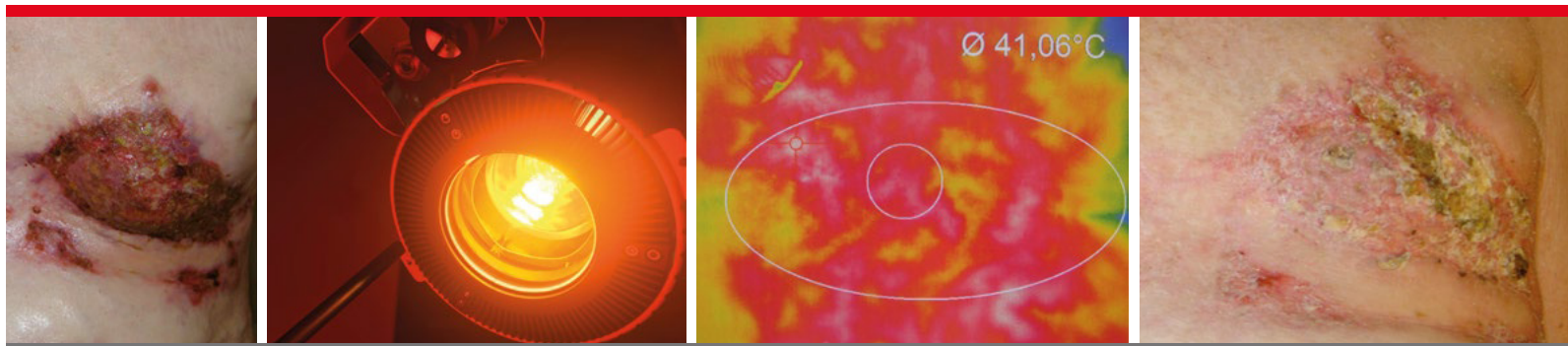


RMS MEDICAL SUPPLIES LTD

Thermography-controlled
Water-filtered Infrared-A Superficial
Hyperthermia
and (Re-)Irradiation

New Option for Effective Control of Locally Recurrent Breast Cancer



hydroSun[®] TWH1500

Thermography-controlled Water-filtered Infrared-A superficial Hyperthermia

heckel

hyperthermia

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Locally Recurrent Breast Cancer (LRBC)

The challenge

Although the general therapeutic options and treatment results of breast cancer have remarkably improved, the treatment of locally recurrent breast cancer (LRBC) – especially in cases of pre-irradiation and resistance to chemo- and hormone therapy – is still a major problem.

Patients suffer from a horrible loss of quality of life (pain, ulceration, bleeding, thoracic constriction, lymphoedema, nerve infiltration).

The therapeutic aim is effective local control

- for improvement of quality of life
- for longer survival and even cure in cases without metastasis



The hurdles

In general, a pre-irradiated area is less perfused and more hypoxic.

Under these unfavourable conditions

- tumours tend to be biologically more aggressive
- anti-tumour immune surveillance is substantially hampered
- the resistance to radiotherapy is significantly increased

Cumulative toxicity and the risk of major side effects often prevent re-irradiation at therapeutically effective dosages.

Often, systemic therapy is either not effective because of the resistance or not acceptable because of the threatening systemic side effects.

In a systematic review, superficial hyperthermia (HT) combined with radiotherapy (RT) in the treatment of LRBC proved efficacy in achieving local control with lower total radiation doses:

Datta NR, Puric E, Klingbiel D, Gomez S, Bodis S: Hyperthermia and radiation therapy in locoregional recurrent breast cancers: A systematic review and meta-analysis. Int J Radiat Oncol Biol Phys. 2016 Apr 1;94(5):1073-87.

In randomized controlled studies (RCT) the CR rate in the combined RT/HT group was significantly higher than in the RT group alone (Jones et al, 2005: 66% compared to 42%). An even significantly higher benefit was shown in patients who had previously been irradiated (68% compared to 28%).

Several single-arm studies confirm the findings of the RCTs.

The authors conclude: „Thermoradiation therapy could therefore be considered as an effective and safe palliative treatment option for LRBCs“.

Proven efficacy in LRBC

Tissue temperatures of superficial hyperthermia using hydrosun® TWH1500 are 39 - 43°C. In this temperature range, hyperthermia enhances cytotoxicity of standard therapies, mainly by

- inhibition of DNA-repair
- improved tissue blood flow and oxygenation
- increased vessel permeability

This is especially true for heavily pre-treated areas where the efficacy of radio- or chemotherapy alone is limited.

In addition, anti-tumor immune responses may be stimulated by hyperthermia.

Datta NR, Kok HP, Crezee H, Gaipl US, Bodis S: Integrating loco-regional hyperthermia into the current oncology practice: SWOT and TOWS analyses. Front Oncol. 2020 Jun 12;10:819.

van Rhoon GC, Franckena M, Ten Hagen TLM: A moderate thermal dose is sufficient for effective free and TSL based thermochemotherapy. Adv Drug Deliv Rev. 2020, Vol 163-164:145-156.

Hyperthermia as a
potent radio- and
chemosensitizer

- DEGRO practical guidelines for radiotherapy of breast cancer VI: therapy of locoregional breast cancer recurrences, 2016
- AGO (Arbeitsgemeinschaft Gynäkologische Onkologie) Guidelines Breast, Version 2020.01, Loco-Regional Recurrence
- Interdisziplinäre S3-Leitlinie für die Früherkennung, Diagnostik, Therapie und Nachsorge des Mammakarzinoms; Langversion 4.3 – Februar 2020

Superficial Hyperthermia
+ (re-)irradiation in
leading breast cancer
guidelines

DEGRO DEUTSCHE GESELLSCHAFT FÜR RADIOONKOLOGIE E.V.

AGO
ARBEITSGEMEINSCHAFT
GYNÄKOLOGISCHE
ONKOLOGIE E.V.

DKG KREBSGESELLSCHAFT

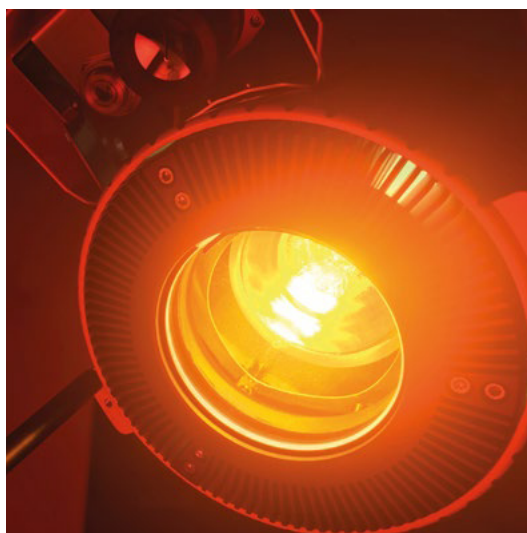
The world-first device for
effective contact-free
superficial hyperthermia

High Efficacy and
Extremely Low Toxicity
even for the treatment
of large-sized and
inflammatory lesions

- Water-filtered Infrared A (wIRA) with a high and most compliant energy input
- Covering large treatment areas independent of heterogenous body contours
- Continuous real-time thermographic control with automatic switch on and off control functions allowing an optimal and safe energy input, achieving an effective heating depth ($>39^{\circ}\text{C}$) of at least 20 mm (maximum skin temperature set at 42°C - 43°C)
- Acute thermal skin damage (TSD) has been reduced to almost 0%. Additionally, the physiological reactions in the treatment area can be observed during hyperthermia treatment and analyzed even afterwards
- Compliant for any patient. The patient does not suffer from any body fixation or painful applicator contact, e.g. with ulcerated lesions. Metal and any implants and pace-makers are not contraindicated
- No shielding required

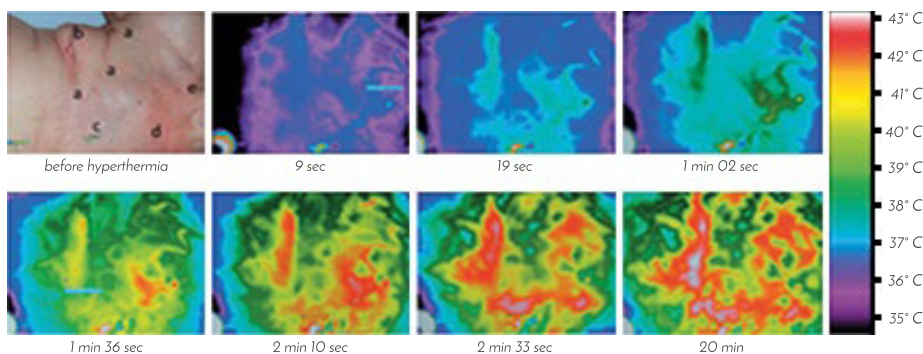


Thermography-controlled Water-filtered infrared-A superficial Hyperthermia - hydrosun®TWH1500



A computer-controlled feedback system registers the detailed temperature distribution of the treated skin area, whereby a ROI can be defined. The programme provides a real-time control of the wIRA radiation unit by switching off and on in a defined range of maximum temperature (42°C - 43°C). Treatment data will be documented and stored. Visual inspections of the colour-coded temperature images could be additionally used to guide the correct adjustment of the wIRA-radiator position and to avoid the potential occurrence of hotspots. Hotspots chiefly occurring in scar tissue with poor perfusion, could be temporally shielded against further wIRA radiation as needed.

TWHControl Software



[Notter et al., 2017]

The unique principle of hydrosun® wIRA is a hermetically sealed water filter that absorbs infrared-B and -C light with wavelengths of > 1380 nm as well as two distinct water absorption bands at 944 and 1180 nm. The energy of these wavelengths would be absorbed in the upper layer of skin and thereby considerably limit the intensity of compliant irradiance.

hydrosun® wIRA Principle

Thermography-controlled wIRA superficial hyperthermia is an approved method in the „Quality assurance guidelines for superficial hyperthermia clinical trials“, issued by ESHO (European Society for Hyperthermic Oncology) and published in Int J Hyperthermia 2017 and Strahlenther Onkol 2017.



Clinical Results

From September 2009 on, heavily pre-irradiated patients with LRBC have been treated using a new treatment schedule with high efficacy and extremely low radiotherapy- and hyperthermia-related toxicity. Results till 07/2015 resp. 09/2019 are published in:

INTERNATIONAL JOURNAL OF HYPERTHERMIA, 2017
VOL. 33, NO. 2, 227-236
<http://dx.doi.org/10.1080/02656567.2016.1225731>

ORIGINAL ARTICLE

Hypofractionated re-irradiation of large-sized recurrent breast cancer with thermography-controlled, contact-free water-filtered infra-red-A hyperthermia: a retrospective study of 73 patients

Markus Nötter^{a,*}, Helmut Piazena^b and Peter Vaupel^c

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cancers

Article

Combined wIRA-Hyperthermia and Hypofractionated Re-Irradiation in the Treatment of Locally Recurrent Breast Cancer: Evaluation of Therapeutic Outcome Based on a Novel Size Classification

Markus Nötter¹, Andreas R. Thomsen^{2,3}, Mirko Nitsche⁴, Robert M. Hermann⁴, Hendrik A. Wolff^{5,6}, Gregor Hahl^{5,7}, Karin Münch¹, Anca-L. Grosu^{2,3} and Peter Vaupel^{2,3,*}

Thermography-controlled wIRA superficial Hyperthermia
45 - 60 min.

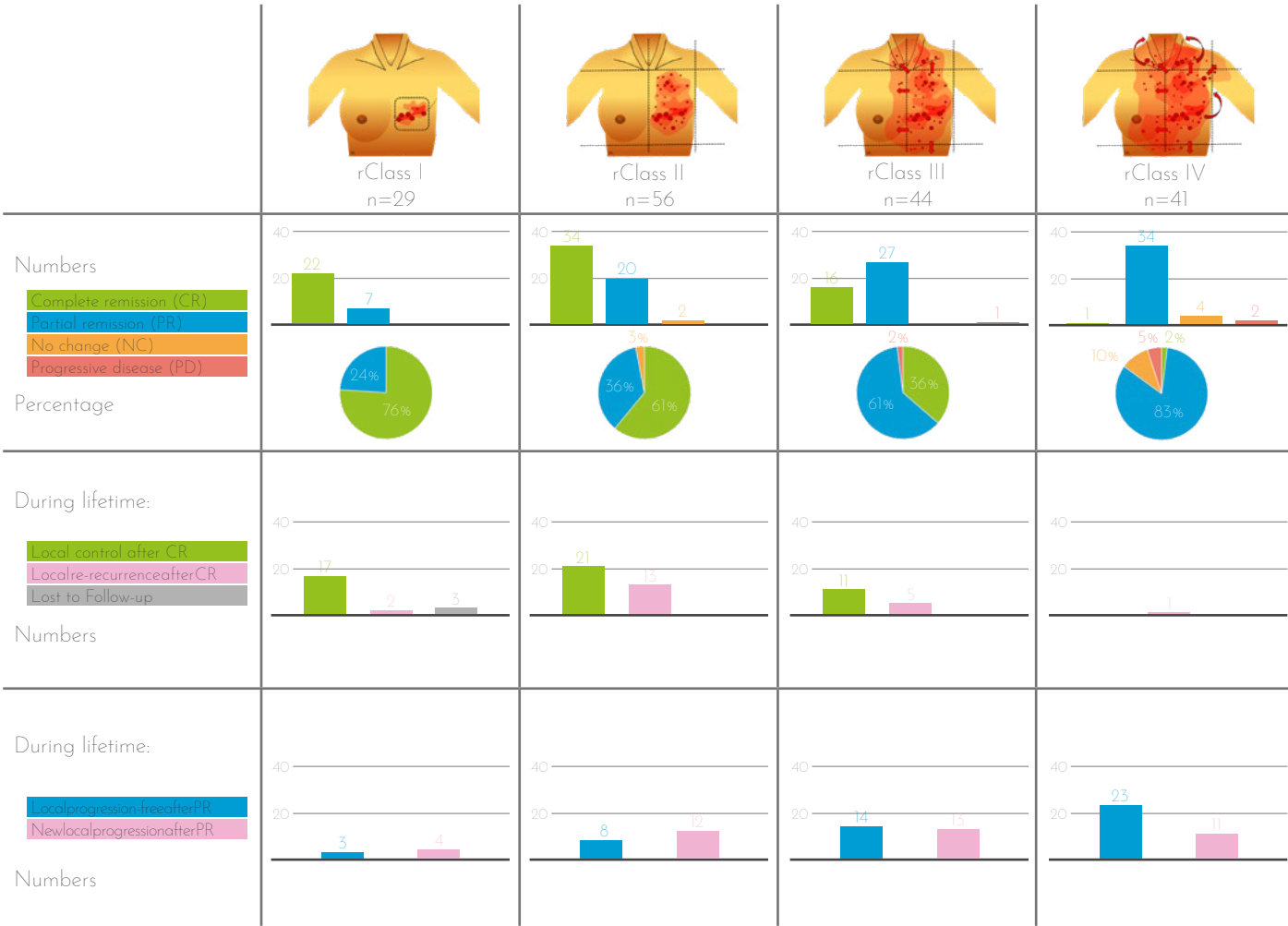
→

1-4 min.
transfer

→

Hypofractionated (re-)irradiation
1 x/week à 4Gy
Total dose: 5 x 4 Gy = 20 Gy

High efficacy



→ 19 of 21 patients with re-recurrences after CR and 24 of 40 patients with new local progression after PR received one or more repeat re-irradiations and wIRA-HT using the same protocol.



■
Extended recurrent breast cancer: Former RT-dose chest wall 50 Gy + 10 Gy boost scar
Before re-RT & wIRA



■
6 weeks after
5 x 4 Gy + wIRA, 1x/wk



■
Recurrent breast cancer en cuirasse: former RT-dose both chest walls: 54 Gy
Before re-RT & wIRA



■
6 weeks after
5 x 4 Gy + wIRA, 1x/wk



■
1st recurrence:
54 Gy + 9 x MW-hyperthermia.
2nd recurrence 4 months later.
Before re-RT & wIRA



■
6 weeks after
5 x 4 Gy + wIRA, 1x/wk

Low toxicity

Acute toxicity occurred in 43% of the patients and was mostly limited to grade 1, few cases of grade 2, no cases of $\geq$ Grade 3.

Thermal skin damage (Grade 2) occurred in 1 patient (<1% of the patients).

Chronic toxicity occurred in 28% of the patients and was mostly limited to grade 1, few cases of grade 2 (teleangiectasia), no cases of $\geq$ Grade 3.

Low toxicity allows for safe and **effective** repeat re-irradiation of re-recurrences.

These results were achieved although – compared to other clinical studies on HT/RT in LRBC – pre-irradiation dosage as well as the size of tumor lesions were highly above-average, whereby the total re-irradiation dose of $5 \times 4 \text{ Gy} = 20\text{Gy}$ was the lowest dose ever applied in a protocol aiming for **effective** tumor control.

hydrosun® TWH1500 is developed and manufactured by Hydrosun Medizintechnik GmbH, Müllheim/Germany, a pioneer and world market leader in water-filtered infrared-A technique.

Hydrosun has a certified Full Quality System as to ISO 13485 and MDD 93/42/EEC, Annex II.

heckel is the exclusive distributor for the superficial hyperthermia device hydrosun® TWH1500 and the whole-body hyperthermia device heckel-HT3000.



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79379 Müllheim / Germany



11.2021

© Image page 2: Alexander Raths/Shutterstock.com, Image page 5: TWH1500 at Ordensklinikum Linz / Austria

heckel

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