Ente Ospedaliero Cantonale

The evolution of the role of RTTs in the context of Thermoradiotherapy

Stefano Leva, RTT
Radiation Oncology Clinic, Ente Ospedaliero Cantonale (EOC-IOSI), Bellinzona-Lugano

OUTLINE

- Hyperthermia and biological rationale
- Our hyperthermia systems and some results
- The role of Radiotherapy Technicians (RTTs) in hyperthermia treatment (HT)
- Future prospective
- Conclusions

HYPERTHERMIA BIOLOGICAL RATIONALE

Hyperthermia (HT), heating tumors in the range 41-43°C, is a **powerful RT and chemo sensitizer**. The effectiveness of HT as well as its safety, in combination with radiotherapy and chemotherapy, has already been proven in phase III clinical trials , particularly in patients with very large or very advanced stages of cancer and recurrent tumors. HT enhances the effect of radiotherapy on the tumor, without additional toxicity for nearby healthy tissue, by multiple synergistic mechanisms.

INHIBITION OF DNA DAMAGE REPAIR:
HT enhances the effectiveness of radiotherapy by inhibiting the repair of DNA damage (2-4-5-6)

REOXYGENATION:
HT increases tissue perfusion resulting in reoxygenation, thereby reducing hypoxia and increasing radiosensitivity (2-6-7)
With regard to chemotherapy, hyperthermia targets its action within the heated tumor region without aggravating systemic toxicity (8)
Local hyperthermia has also been shown to be capable of inducing systemic anti- tumor immune responses (1)

DIRECT CELL KILLING:
HT selectively kills radioresistant hypoxic tumor cells

1)Datta, N. R. et al., 2015. Local hyperthermia combined with radiotherapy
2) Crezee, H. et al., 2015. Thermoradiotherapy planning
3) Issels, R. D. et al., 2018. Effect of Neoadjuvant Chemotherapy Plus Regional Hyperthermia
4) Krawczyk, P. M. et al., 2011. Mild hyperthermia inhibits homologous recombination, induces BRCA2 degradation, and sensitizes cancer cells to poly (ADP-ribose) polymerase-1 inhibition
5) Oei, A. L. et al., 2015. Effects of hyperthermia on DNA repair pathways
6) Franken, N. A. P. et al., 2013. Cell survival and radiosensitisation
7) Vujaskovic, Z. & Song, C. W., 2004. Physiological mechanisms underlying heat-induced radiosensitization
8) Issels, R. D., 2008. Hyperthermia adds to chemotherapy

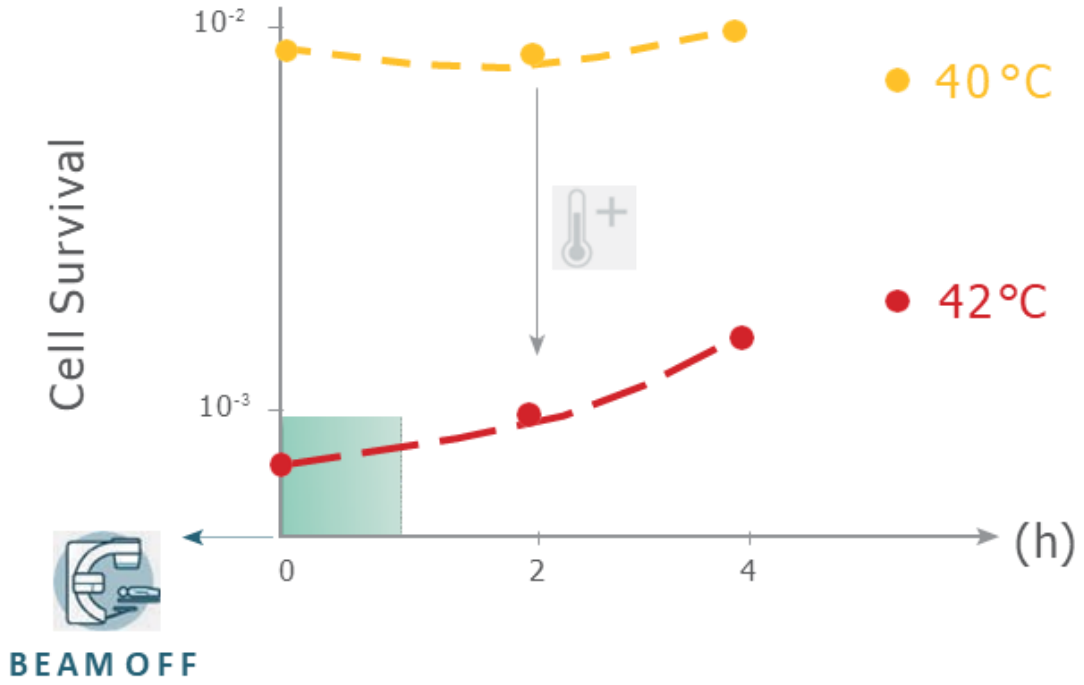
BOOST UP TO 10/20 Gy OR MORE WITH NO ADDITIONAL TOXICITY

HIGHER THERMO-DOSE

Higher temperature for reoxygenation and more direct cell killing for an effective thermodose escalation.

SHORT TIME INTERVAL

Achievable as the units allow for a short preparation time and ultrafast and precise Hyperthermia treatment delivery.



Van Leeuwen et al. International Journal of Hyperthermia, 2017

OUR HT TECHNOLOGY: 1 DEEP – 2 SUPERFICIAL

EOC BELLINZONA

EOC LUGANO

Phased array of 4 antennas emitting at 70 MHz, for deep tumors

One antenna emitting at 434 MHz, for superficial tumors

HT TREATMENT @ EOC-IOSI

DEEP HT TREATMENT

- 10 cases
- Carcinoma, melanoma, adenocarcinoma
- Mean beam-off time: 40 min

SUPERFICIAL HT TREATMENT

- 20 cases
- Adenocarcinoma, leiomyosarcoma, melanoma, ductal carcinoma
- Mean beam-off time: 17 min

BEAM OFF

Beam-off time : interval time between the end of the radiotherapy and the start of the HT treatment

Role of RTTs in HT: many tasks during HT treatment

Positioning the patient in the HT room

Measuring the temperature through thermocouples on the skin or in the natural cavities of the patient

Monitoring the patient throughout the treatment, maintaining patient comfort

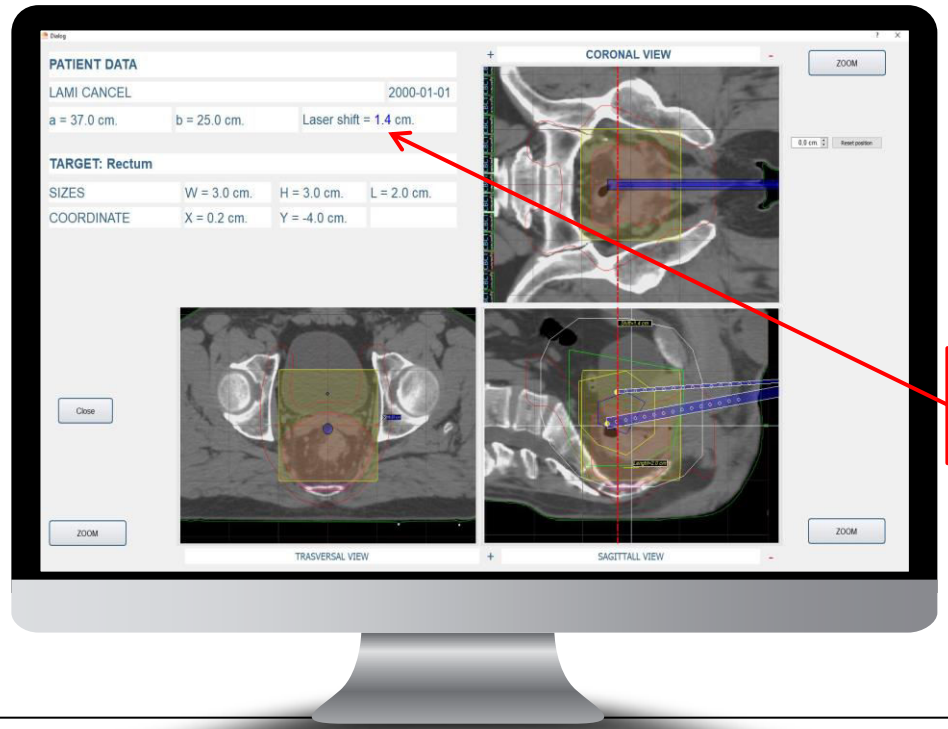
Setting and changing the machine parameters (power, phases, water temperature), to obtain the most effective treatment

Sinergy and coordination of the whole team: Clinicians - Physicists - Biomedical Engineers - Nurses - RTTs

Role of RTTs in HT: Positioning of the patient

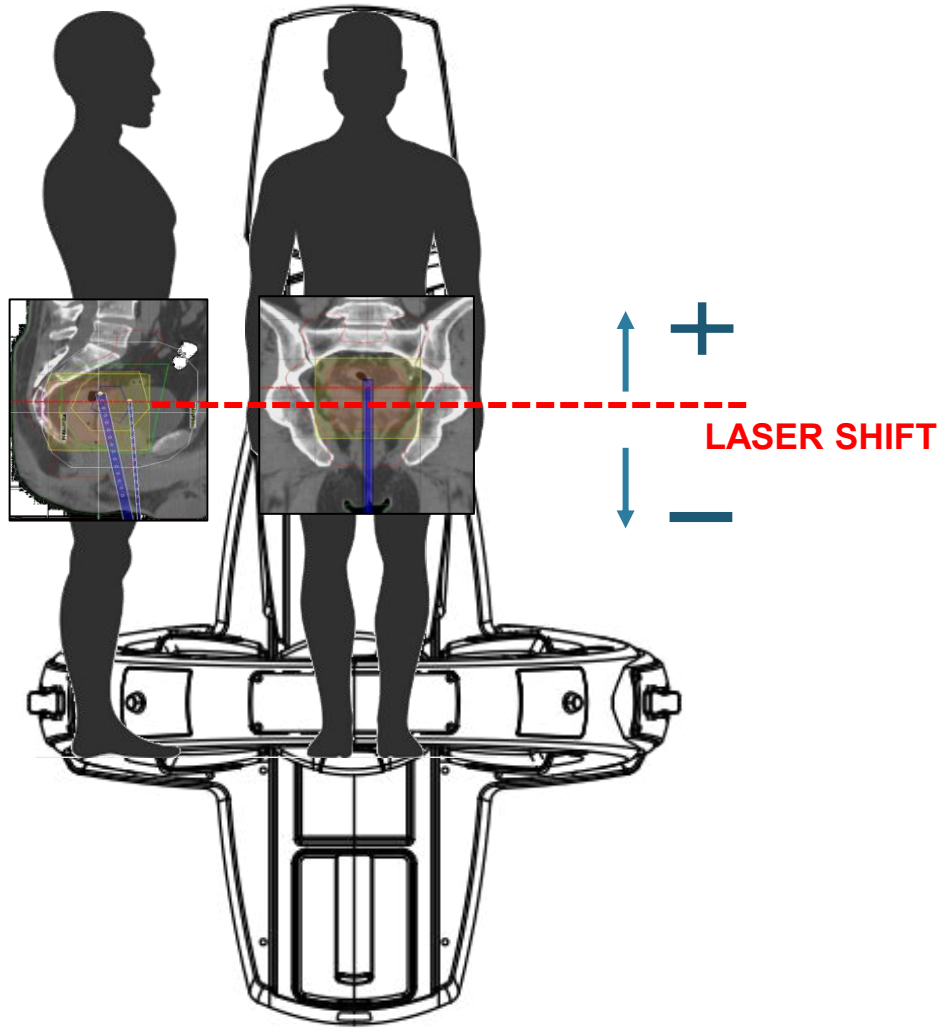
TREATMENT ROOM MONITOR

DATA DISPLAYED TO **ALIGN**
TUMOR CENTER (AXIAL VIEW) WITH THE CENTER OF THE GANTRY



LASER SHIFT

Laser shift = 1.4 cm.

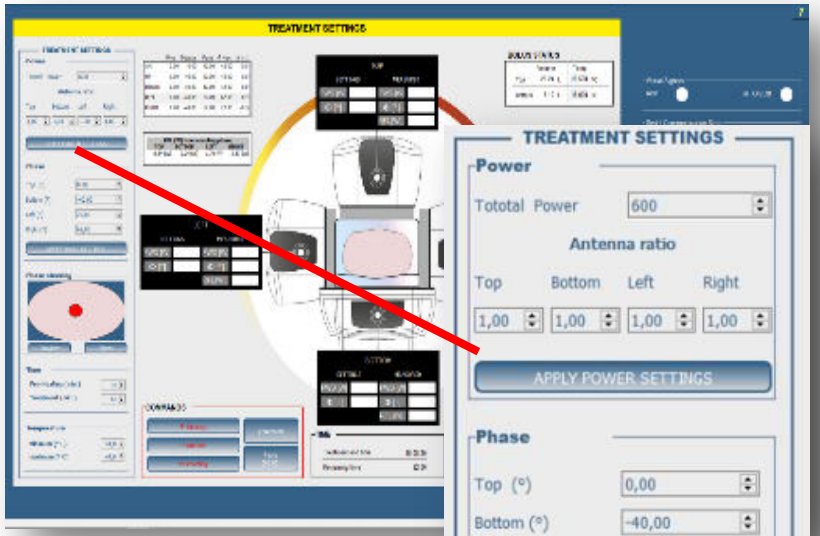


Role of RTTs in HT: Positioning of the patient

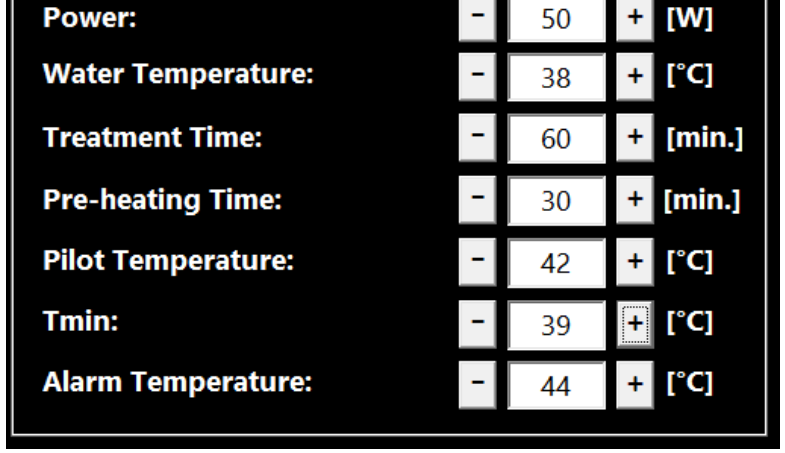
For the superficial system, the RTT places the temperature probes and the antenna on patient's skin, as previously planned.

By modifying the antenna positioning angle on the skin, the reflected power can be minimized and the best coupling can be reached

Role of RTTs in HT: Parameters setting and changing



- Total power
- Power ratio of sing
- Phases



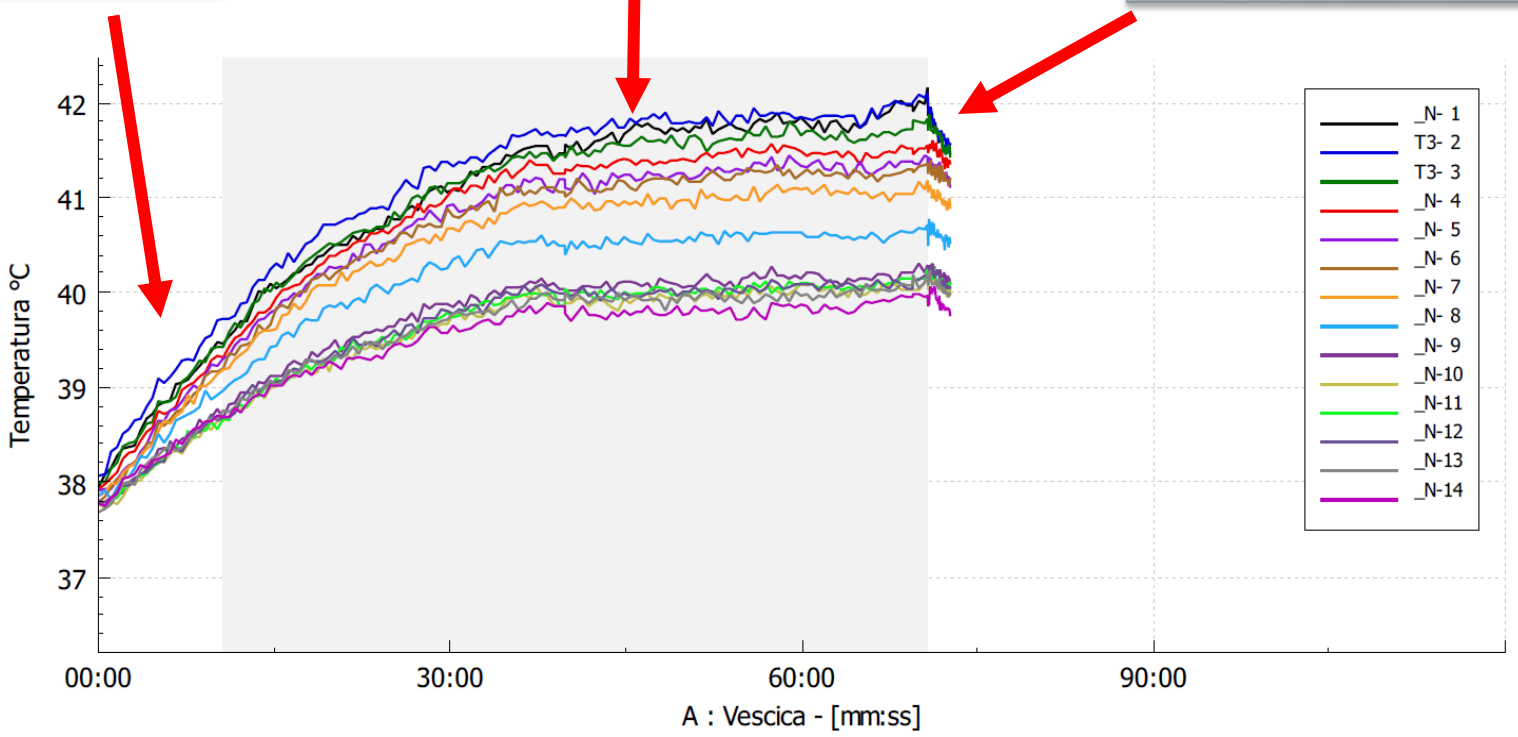
- Total power
- Water temperature
- T pilot
- T min
- Alarm temperature

Role of RTTs in HT: Temperature monitoring

PREHEATING:
5-15 min

STEADY STATE:
60 min

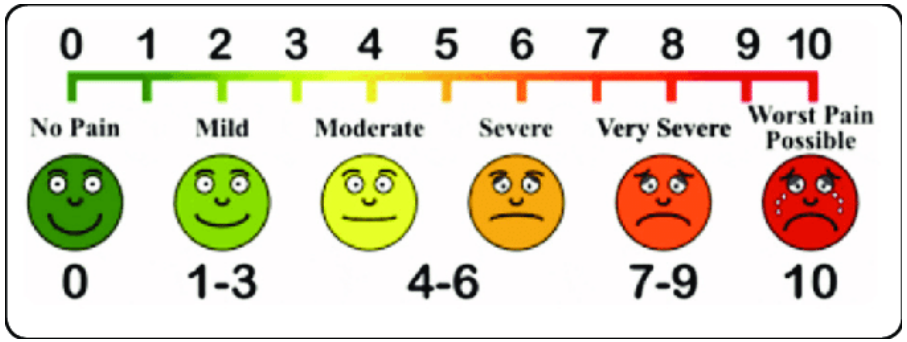
POSTHEATING:
2 min



During the treatment, RTTs monitors the temperature graphs of all the probes, in order to have the temperature in 41-44 C range.

Role of RTTs in HT: Patient comfort

Patient comfort is crucial for a good outcome of the treatment. High temperature (>44 C) may cause pain and discomfort.
The patient could also ask to stop the treatment due to pain, and the technician should avoid it, carrying out the HT treatment.



The VAS scale is a useful tool to assess the pain felt by the patient during the HT treatment, and can help the RTTs to change some parameters in order to ensure the best comfort for the patient (i.e. power, phases, water temperature, etc)

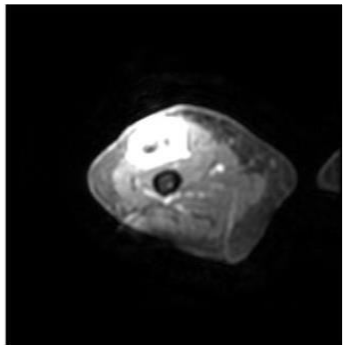
Future prospective: Advanced MRI in combination with HT

Advanced MRI techniques are able to assess the response to the HT treatment by evaluating the tissue changes.

- Dynamic Contrast Enhancement Magnetic Resonance Imaging (DCE-MRI) : tumor perfusion and vascularity
- Diffusion Weighted Imaging (DWI): motility of water molecules in tissue
- Other advanced MRI sequences : dielectric properties of tissue perfusion and diffusion can be altered in tumor tissues.

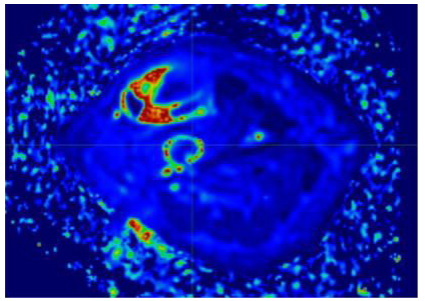
Dedicated software are able to segment ipo-vascularized volume and produce perfusion maps, obtained by DCE-MRI.

By comparing pre-/post- treatment ipo-vascularized volume maps, the HT treatment outcome can be assessed

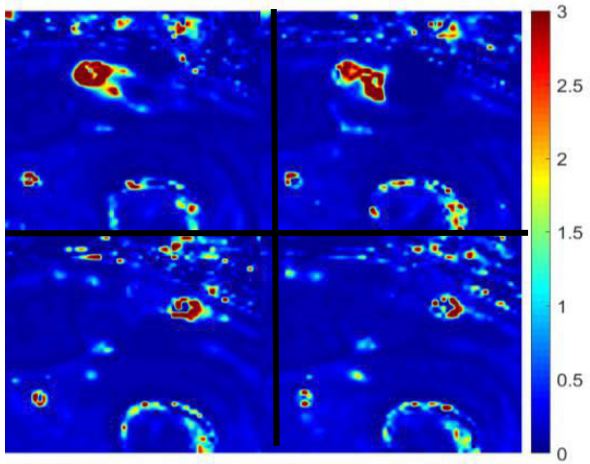


DCE-MRI

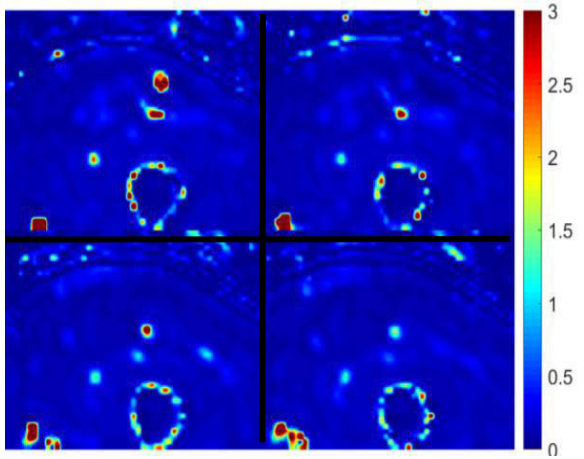
Post-processing software



Volumetric perfusion map



Pre-treatment vascularized map of a fibrosarcoma

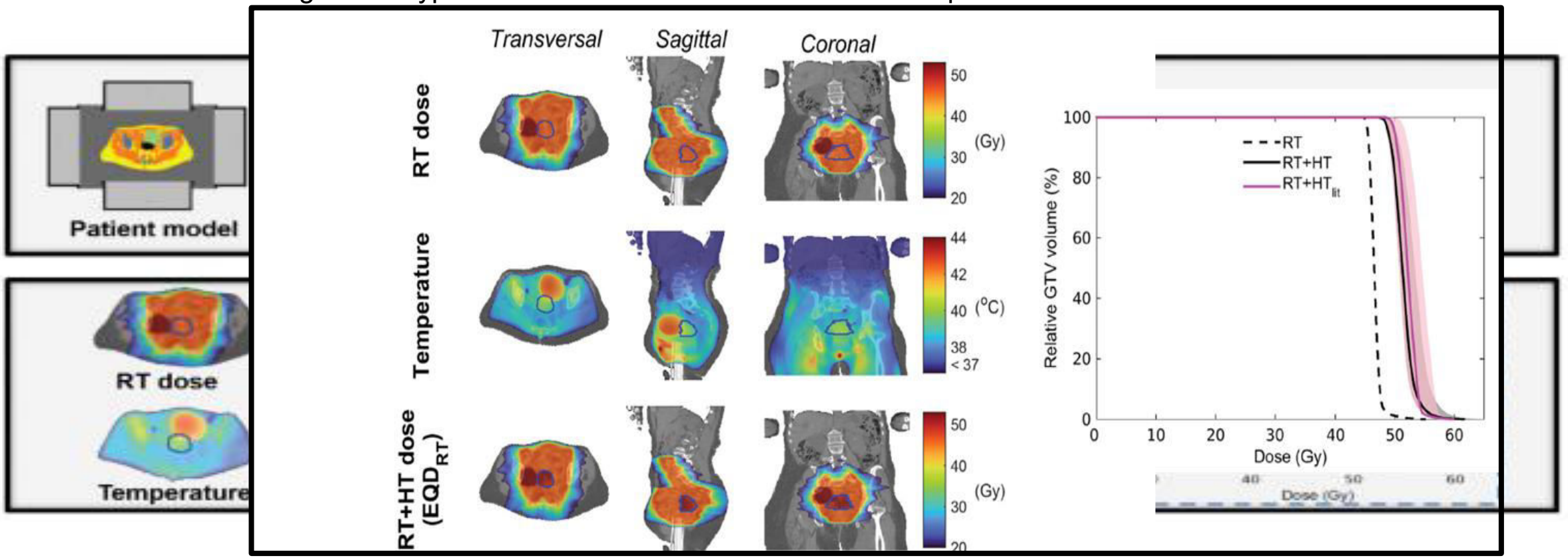


Post-treatment vascularized map of a fibrosarcoma

Future prospective: Advanced MRI in combination with HT

The integration of MRI into the Hyperthermia Treatment Planning workflow influences:

- conductivity information
- heat transfer modeling of the vasculature
- modeling of the hyperthermia treatment effect in terms of equivalent radiation dose



Gavazzi et al. Advanced patient-specific hyperthermia treatment planning, International Journal of Hyperthermia, 2020

CONCLUSIONs

- HT treatment enhances the efficacy of radiotherapy, without adding toxicity
- HT treatment can improve patient's quality and time of life
- The role of RTTs are crucial for the best HT treatment
- RTTs should ensure the best comfort for the patient, in order to carry out the HT treatment
- The combination of HT with advanced MRI techniques may improve the HT treatment planning and treatment outcome assessment
- Advanced MRI techniques will estimate the dielectric properties of tissue, patient-specific, and evaluate the SAR distribution

Thank you for the attention

Disclosure

I have no actual or potential conflict of interest in relation to this presentation.