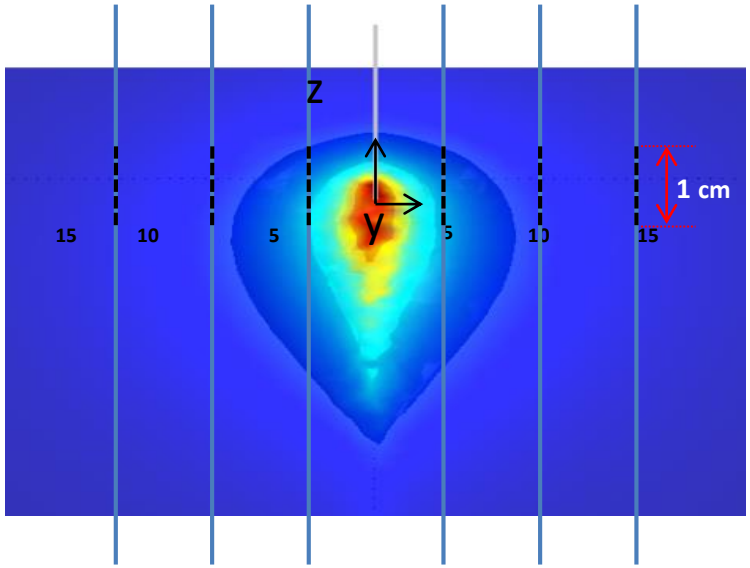


•Thermometry during laser therapy: fiber optic sensors

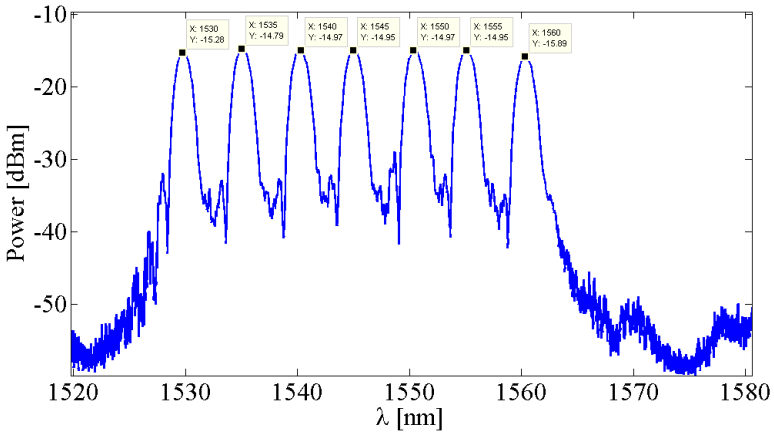


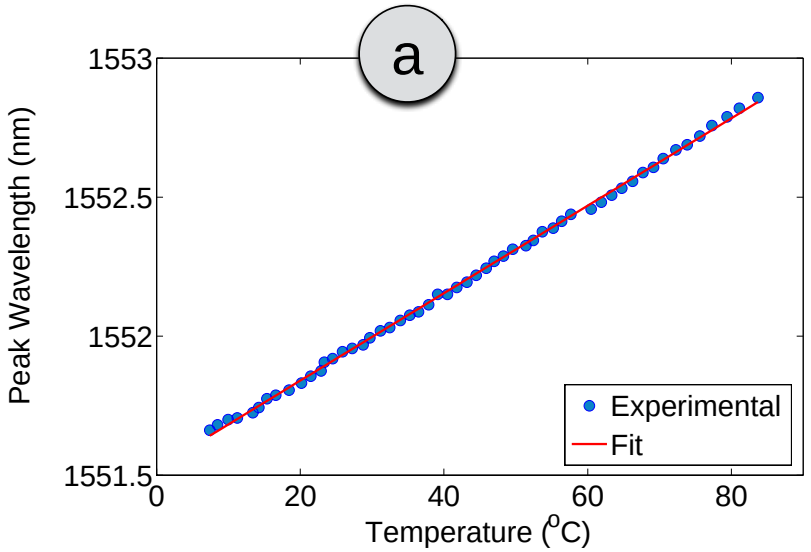
•Thermometry during laser therapy: fiber optic sensors



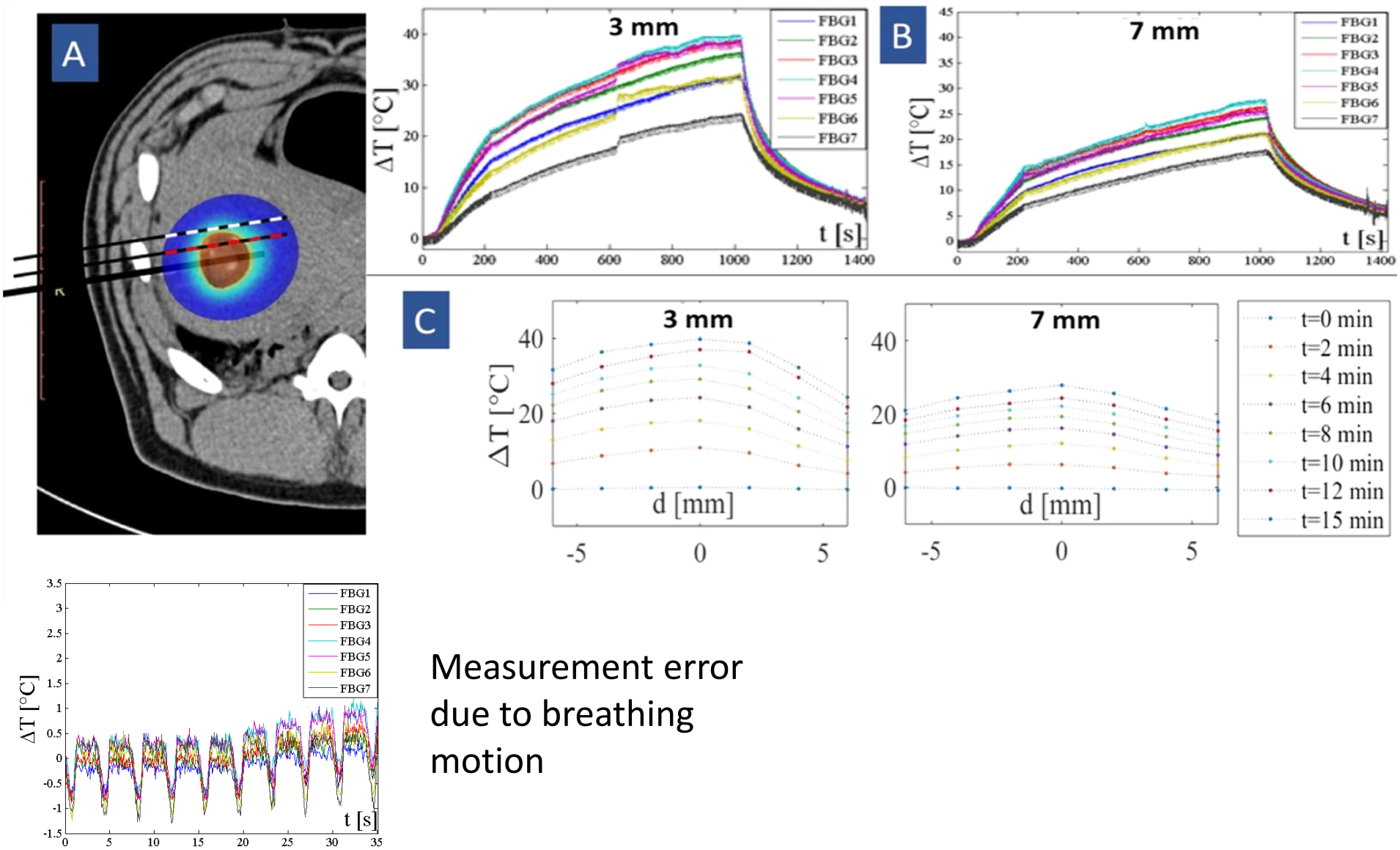


$$\frac{\Delta\lambda_B}{\lambda_B} = (1-p_e)\cdot\varepsilon + ((1-p_e)\cdot\alpha_\Lambda + \alpha_n)\cdot\Delta T$$





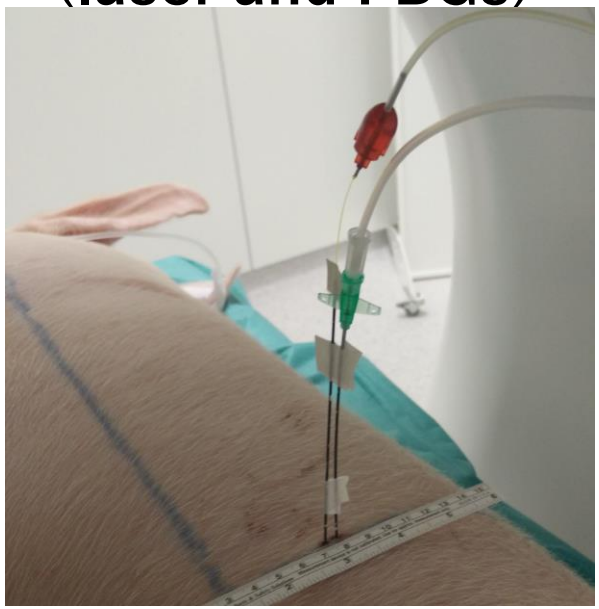
•Thermometry during laser therapy: fiber optic sensors



Measurement error due to breathing motion

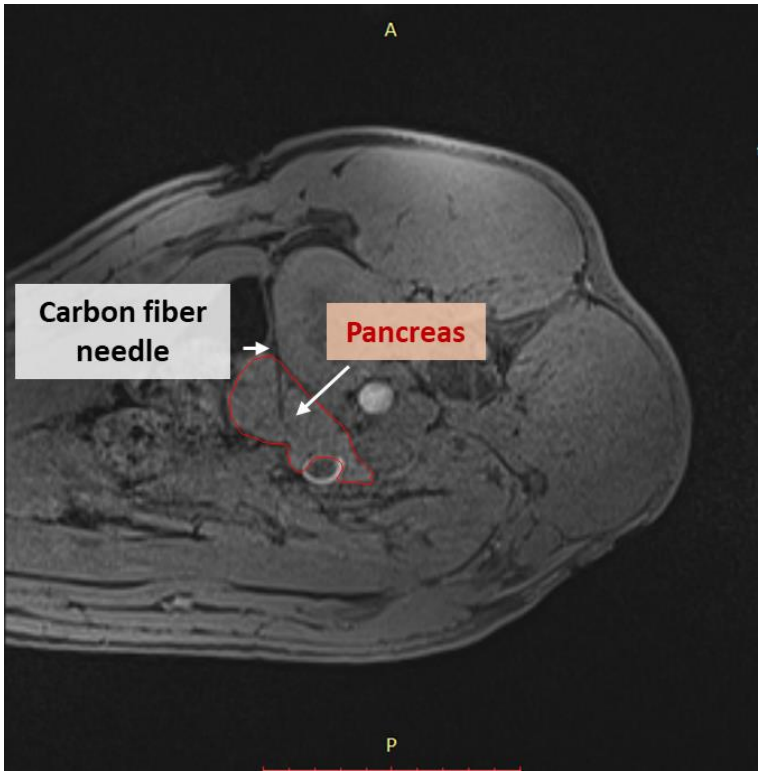
MR imaging and in vivo laser ablation

Needles placement (laser and FBGs)



Anaesthetized animal
Compliance with directive 2010/63/EU and 3Rs principles

MR imaging



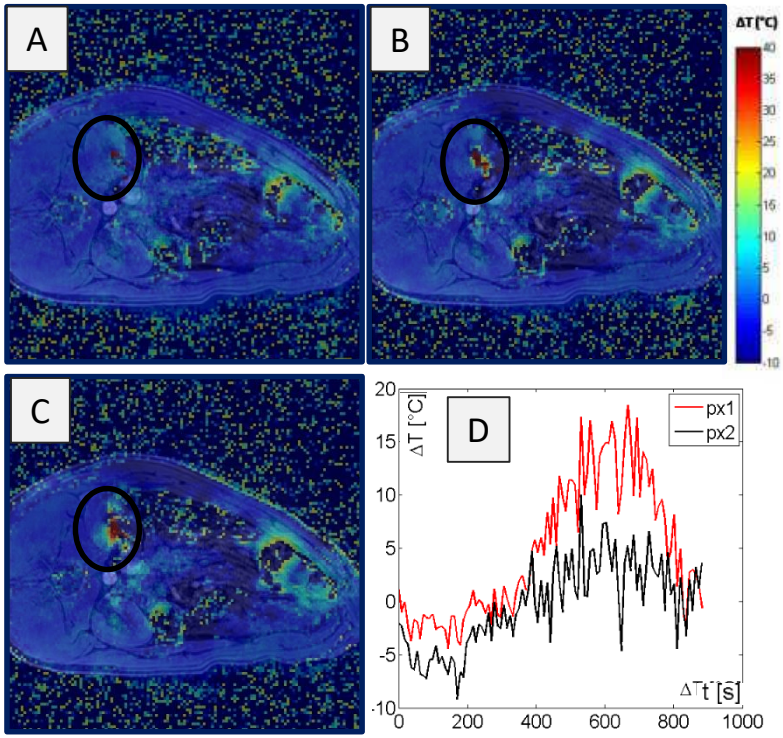
Laser Ablation

2-3 W
1000-1200 J

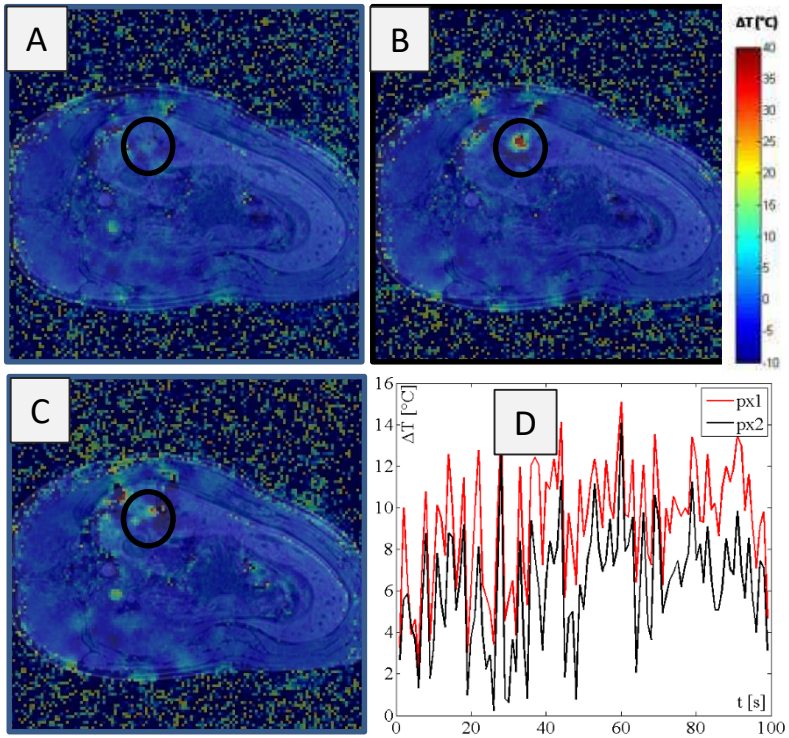
Nd:YAG, 1064 nm, CW
265 µm fiber

MR thermometry

Kidney



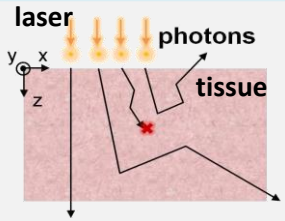
Liver



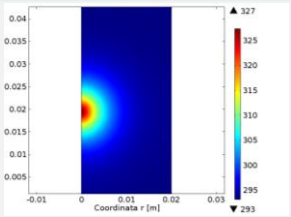
•Laser tissue-interaction: from mathematical model to clinical practice

Laser energy

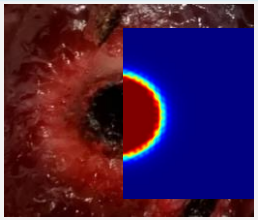
Absorption



Temperature increase



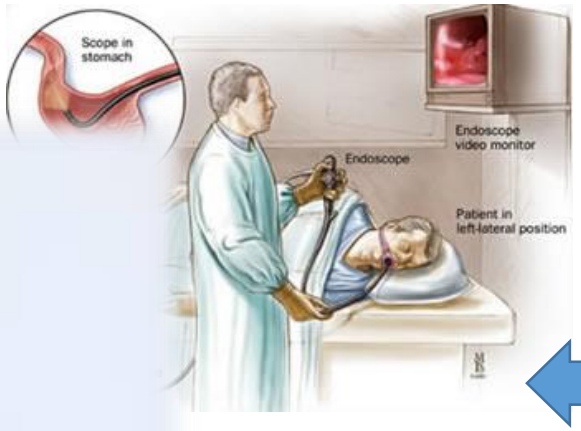
Thermal damage



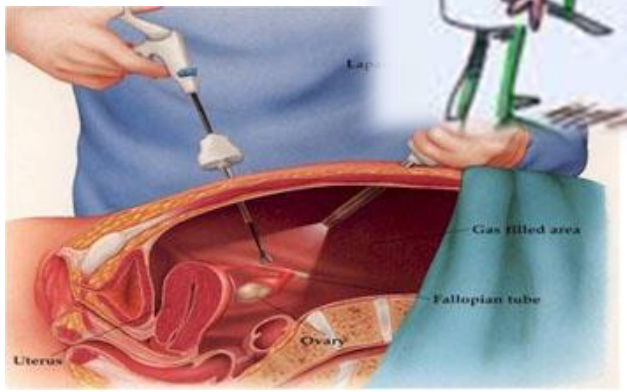
Patient

Laparotomy

Endoscopy/Percutaneous

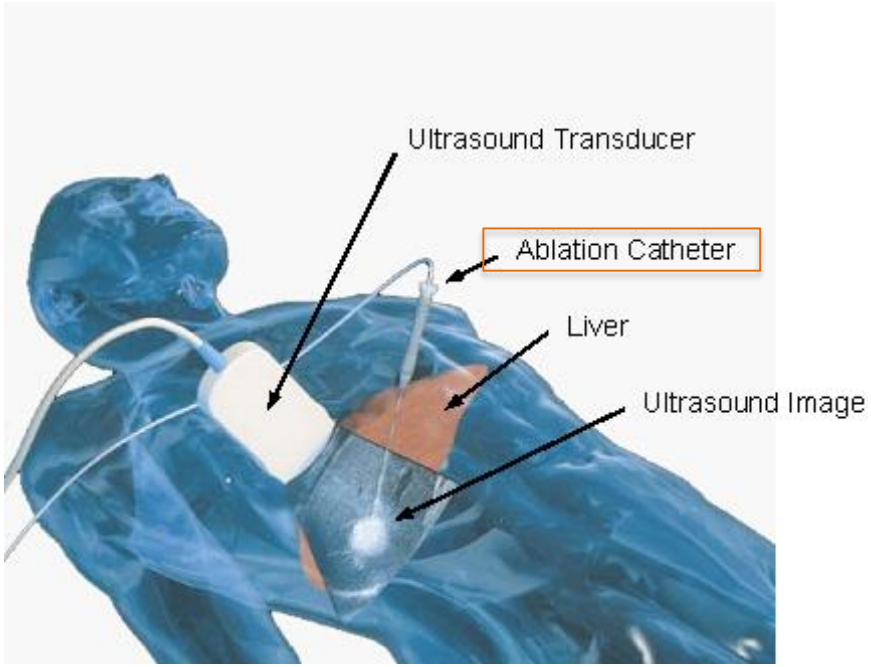


Laparoscopy



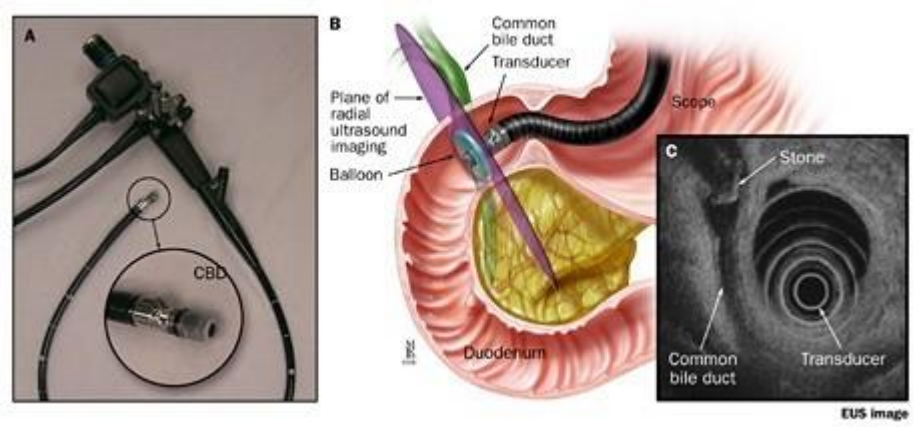
Robotics

Surgical diseases treatment evolution



Which approach?

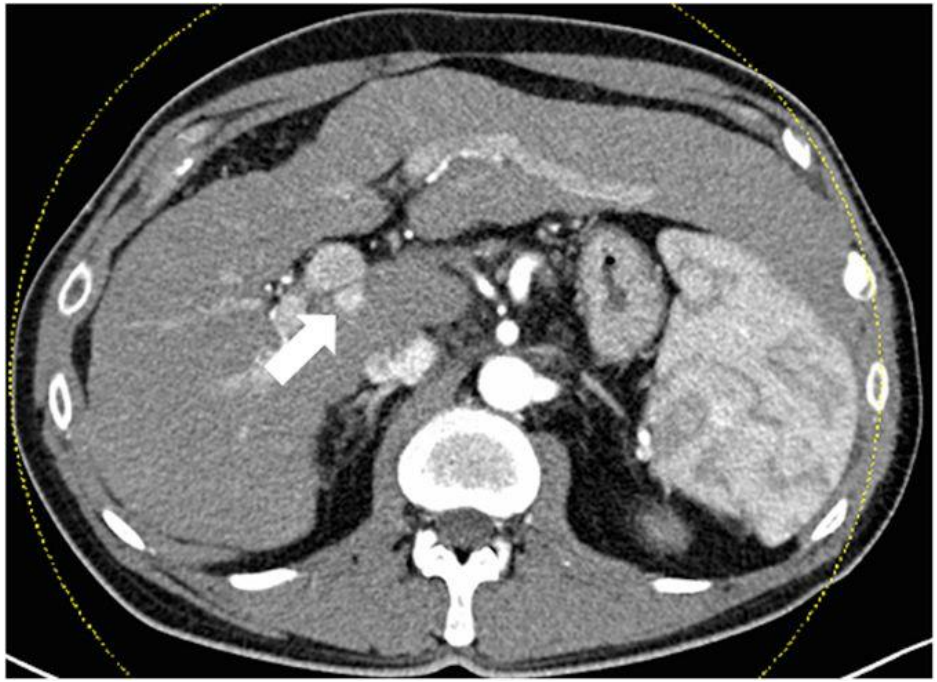
Echoendoscopy



Percutaneous approach

Why laser ablation for malignancies treatment?

Capability to reach "difficult locations"

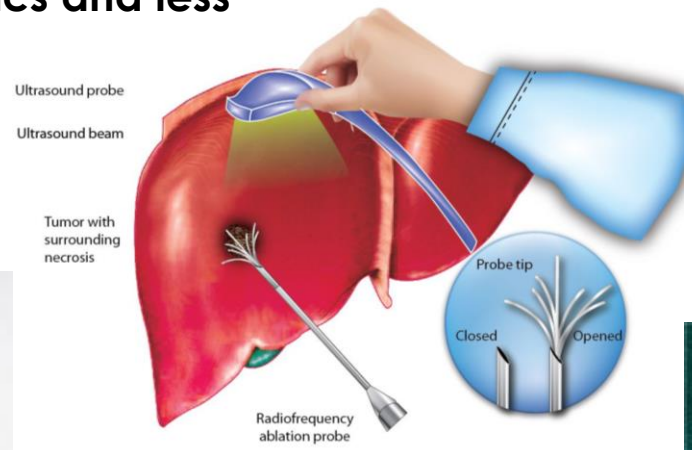


Overall, it is believed that between 10% and 25% of patients with HCC may not be eligible for RFA because of tumor location

Why laser ablation for malignancies treatment?

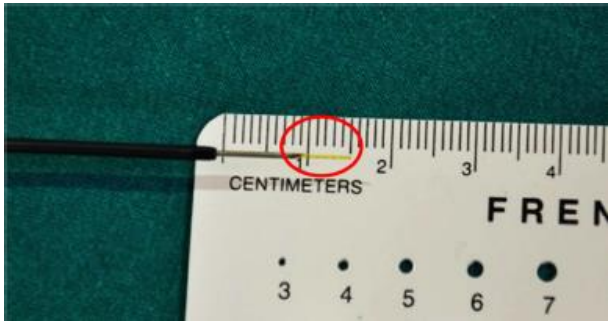
Major operator ergonomics and less patient's trauma

RFA probe



We believe that the main advantage of laser ablation is the use of multiple fine needles, which are less traumatic in cirrhotic patients at risk of bleeding and may be handled more easily by the operator to reach difficult sites. In addition, using multiple thermal sources makes it possible to better tailor energy delivery to the volume and shape of the target nodule.

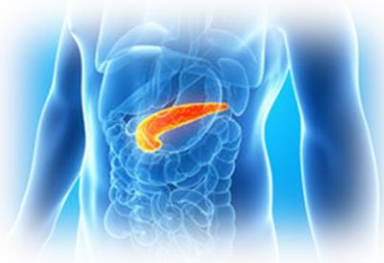
Laser probe



Clinical application of LA

Hepatocellular Carcinoma
Liver Metastases

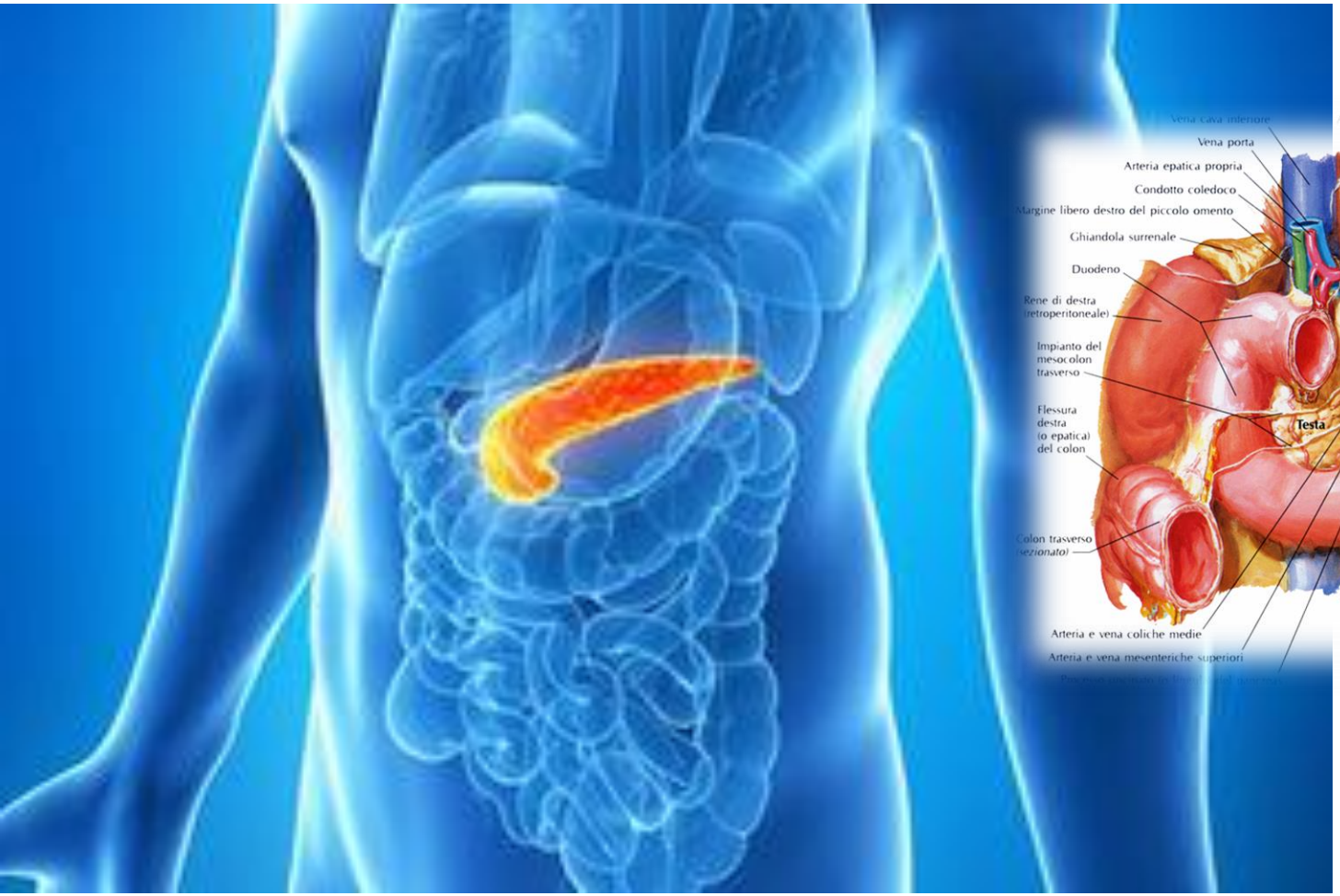
Thyroid nodules

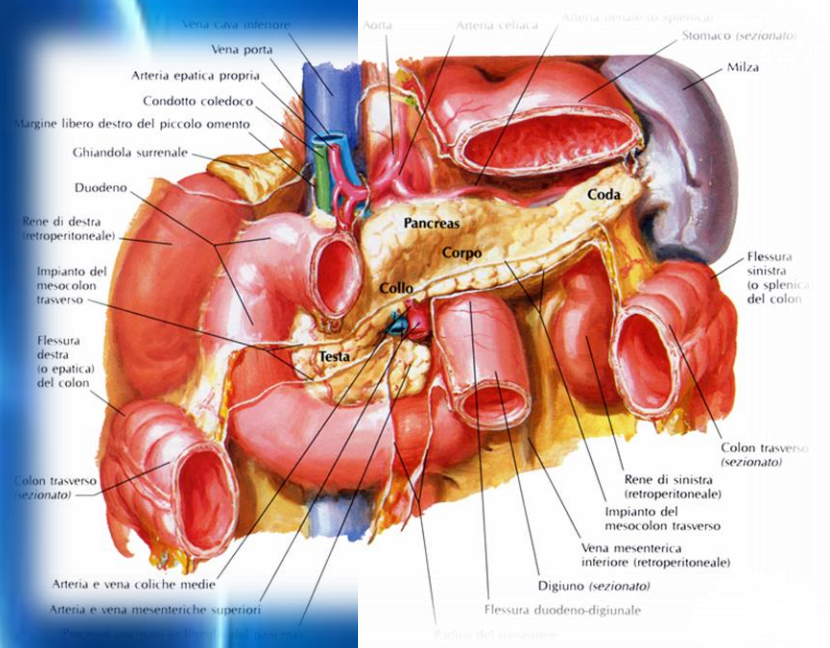


Pancreatic diseases

Biliary tree tumors

Pancreatic diseases



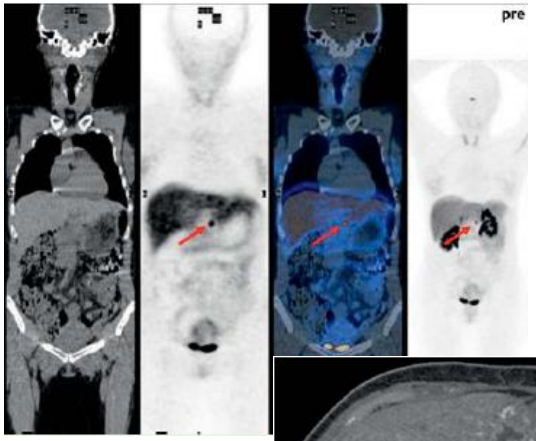


•Laser tissue-interaction: from mathematical model to clinical practice

Endoscopic ultrasound-guided Nd:YAG laser ablation of recurrent pancreatic neuroendocrine tumor: a promising revolution?

Endoscopy 2014; 46: E380–E381

Francesco Di Matteo[1], Francesca Picconi[1], Margareth Martino[1], Monica Pandolfi[1], Claudio Maurizio Pacella[2], Emiliano Schena[3], Guido Costamagna[4]



Laser settings: Nd:YAG, 4W for 300 secs

Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore

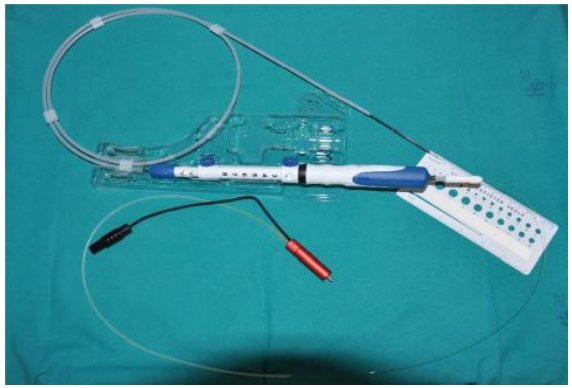
LASER optima GA 759159
erc European Research Council

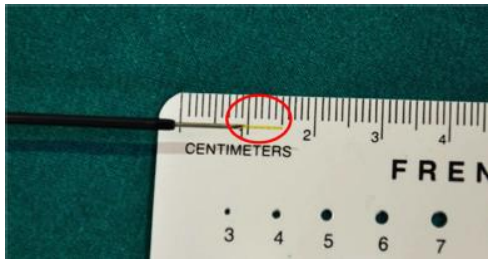
Feasibility of EUS-guided Nd:YAG laser ablation of unresectable pancreatic adenocarcinoma

Francesco Maria Di Matteo, MD, Paola. Saccomandi, Prof, Margareth Martino, MD, Monica Pandolfi, MD, Margherita Pizzicannella, MD, Valerio Balassone, Md, PhD, Emiliano Schena, Prof, Claudio Marcello Pacella, MD, Sergio Silvestri, Prof, Guido Costamagna, Prof.

Laser settings: 2W for 800 J, 1000 J and 1200 J or 3W for 800 J, 1000 J and 1200 J or 4W for 800 J, 1000 J and 1200 J

9 patients





INSTITUT DE CHIRURGIE GUIDÉE PAR L'IMAGE

Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore

Feasibility of EUS-guided Nd:YAG laser ablation of unresectable pancreatic adenocarcinoma

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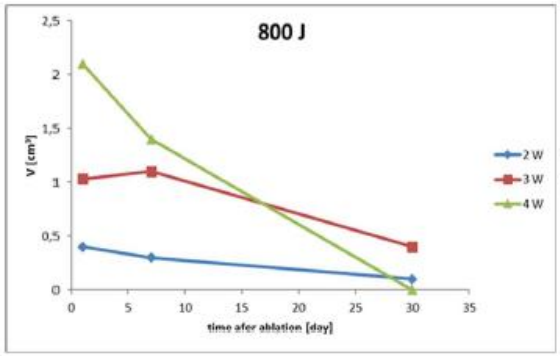
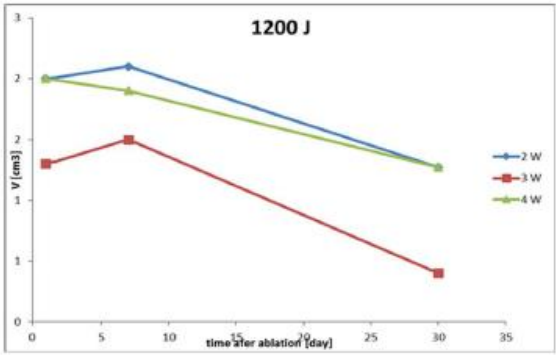
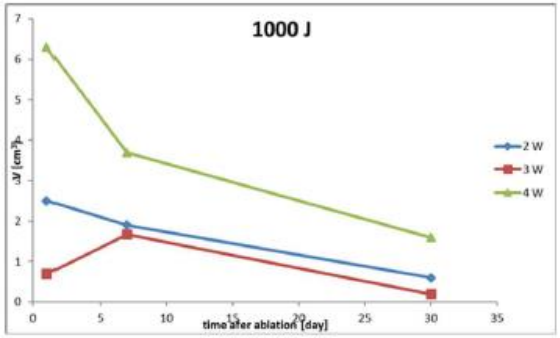
No intraprocedural complications

Post-procedure morbidity:

- 3 peripancreatic fluid collections
- 2 mild grade pancreatitis







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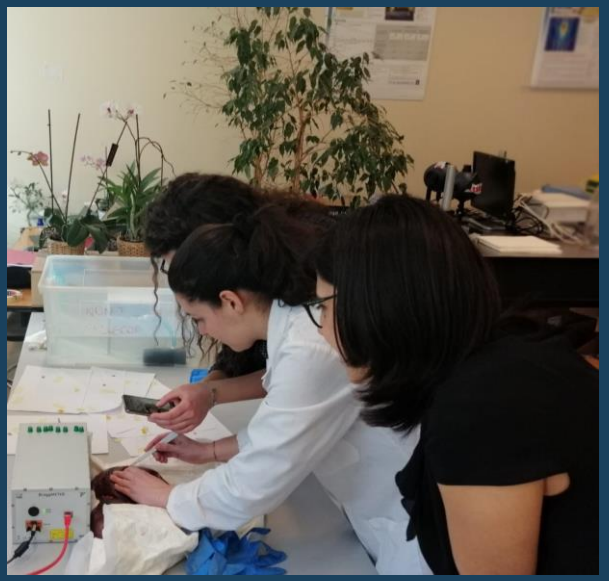
European Research Council
Established by the European Commission

Laser *su misura* per il trattamento dei tumori

Grazie!



Paola Saccomandi, PhD

Politecnico di Milano
Department of Mechanical Engineering

http://www.laseroptimal.polimi.it/

27/03/2019, Milano