Short term treatment with modulated electro-hyperthermia in triple negative breast cancer bearing mice

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Introduction: The effective therapy of triple-negative breast cancer (TNBC) has not yet been achieved. Modulated electro-hyperthermia (mEHT) is a novel adjuvant antitumor therapeutic approach, based on the highly selective effects on tumor cells by a 13.56 MHz radiofrequency current promoted electric field.

Aims: Our aim was to investigate the effects of mEHT on a triple-negative mammary carcinoma bearing mouse model.

Method: 4T1 cells transfected with firefly luciferase were inoculated orthotopically in immunocompetent female Balb/c mice. The isografts were treated with mEHT on day 3 and 5 after inoculation. Treatments were performed with 1.0±0.5W power to reach 40°C of the skin above the tumor, treatment length was 30 minutes. Tumor growth was measured in vivo by IVIS Lumia system (Perkin Elmer), digital caliper and ultrasound (Phillips Sonos 5500) before and after treatments. Mice were euthanized on day 7 after inoculation and the tumors were harvested and processed for histology. The ratio of the damaged area compared to the whole tumor area (Tissue Damage Ratio, TDR) was evaluated on H&E stained sections, while HSP70 was analyzed on immunohistochemical staining with HistoQuant module of CaseViewer Software (3DHistech).

Results: There was a significant decrease in tumor growth measured by IVIS in the mEHT treated group (mEHT: 7.1*108 p/s vs sham: 13.5*108 p/s, $p<0.05$), which couldn't be detected by the less sensitive caliper (mEHT: 51.17±4.86 mm3 vs sham: 52.36±10.25 mm3, $p=0.93$) and ultrasound (mEHT: 73.29±22.18 mm3 vs sham: 74.87±7.95 mm3, $p=0.52$) measurements. Furthermore, the tumor damage ratio (fold change: 4.1, $p<0.05$) and the HSP70 positive signal around the damaged area (fold change: 12.9, $p<0.05$) was significantly higher in the mEHT treated group compared to the sham group.

Conclusion: Our findings suggest, that modulated electro-hyperthermia could be a possible alternative adjuvant therapeutic strategy for TNBC cancer patients. We plan next generation sequencing to elucidate the molecular mechanisms behind the effects of mEHT.
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oral presentation

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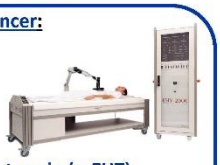
Introduction

Triple negative breast cancer:

- 15% of breast cancer
- Highly agressive
- High mortality

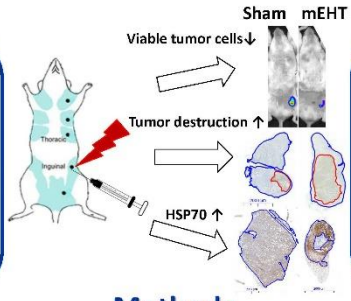
poor clinical outcome

- No targeted therapy



Modulated electro-hypertermia (mEHT)

- Non-invasive therapeutic option
- Electromagnetic field generated by amplitude modulated 13.56 MHz radiofrequency.



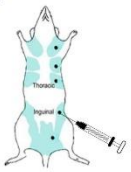
Discussion

2x mEHT treatment induced:

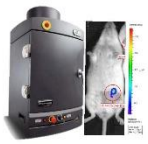
- Decrease in the number of viable tumor cells (IVIS)
- Significant damage in the tumor tissue (TDR)
- Heat shock response (HSP70)

mEHT: a new, adjuvant treatment for TNBC patients.

Methods



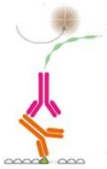
4T1 cells (10^6/50 µl Matrigel:PBS)
♀ Balb/c mice
4th mammary gland



Fluorescent, viable cells In Vivo Imaging System (IVIS)

Treatments
Pole electrode
Lab-EHY200

Tumor size measurement
Ultrasound
Digital caliper



Immunohisto-chemistry
HSP70, cC3

Day after inoculation	0	3	5	7
4T1 cell inoculation	x			
IVIS	x	x	x	x
Tumor size (US, caliper)		x	x	x
mEHT			x	
Harvest				x

Experimental protocol, 1 treatment

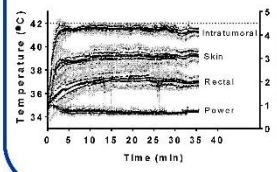
Day after inoculation	0	3	4	6	7
4T1 cell inoculation	x				
IVIS		x			x
Tumor size (US, caliper)					x
mEHT			x	x	
Harvest					x

Experimental protocol, 2 treatments

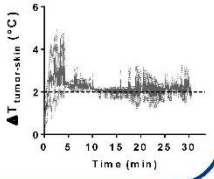
Results

Two treatments

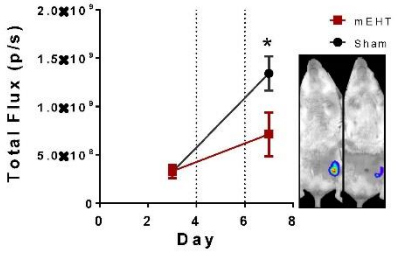
Temperatures of the tumor, skin and rectum



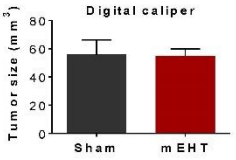
Temperature gradient btwn skin and tumor



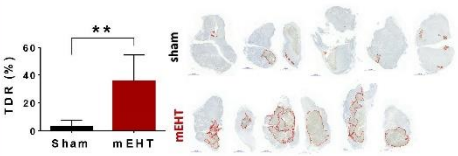
Viable cells measured by IVIS

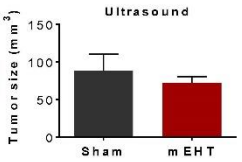


Tumor size and weight

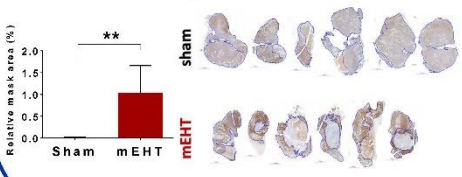


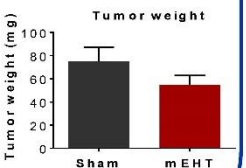
Tumor destruction (cC3, immunohisto)





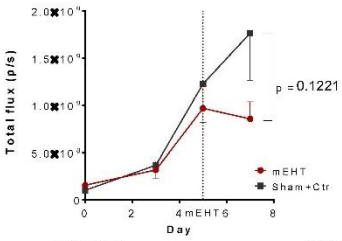
Heat shock response (HSP70, immunohisto)



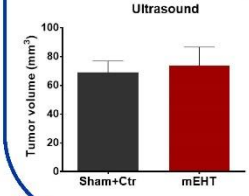


One treatment

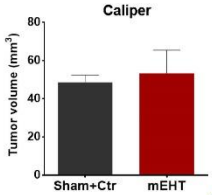
Number of viable cells measured by IVIS



Ultrasound



Caliper



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