Integrating loco-regional hyperthermia into the current oncology practice: A SWOT and TOWS analysis

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Friedrich-Alexander-Universität,
Erlangen-Nürnberg, Germany

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www.oncotherm.com/sites/oncotherm/files/2021-02/Datta_Integrating

Abstract

Moderate hyperthermia at temperatures between 39 and 45°C is a multifaceted therapeutic modality. It is a potent radiosensitizer, interacts favorably with a host of chemotherapeutic agents and with RT enforces immunomodulation akin to "in situ tumor vaccination." By sensitizing hypoxic tumor cells and inhibiting repair of radiotherapy-induced DNA damage, the properties of hyperthermia delivered with photons provides a tumor-selective therapeutic advantage analogous to high LET neutrons, but without normal tissue toxicity. Furthermore, the high LET attributes of hyperthermia thermoradiobiologically enhance low LET protons; thus, proton thermoradiotherapy mimics 12C ion therapy. Hyperthermia with radiotherapy and/or chemotherapy substantially improves therapeutic outcomes without enhancing normal tissue morbidities yielding level I evidence as reported in several randomized clinical trials, systematic reviews and meta-analyses for various tumor sites. Further, hyperthermia along with immune check point inhibitors and DNA damage repair inhibitors could further augment the therapeutic efficacy resulting in synthetic lethality. Besides technological advancements in hyperthermia delivery, complemented by hyperthermia treatment planning, its integration with radiotherapy treatment plans, online thermometry and adherence to quality assurance guidelines have all ensured safe and effective delivery of hyperthermia to the target region. Additionally, hyperthermia induced by magnetic nanoparticles coupled to selective payloads provides a comprehensive tumor-specific theranostic modality akin to "magic (nano)bullets." To get a realistic overview of the strength (S), weakness (W), opportunities (O) and threats (T) of hyperthermia, a SWOT analysis has been undertaken. Additionally, a TOWS analysis categorizes future strategies to facilitate further integration of hyperthermia with the current treatment modalities. These could gainfully accomplish a safe, versatile and cost-effective enhancement of the existing therapeutic armamentarium to improve outcomes in clinical oncology.

Keywords: hyperthermia, radiation therapy, chemotherapy, immunotherapy, radiosensitizer, hyperthermia treatment planning, SWOT analysis, clinical trials

SWISS HYPERTHERMIA NETWORK

Kantonsspital Aarau

38. ICHS Meeting (Online!)

Integrating loco-regional hyperthermia into current oncology practice: A SWOT and TOWS analysis

2020 update of oncologic thermotherapy activities in EU/CH

Stephan Bodis on behalf of the Swiss Hyperthermia Network (SHN)
5.11.2020

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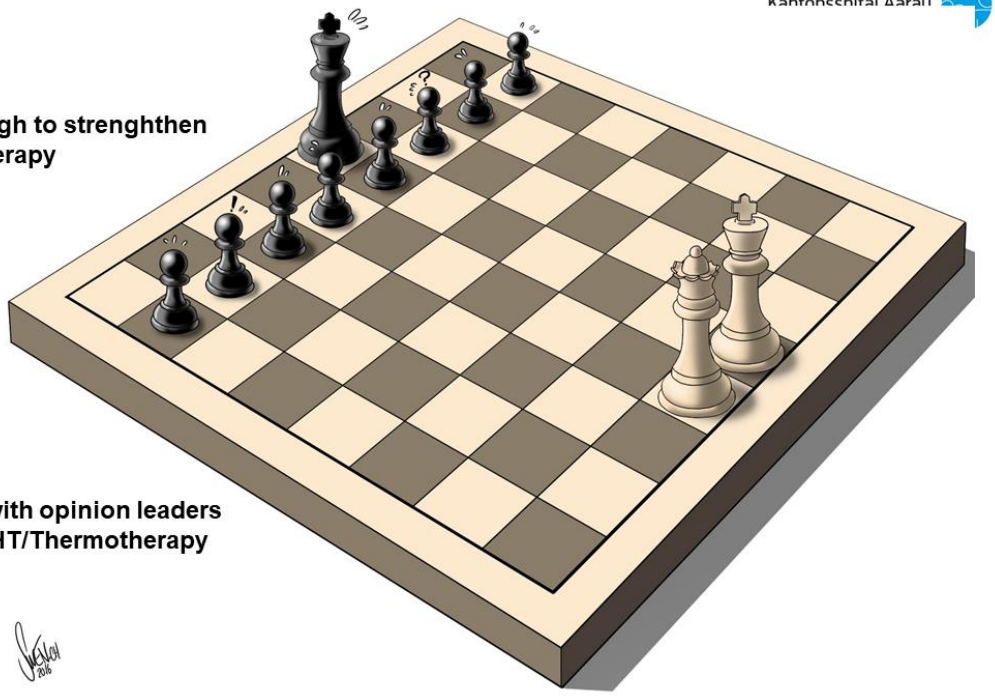
1 strong partner is enough to strenghthen oncologic HT/Thermotherapy



Use meeting debates with opinion leaders to promote oncologic HT/Thermotherapy

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The future of Oncologic Thermotherapy is Technology

Niels Kuster

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Niels Kuster

Prof. Niels Kuster is the founder and Director of the Foundation for Research on Information Technologies in Society (IT'IS Foundation) in Zurich, Switzerland, and Associate Professor of the Department of Information Technology and Electrical Engineering at ETH Zurich.

His research covers many aspects of electromagnetics and computational life sciences, and focus, in particular, on the modeling of both internal and external physical factors that affect human physiology. These include electromagnetic fields (e.g. MR safety assessments), tissue heating and cooling (e.g. hyperthermia and ablation), acoustics in biology (e.g. focused ultrasound/pressure waves), biofluid dynamics (e.g. blood flow and aneurysm), biomechanics (e.g. bone, ligaments, and arterial walls), and dynamic tissue models (e.g. nerve models and tumor growth).

Prof. Kuster has published over 700 publications in books, journals, and proceedings on measurement techniques, computational electromagnetics, dosimetry, exposure assessments, and bioexperimentation. He is a long-time member of several standardization bodies and serves as a consultant on exposure safety assessment for governmental agencies around the globe.

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The future of Oncologic Thermotherapy is Biology

Jean Bourhis

5

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Jean Bourhis

Prof. Bourhis has been Chairman of the Radiation Oncology at the Institute Gustave Roussy (Villejuif, France), one of the most prominent Cancer Center in Europe, and moved in 2012 to the CHUV as Head of Radiation Oncology.

His clinical activity is focused on Radiation Oncology Head and Neck cancers, he is chairman of the GORTEC, a cooperative group dedicated to Head and Neck Oncology.

Prof. Bourhis has been for 15 years also Director of a laboratory dedicated to Translational Research in Radiation Oncology. He authored more than 300 scientific papers.

Prof. Bourhis is also Past President of the European Society for Radiotherapy and Oncology (ESTRO), Past President of the ESTRO Cancer Foundation and currently serves as SASRO President."

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frontiers in Oncology

Datta et al.
June 2020

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

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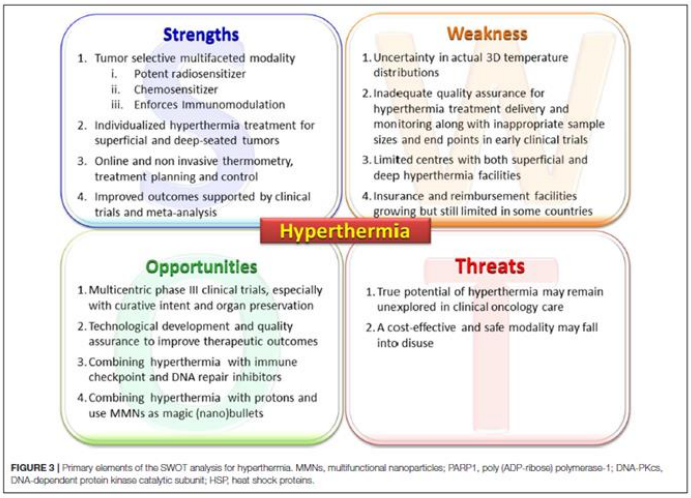
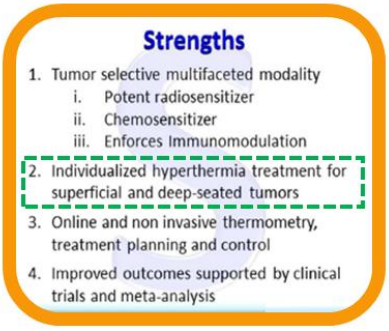
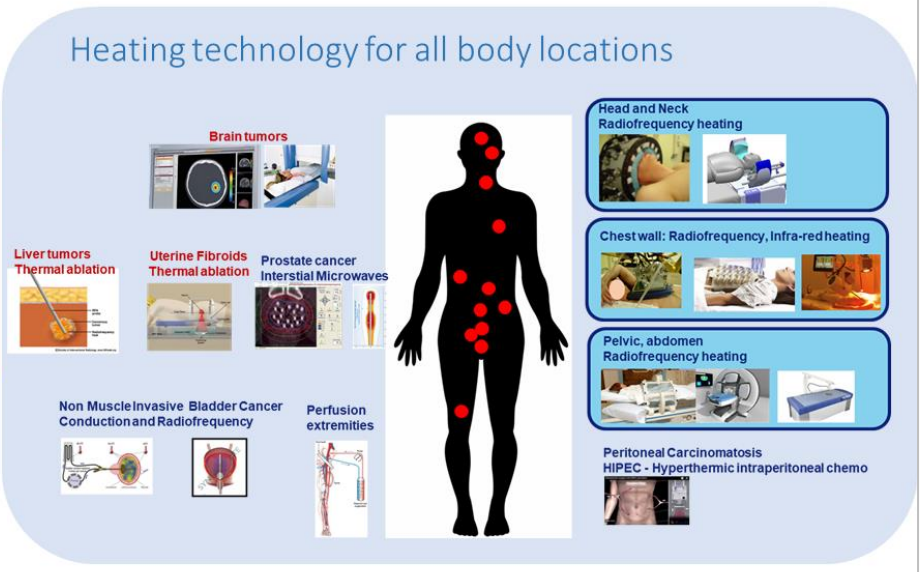


FIGURE 3 | Primary elements of the SWOT analysis for hyperthermia. MMNs, multifunctional nanoparticles; PARP1, poly (ADP-ribose) polymerase-1; DNA-PKcs, DNA-dependent protein kinase catalytic subunit; HSP, heat shock proteins.

Review Hyperthermia, Datta et al

Frontiers in Oncology 2020





Review Hyperthermia, Datta et al

Frontiers in Oncology 2020

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

Clinical evidence hyperthermia

> 27 positive randomized trails RT or CT ± HT

Reference	Treatment	Tumor	Endpoint	Lesions	RT/CT	RT/CT+HT
Van Driel (2018)	CT (hipec)	Ovarian	med Surv.	245	33.9m	45.7m
Issels (2018)	CT	Soft tissue sarcoma	med. Surv.	329	6.2yrs	15.4yrs
Chi (20018)	RT	Painful Bony mets	Time2pain prog	57	55d	>168d
Zhao (2014)	RT	Nasopharynx	3yr OS	83	54%	73%
Kang (2013)	RT+CT	Nasopharynx	5yr OS	154	50%	68%
Hua (2011)	RT+CT	Nasopharynx	5yr PFS	180	63%	73%
Huilgol (2010)	RT	Head and Neck	CR	54	42%	79%
Jones (2005)	RT	Various	CR	109	42%	64%
		previously irradiated		39	24%	68%
Colombo (2003)	CT	Bladder	2yr OS	75	40%	83%
Verwaal (2003)	CT (hipec)	Colorectal peri. car.	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	112	15%	31%
Vernon (1996)	RT	Breast	CR	308	41%	59%
		previously irradiated		39	39%	79%
Wang (1996)	RT	Oesophagus	3yr S	125	24%	42%
Overgaard (1995)	RT	Melanoma	2 yr NED	134	28%	48%
Kitamura (1995)	RT,CT	Oesophagus	CR	66	6%	25%
You (1993)	RT, surg.	Rectum	pCR	122	5%	23%
Sugimachi (1992)	RT, CT, surg.	Oesophagus	Palliation	53	8%	70%
Strotsky (1991)	RT, surg.	Bladder	3yr S	102	67%	94%
Berdow (1990)	RT, surg.	Rectum	5yr S	115	7%	36%
Kakehi (1990)	RT	Rectum	Response	14	20%	100%
Engelhardt (1989)	CT	Lung	Response	44	36%	60%
Egawa (1989)	RT	Various	Response	92	63%	82%
Valdagni (1988)	RT	Hoofd-hals	CR	44	41%	83%
Datta (1987)	RT	Cervix	CR	64	31%	55%
Kohno (1984)	CT	Vulva/vagina	Response	65	19%	59%

Review Hyperthermia, Datta et al

Frontiers in Oncology 2020

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All clinical studies report no relevant increase of side effects

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

Review Hyperthermia, Datta et al

Frontiers in Oncology 2020

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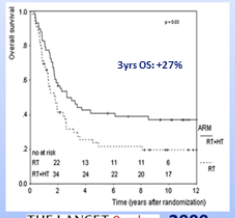
Clinical evidence hyperthermia >27 positive randomised trials RT or CT ± HT

Radiotherapy

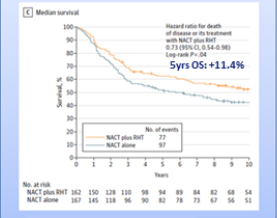
vd Zee et al. Franckena et al. Dutch Deep Hyperthermia Trial RT±HT in LACC: long term follow-up



THE LANCET Oncology 2000
Radiation Oncology ASTRO 2008

Chemotherapy

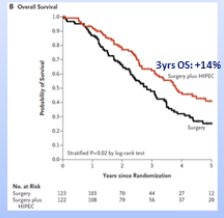
Issels et al. NAC+RHT: Long-term Outcomes Localized High-Risk Soft Tissue Sarcoma



JAMA Oncology 2018

Chemotherapy

Van Driel et al. Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer



The NEW ENGLAND JOURNAL of MEDICINE 2018

Review Hyperthermia, Datta et al

Frontiers in Oncology 2020

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Chemotherapy

Van Driel et al. Hyperthermic Intraperitoneal Chemotherapy in Ovarian Cancer

RT+HT regular care in NL, CH for patients with locally advanced cervical cancer refractory for chemo-radiation

July 2018 Every German Sarcoma cancer centre must provide access to hyperthermia

Jan 2018 Reimbursed in NL for abdominal metastasized Ovarian ca.

Review Hyperthermia, Datta et al

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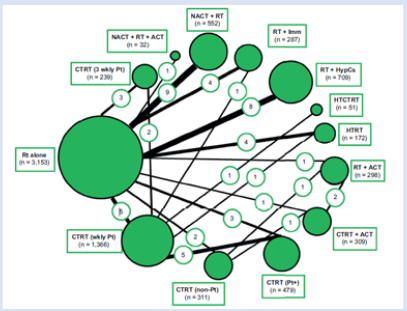
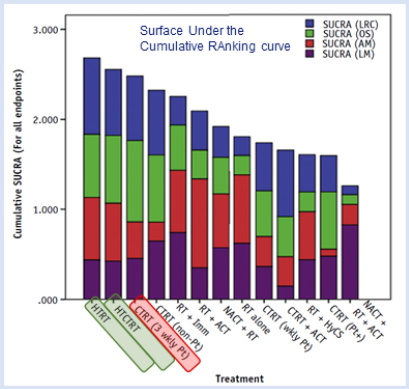
Systematic Review and Network Meta-Analysis of Randomized Clinical Trials
Locally Advanced Cervical Cancer



59 RCTs in LACC
9894 patients evaluated



Datta et al., Int. J. Radiation Oncology Biology Physics, 2019

Review Hyperthermia, Datta et al

Adding hyperthermia gives the best results

Strengths

trials and meta-analysis

Systematic Review and Network Meta-Analysis of Randomized Clinical Trials
Locally Advanced Cervical Cancer

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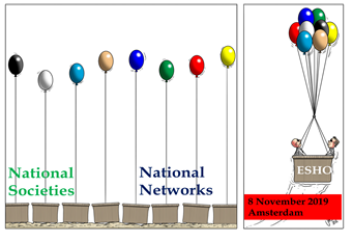
Datta et al., Int. J. Radiation Oncology Biology Physics, 2019

Review Hyperthermia, Datta et al

Frontiers in Oncology 2020

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



ESHO and Atzelsberg Circle combine efforts for CT-RT trials including hyperthermia (HT). Kick- off in Amsterdam 11-2019

Evaluating
- **Natl. phase II study RT+HT in rectum cancer Germany**
- **Int. study CT+HT: HEAT trial in pancreatic tumors Germany, Poland**

Running
- **Int. study RT+HT in anal cancer Germany, Italy, CH**
- **Natl. phase II study CRT+HT inop Rectum Ca. Germany**
- **Natl. study HyperThermia Enhanced Trabectedin for STS**

Initiatives
- **Int. study proton+HT in sacral chordoma patients CH, Netherlands, USA**
- **Intl. study RT/CT-HT for muscle invasive bladder cancer**
- **Natl. RTCT-HT for local advanced non metastastic pancreatic cancer (HEATPAC)**

Exclusive company initiated clinical trials.

Review Hyperthermia, Datta et al

Frontiers in Oncology 2020

Opportunities

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Non-invasive thermometry by MRI research

- Munich
- Rotterdam
- Dusseldorf
- Tubingen
- Erlangen

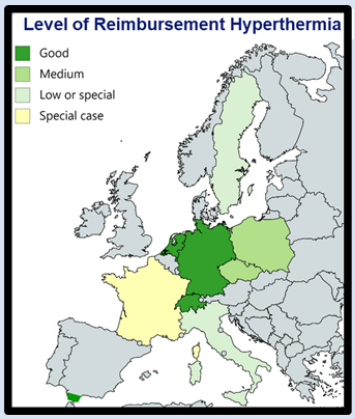
Review Hyperthermia, Datta et al

Frontiers in Oncology 2020

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.**

Summary

1. Recent **Phase III trials** confirm the potential of Hyperthermia to boost effectiveness of Radiotherapy and Chemotherapy
2. **New multicentric intl. phase III trials are mandatory to keep up to momentum**. Sites could be stratified for technology used. Central QA mandatory.
3. **Reimbursement** of hyperthermia is improving. A long way to go…
4. **Innovation** is needed to improve workflow for all staff (patients, physicians, physicist, RTT) and to therapy algorhythms (prescription, planning, execution, QA) for HT combined with RT/CT
5. **Quality assurance** is essential for good clinical practice of all devices

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Oncologic Thermotherapy/Hyperthermia 2020

Selected Swiss Activities

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Reimbursement of Oncologic Hyperthermia (HT combined with RT) in CH

2020: 4 indications for superf. HT approved 2016, 7 for deep HT final approval pending

Massnahmen	Leistungs-pflicht	Voraussetzungen	gültig ab
		Die Behandlungen erfolgen im Rahmen einer Klinik, die dem Swiss Hyperthermia Network angeschlossen ist. Indikationsstellung durch dessen Tumorboard.	
Regionäre Tiefen-hyperthermie zwecks Tumortherapie in Kombination mit externer Strahlen therapie oder Brachytherapie	Ja	Bei folgenden Indikationen: – Cervix-Karzinom, bei Kontraindikation für Chemotherapie oder lokal vorbestrahlt – Blasen-Karzinom (Funktionserhalt), bei Kontraindikation für Chemotherapie oder lokal vorbestrahlt – Rektum-Karzinom (Funktionserhalt), bei Kontraindikation für Chemotherapie oder Lokalrezidiv in vorbestrahltem Areal – Weichteil-Sarkom (Funktionserhalt), bei Kontraindikation für Chemotherapie – Pankreas-Karzinom, lokal fortgeschrittener, primär inoperabler Tumor Die Behandlungen erfolgen im Rahmen einer Klinik, die dem Swiss Hyperthermia Network angeschlossen ist. Indikationsstellung durch dessen Tumorboard.	1.1.2017 bis 31.12.2018

Diese Änderung tritt am 1. Januar 2017 in Kraft. Bitte beachten Sie, dass die Leistungspflicht für die regionäre Tiefenhyperthermie erst provisorisch mit einer Befristung bis Ende 2018 gilt. Wir bitten Sie, dem BAG bis spätestens Ende März 2017 ein vollständig dokumentiertes Antragsdossier zur erneuten Beurteilung der Wirksamkeit, Zweckmässigkeit und Wirtschaftlichkeit dieser Leistung durch die ELGK einzureichen.

Freundliche Grüsse

Abteilung Leistungen
Sektion Medizinische Leistungen

Felix Gurtner

Von: felix.gurtner@bag.admin.ch <felix.gurtner@bag.admin.ch>
Gesendet: Dienstag, 18. August 2020 10:51
An: Bodis Stephan <stephan.bodis@ksa.ch>
Betreff: Tiefen-Hyperthermie

Sehr geehrter Herr Prof. Bodis

Wegen Überlastung unseres Teams konnten nicht alle ursprünglich vorgesehenen Themen für die Beratung in der Eidg. Leistungs- und Grundsatzkommission (ELGK) vorbereitet bzw. in der ELGK beraten werden. Da in Zusammenhang mit der Tiefen-Hyperthermie keine hohe medizinische oder gesundheitspolitische Dringlichkeit besteht, wurde die Beratung dieses Themas auf die ELGK-Sitzung im November vertagt. Damit keine Leistungslücke entsteht, werden wir dem Eidg. Departement des Innern (EDI) empfehlen, die aktuell gültige, befristete Leistungspflicht für die Tiefenhyperthermie vorerst bis Mitte 2021 zu verlängern und erst auf dieses Datum hin anhand der Empfehlung der ELGK die Leistungspflicht definitiv zu regeln.

Wir werden Sie orientieren, sobald die ELGK das Thema beraten hat und sobald das Departement über die Verlängerung der Leistungspflicht entschieden hat.

Freundliche Grüsse

Felix Gurtner

Dr. med. Felix Gurtner, MSc
Facharzt für Prävention und Gesundheitswesen
Wissenschaftlicher Mitarbeiter

Eidgenössisches Departement des Innern EDI
Bundesamt für Gesundheit BAG
Direktionsbereich Kranken- und Unfallversicherung
Abteilung Leistungen Krankenversicherung
Sektion Medizinische Leistungen

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felix.gurtner@bag.admin.ch
www.bag.admin.ch

SWISS HYPERTHERMIA NETWORK

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ISO-Certification DIN EN ISO 9001:2015 of our Hyperthermia Unit in 2020 (Radiation Oncology Center Aarau and Baden) Increased acceptance of HT at least by hospital administrators and QA management

CLARCERT

ZERTIFIKAT

Auf Grundlage der Zertifizierungsentscheidung vom 01.07.2020 bescheinigt die ClarCert GmbH, dass das

Kantonsspital Aarau

Tellstrasse 25, CH-5001 Aarau

für das

Radio-Onkologie-Zentrum KSA-KSB

für den Geltungsbereich

Anwendung der Hyperthermie

ein Qualitätsmanagementsystem nach

DIN EN ISO 9001:2015

erfolgreich eingeführt hat und anwendet.

Gültigkeitsdauer: 10.06.2021
Registrier-Nummer: ISO-091-3
Datum der Ausstellung: 30.07.2020

Neu-Ulm, den 30.07.2020

DAkkS Deutsche Akkreditierungsstelle D-ZM-16034-01-01

Dieses Zertifikat ist ein Unterzertifikat und nur in Verbindung mit dem Hauptzertifikat mit der Registriernummer ISO-091-3 gültig.

Jürgen Fischer Geschäftsführer ClarCert GmbH

ClarCert GmbH · Gartenstraße 24 · D-89231 Neu-Ulm

SWISS HYPERTHERMIA NETWORK

SHN/SHRN activities with partners in intl. networks

Kantonsspital Aarau

Workshop ESHO 2019 : Strengthen the ESHO clinical trial committee
Intl. clinical study projects development for Hyperthermia combined with Radiotherapy

- F/u meeting in Amsterdam 11/2019 with a voting on presented clinical protocols (active, finalised not yet activated, in development) for phase I/II/III clinical trials
- Joint ESHO/Atzelsberg effort: Launch/conduct intl. multicentric trials in oncologic HT combined with RT and/or CT

EU Horizon 2020 Grant H2020-MSCA-ITN-2020-955625
Research and Innovation Framework Programme
Hyperthermia boosting the effect of radiotherapy
Swiss members: RAO KSA-KSB and ZHAW

ESTRO 2021
Scientific session: Current status of hyperthermia in radiation oncology
Interdisciplinary Symposium on Oncologic Hyperthermia as plenary session jointly with opinion leaders from Japan and USA

ESTRO 2021: ESTRO - JASTRO Hyperthermia Symposium

Biological rational for combining heat and radiation
Jens Overgaard DK

Clinical heating techniques, thermometry and quality assurance
Hans Creeze NL

Status of clincial Hyperthermia in Japan
Hideyuki Sakurai Jp

Thermoradiotherapy: Clinical evidence and potential indications
Zeljko Vujaskovic USA

Conclusions
Ben Slotman NL

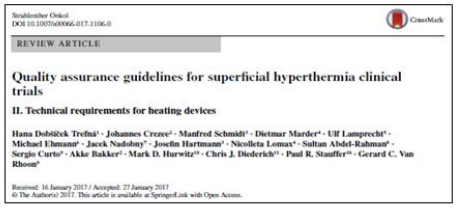
Chairs: Naojuki Shimegatsu Jp and Stephan Bodis CH

SHN | SWISS HYPERTHERMIA NETWORK

Kantonsspital Aarau

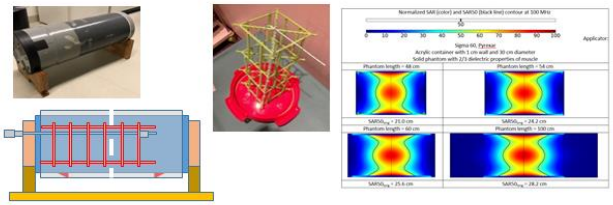
ESHO technical committee guidelines

Superficial HT - Current guideline 2017



Deep HT - Current guideline 2012

Currently under revision – new release 2021 planned



HYPERBOOST

Hyperthermia boosting the effect of Radiotherapy

H2020-MSCA-ITN-2020-955625

6 countries
11 beneficiaries
14 PhD students
Budget: € 3,761,881.56

Project coordination:
Hans Crezee
Amsterdam UMC

SHN SWISS HYPERTHERMIA NETWORK

Kantonsspital Aarau

EU Horizon 2020 Programme

Grant approved for Hyperthermia

Associated with document Ref. Ares(2020)2474290 - 11/05/2020

Proposal Evaluation Form

EUROPEAN COMMISSION

Horizon 2020 - Research and Innovation Framework Programme

Evaluation Summary Report

Call: H2020-MSCA-ITN-2020
Type of action: MSCA-ITN-ETN
Proposal number: 955625
Proposal acronym: HYPERBOOST
Duration (months): 48
Proposal title: Creation of advanced cancer treatment planning to boost the effect of Radiotherapy by combining with hyperthermia, heating the tumor.
Activity: MSCA-ITN-ETN: LIF

N.	Proposer name	Country	Total Cost	%	Grant Requested	%
1	ACADEMISCH MEDISCH CENTRUM BIJ DE UNIVERSITEIT VAN AMSTERDAM	NL	531,239.76	14.12%	531,239.76	14.12%
2	AARHUS UNIVERSITETSHOSPITAL	DK	595,044	15.82%	595,044	15.82%
3	Kantonsspital Aarau AG	CH	281,276.64	7.48%	281,276.64	7.48%
4	UNIVERSITAETSKLINIKUM ERLANGEN	DE	505,576.8	13.44%	505,576.8	13.44%
5	ZURCHER HOCHSCHULE FUR ANGEWANDTE WISSENSCHAFTEN	CH	281,276.64	7.48%	281,276.64	7.48%
6	Dr. Sennewald Medizintechnik GmbH	DE	252,788.4	6.72%	252,788.4	6.72%
7	Medlogix srl	IT	261,499.68	6.95%	261,499.68	6.95%
8	CHARITE - UNIVERSITAETSMEDIZIN BERLIN	DE	252,788.4	6.72%	252,788.4	6.72%
9	CHALMERS TEKNISKA HOEGSKOLA AB	SE	281,982.96	7.50%	281,982.96	7.50%
10	ERASMUS UNIVERSITAIR MEDISCH CENTRUM ROTTERDAM	NL	265,619.88	7.06%	265,619.88	7.06%
11	MAX DELBRUECK CENTRUM FUER MOLEKULARE MEDIZIN IN DER HELMHOLTZ-GEMEINSCHAFT (MDC)	DE	252,788.4	6.72%	252,788.4	6.72%
	Total:		3,761,881.56		3,761,881.56	

Abstract:
Hyperthermia (HT), heating tumors to temperatures of 40-44 °C, is an oncological treatment used in combination with radiotherapy (RT) and chemotherapy to enhance their efficacy. Clinical effectiveness of HT has been demonstrated in randomised studies and HT is currently applied for many clinical indications, like cervical cancer and recurrent breast cancer. Clinical results can be further improved as application of HT with well-controlled tumor temperatures and optimal timing and sequence realising full synergy of RT+HT is challenging. Optimal HT delivery requires accurate planning, moreover preclinical research has shown that many mechanisms are responsible for the therapeutic effect of HT, all presumably with a different temperature-effect relationship and with different optimal timing between RT and HT. Optimisation of clinical RT+HT treatments therefore requires a quantum leap in understanding and in clinical application.
Scientific objective of this multidisciplinary project with contributions from all sectors and disciplines (biology, physics and oncology) is to combine training and research into the synergistic molecular mechanisms responsible for the therapeutic effect of HT on RT with the development of a versatile and innovative planning platform which utilises biological knowledge to achieve optimal patient-specific treatment delivery and ultimately application in a clinical registration study in a network of European centres implementing this treatment planning software to ensure optimal treatment delivery.
This ground-breaking and multidisciplinary project with contributions from biology, physics and oncology will create a versatile and innovative planning platform, enhance fundamental knowledge and create practical tools to achieve personalised treatment, thereby augmenting treatment delivery and clinical results. The projects will also educate 15 highly skilled professionals capable of addressing and solving complex oncological issues.

Evaluation Summary Report

Evaluation Result

Total score: 96.00% (Threshold: 70/100.00)

HYPERBOOST

Hyperthermia boosting the effect of Radiotherapy

H2020-MSCA-ITN-2020-955625

Key objectives "*HYPERBOOST*"

- Train and equip early stage researchers with transferable, multi-disciplinary skills essential in high-end biomedical engineering, clinical hyperthermia and translational oncology (**WP2**)
- Obtain and validate new insights into clinical working mechanisms of hyperthermia (**WP3**)
- Translate preclinical and clinical results (**WP3**, **WP5**) into mathematical relations and treatment planning models (**WP4**)
- Apply novel treatment planning models for personalised treatment (**WP4**) clinically to improve the efficacy of clinical treatments (**WP5**)
- Initiate, stimulate and profit from **multidisciplinary cross-pollination** between the disciplines involved in hyperthermic oncology (**WP3-5**)
- Consolidate and expand the **European infrastructure** and industry for hyperthermia research and clinical application (**WP 2-6**)