

39. ICHS Conference It's time for prime time for oncologic hyperthermia/thermotherapy

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39. ICHS Conference

It's time for prime time for oncologic hyperthermia / thermotherapy?

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Conflicts of Interest Declaration

ElmediX - Member Advisory Board
ITIS Foundation - Member ITIS Foundation Board
Sensius - Member Thermotherapy Leadership Council

2

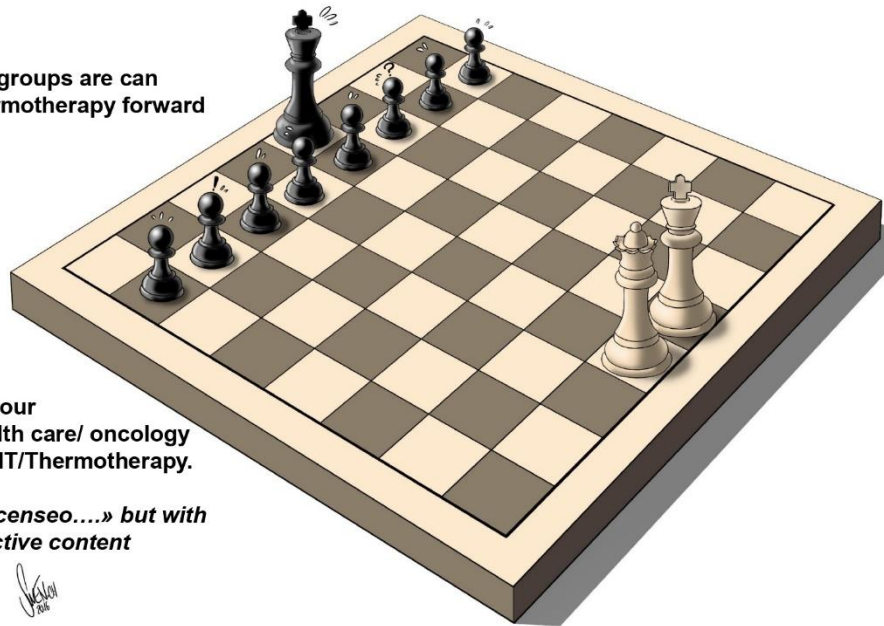


SWISS
HYPERTHERMIA
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**2 strong united leaders/groups are can
push oncologic HT/Thermotherapy forward**

**Use discussions with your
National leaders in health care/ oncology
to promote oncologic HT/Thermotherapy.**

***Like Cesars «Ceterum censeo....» but with
a positive and constructive content***



SWISS
HYPERTHERMIA
NETWORK

How do we handle HT / TT in Switzerland ?

“Material and Methods of Thermotherapy (TT) within SHN”

SHN thermotherapy units are embedded within a Swiss Radiation Oncology

Use of superficial IR and RF and deep RF TT

Use of fractionated, moderate heated, regional TT

Planning “library” for specific tumors in defined anatomic regions

Experimental personalized (RT-like) planning selected for combined Proton-TT

Online temp. point measurements (at tumor and surrounding healthy tissue)

4

What is needed for prime time?

7 Bullet Points

1. Need for evidence based medicine
2. Need for multicentric-prospective-randomised clinical trials
3. Need for Iso-certification for clinical thermotherapie units
4. Need for clinical European Research Networks
5. Need for re-imbursement for defined indications
6. Need for standardization of hard-software
7. Need for standardisation of patient workflow and QA

5

Bullet point 1

Need for Evidence Based Medicine

2 slides



Integrating Loco-Regional Hyperthermia Into the Current Oncology Practice: SWOT and TOWS Analyses

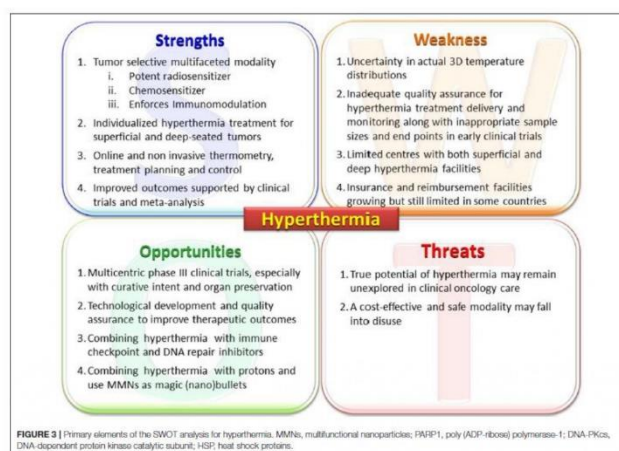
Nilesh R. Datta¹, H. Petra Kok², Hans Crezee³, Udo S. Gaipl⁴ and Stephan Bodis⁵

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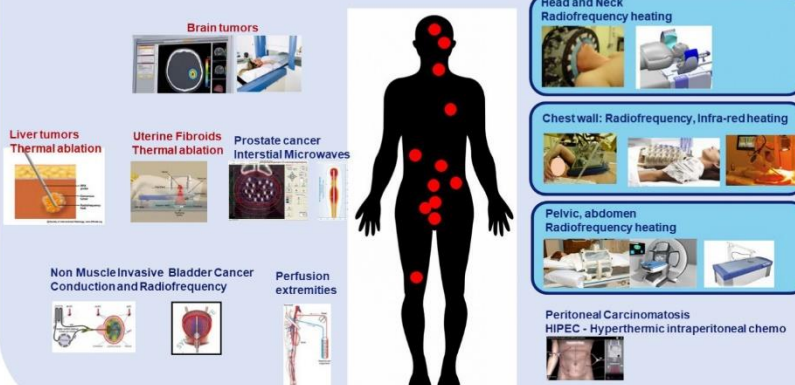
Make your own SWOT analysis to push HT/TT



Heating technology for all body locations

Strengths

1. Tumor selective multifaceted modality
 - i. Potent radiosensitizer
 - ii. Chemosensitizer
 - iii. Enforces Immunomodulation
2. Individualized hyperthermia treatment for superficial and deep-seated tumors
3. Online and non invasive thermometry, treatment planning and control
4. Improved outcomes supported by clinical trials and meta-analysis



Make your own SWOT analysis to push HT/TT

* Bullet point 2*

Need for multicentric prosp. rand. clinical trials
3 slides

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Clinical evidence hyperthermia

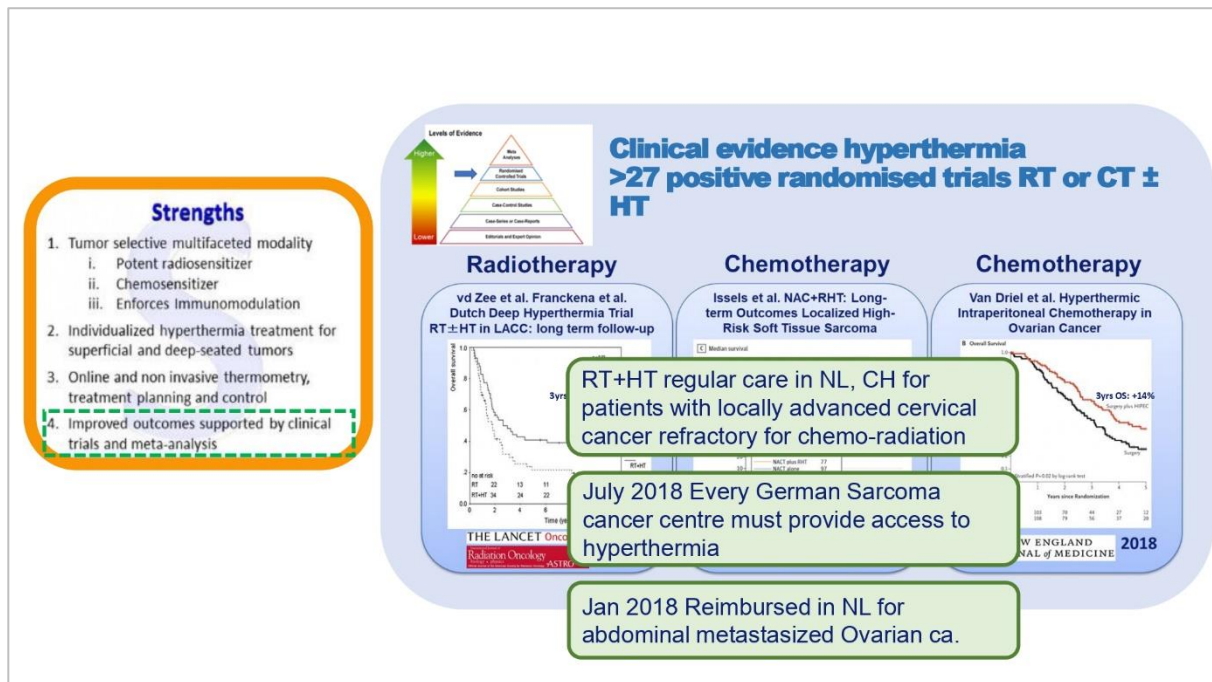
> 27 positive randomized trials RT or CT \pm HT

Reference	Treatment	Tumor	Endpoint	Lesions	RT/CT	RT/CT+HT
Van Driel (2018)	CT (hipec)	Ovarian	med Surv.	245	33.9m	45.7m
Isola (2018)	CT	Soft tissue sarcoma	med. Surv.	329	6.2yr	15.4yr
Chi (2018)	RT	Painful Bony mets	Time2pain prog	57	55d	>166d
Zhao (2014)	RT	Nasopharynx	3yr OS	83	54%	73%
Kang (2013)	RT+CT	Nasopharynx	5yr OS	154	50%	68%
Hsu (2011)	RT+CT	Nasopharynx	5yr PFS	180	63%	73%
Huigol (2010)	RT	Head and Neck	CR	54	42%	79%
Jones (2005)	RT	Various	CR	109	42%	64%
Colombo (2003)	CT	Bladder	2yr OS	39	24%	68%
Verwaal (2003)	CT (hipec)	Colorectal peri. cat.	med. Surv.	105	12.6m	22.3m
Harima (2001)	RT	Cervix	CR	40	50%	85%
Van der Zee (2000)	RT	Blad., Cerv., Rect.	3yr OS	358	24%	30%
Sneed (1998)	RT	Glioblas	2yr S	117	15%	31%
Vernon (1996)	RT	Breast	CR	308	41%	59%
Wang (1996)	RT	previously irradiated	CR	39	39%	79%
Overgaard (1995)	RT	Osteosarcoma	2yr S	125	24%	42%
Kihmura (1993)	RT	Melanoma	2 yr-NED	134	70%	25%
Yon (1993)	RT	Various	Response	92	63%	82%
Sugimachi (1993)	RT	Various	Response	92	63%	82%
Strotsky (1993)	RT	Various	Response	92	63%	82%
Berdow (1993)	RT	Various	Response	92	63%	82%
Kakehi (1993)	RT	Various	Response	92	63%	82%
Engelhardt (1993)	RT	Various	Response	92	63%	82%
Egawa (1989)	RT	Various	Response	92	63%	82%
Valdagni (1987)	RT	Various	Response	92	63%	82%
Datta (1987)	RT	Various	Response	92	63%	82%
Kohno (1984)	RT	Various	Response	92	63%	82%

All clinical studies report no relevant increase of side effects

re-RT+HT Standard of care for recurrent tumors in several European Countries





Phase III trials: Randomised, prospective, multicentric, standardised, international

Phase III trials with long term f/u and subsequent Metanalysis

- Critical for acceptance of TT/HT for stakeholders in oncology care, oncology politics, health care politics
- Critical for negotiations with national ministries of health care (They dont care about promising data)

(Also needed are Phase I / II trials)

...with an innovative potential for a better outcome, a better efficacy, better economics

Loco-regional moderate temperature HT/TT

- Proton Therapy, FLASH - RT
- Trimodality Therapy RT - Systemic Therapy - HT/TT
- Novel low budget RT and novel forms of Thermo-therapy (also) for use in LMI countries

Local high temperature/ablative HT/TT

Whole body low to moderate HT/TT

- Oncologic setting combined with systemic therapy +/- RT
- Novel applications in medicine (E.g. multiresistant bacterial infections)

ISO-Certification DIN EN ISO 9001:2015 of a Hyperthermia Unit in 2020 (Radiation Oncology Center Aarau and Baden)

Bullet point 3

Increased acceptance of TT/HT by hospital administrators and QA management

Need for Iso-Certification in clinical hyperthermia/thermotherapy units
1 slide

Comments from opinion leaders of our local tumor boards

- This was a good step for you
- We (start to) consider HT/TT now more seriously
- We understand now that you don't harm patients



Need for International HT/TT Research Networks

3 slides

Bullet point 4

Current SHN activities within intl. networks

2019 ESHO Workshop to promote/endorse European clinical trials:

- **Need for international multicentric clinical trials in oncology for Hyperthermia combined with Radiotherapy (endorsed by ESHO)**
- F/u meeting and joining forces between the ESHO Clinical Trial Committee and the Atzelsberg Group from Germany

EU Horizon 2020 Grant H2020-MSCA-ITN-2020-955625 (The EU Research and Innovation Framework Programme)

- **Hyperthermia boosting the effect of radiotherapy**

ESTRO 2021

Interdisciplinary Symposium in Oncologic Hyperthermia: A session jointly with leaders from Europe, Japan and USA

Current status of hyperthermia in radiation oncology

CANCERS 2022 (IF > 6)

Special issue dedicated to Oncologic Thermo-Radiotherapy

HYPERBOOST
Hyperthermia boosting the effect of Radiotherapy
H2020-MSCA-ITN-2020-955625

6 countries
11 beneficiaries
14 PhD students
Budget: € 4 million

Project coordination:
Hans Crezee
Amsterdam UMC

B2 Århus University

B1 Amsterdam UMC

B10 EMC Rotterdam

B3 RAO KSAKSB Aarau

B5 ZHAW Zurich

B7 Medlogix Rome

B9 Chalmers Göteborg

B8 Charité Berlin

B11 MDC Berlin

B4 UKER Erlangen

B6 Sennewald Munich



ESTRO 2021

Joint ESTRO-JASTRO Hyperthermia Symposium

Current status of hyperthermia in radiation oncology

Biological rational for combining heat and radiation

Jens Overgaard DK

Clinical heating techniques, thermometry and quality assurance

Hans Crezee NL

Status of clinical Hyperthermia in Japan

Hideyuki Sakurai Jp

Thermoradiotherapy: Clinical evidence and potential indications

Zeljko Vujaskovic USA

Conclusions by the ESTRO President

Ben Slotman NL

↓ 69% 20:45

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Session

Sunday 14:15 - 15:30
August 29 N101-102

ESTRO-JASTRO - Current status of hyperthermia in radiation oncology

Chair: Stephan Bodis, Switzerland;
Chair: Yasushi Nagata, Japan

Session Code: 1630

Session Type: Joint symposium

Track: Interdisciplinary

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Special Issue

mdpi.com/si/87409

Invitation to submit

Bullet point 5

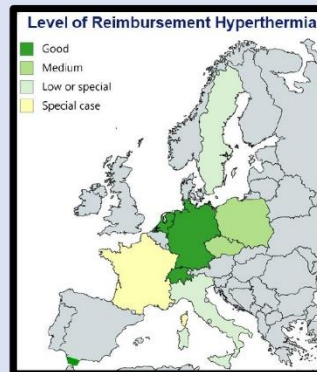
Need for re-imbursement for defined indications

2 slides

Weakness

1. Uncertainty in actual 3D temperature distributions
2. Inadequate quality assurance for hyperthermia treatment delivery and monitoring along with inappropriate sample sizes and end points in early clinical trials
3. Limited centres with both superficial and deep hyperthermia facilities
4. Insurance and reimbursement facilities *growing but still limited in some countries*

Reimbursement hyperthermia



Netherlands: HT reimbursed with radiotherapy. Regional deep and superficial hyperthermia, from January 1st 2010 onwards:

- Locally advanced cervical cancer for patients that are refusing or refractory for chemoradiation

Any recurrent tumor in previously irradiated areas:

- breast ca.
- lymph node metastasis of Head & Neck ca.
- tumors causing local complaints as palliation
- Rectum ca.
- Superficial local recurrence of mesothelioma
- Lymph node met's or recurrent malig. melanoma

Hyperthermic Intraperitoneal Chemotherapy:

- Peritoneal metastasis colon ca, mesothelioma
- Since 2019: ovarian ca.



SWISS
HYPERThERMI
NETWORK

Status reimbursement Thermotherapy in CH (only combined TT + RT) in 2021

4 indications for superficial HT approved 2016 (unlimited)

Curative: Recurrent Melanoma, H/N recurrences (Pre-RT), Chest wall BC recurrences (Pre-RT)

Palliative: Local tumor recurrence with compression symptoms

2 indications for deep HT approved 2021 (unlimited)

Curative: Cervix Cancer if contraindication for concurrent CT-RT

Palliative: Painfull bone metastases of spine and pelvis

2 indications approved (limited 2021-2023)

Curative Soft Tissues Sarcomas (To preserve anatomical functionality) only in clinical trials (incl. protontherapy!)

Palliative: Local tumor recurrence with compression symptoms

All indications restricted to synchronous RT and HT/TT

All patients must be presented and discussed @ the local tumorboard of an accredited oncology center

Hyperthermia/Thermotherapy Center must be an accredited member of the Swiss Hyperthermia Network

Bullet point 6

Need for standardisation of all clinically used hard-software

2 slides

Opportunities

1. Multicentric phase III clinical trials, especially with curative intent and organ preservation
2. Technological development and quality assurance to improve therapeutic outcomes
3. Combining hyperthermia with immune checkpoint and DNA repair inhibitors
4. Combining hyperthermia with protons and use MMNs as magic (nano)bullets

Non-invasive thermometry by MRI research



No sling

Munich

Rotterdam

Dusseldorf

Tubingen

Erlangen

A new software ?

We need a standardisation of our HT/TT vocabulary

We need a glossary/encyclopedia dedicated to HT/TT (in progress by ESHO)

- We should harmonise our technical terms
- We should harmonise our keywords
- We should create new and commonly accepted terms where needed

Crucial for the promotion a global HT/TT «language» understood and accepted by all stakeholders including our patients and their families

Only possible with a joint effort between science and industry
(including all major societies dedicated to oncology HT/TT)

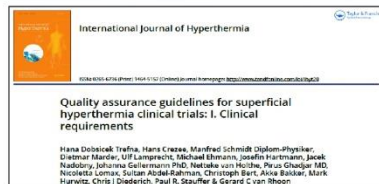
Bullet point 7

Need for standardisation
of workflow and QA

1 slides and discussion

ESHO technical committee guidelines (lead - guidelines)

Superficial HT - Current guideline 2017



Deep HT - Current guideline 2012



New release 2021



Coordination with industry/matrix standards
Coordination with national guidelines
Coordination with ISO-certifications

As an oncologic «underdog»
And with a strategy and a vision
All we should care is

- Evidence and Empathy
- Quality- and Outcome Analysis
- Cooperation and Communication

and thereby push HT/TT into prime time



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If we join forces it might be a good time for prime time
for hyperthermia/thermotherapy



Thank you for your attention