## INFORMATION BRIEF (RAPID REVIEW)

# REMISSION 1°C HYPERTHERMIA HIGH-FREQUENCY DEVICE FOR CANCER TREATMENT (UPDATE)

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**Medical Development Division**
**Ministry of Health Malaysia**
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# TITLE: REMISSION 1°C HYPERTHERMIA HIGH-FREQUENCY DEVICE FOR CANCER TREATMENT

## PURPOSE

To provide update in evidence on the effectiveness, safety, and cost-effectiveness of Remission 1°C hyperthermia high-frequency device for cancer treatment following a request from Deputy Director of MaHTAS.

## BACKGROUND

Hyperthermia as a cancer treatment (also called thermal therapy) refers to the use of high temperatures to treat the disease. It may be used alone or in combination with chemotherapy, immunotherapy, radiation therapy or other treatments, and can be delivered locally, regionally, or to the whole body depending on the type and stage of the cancer being treated. In the early days, hyperthermia alone (at 42-44°C) was performed against recurrent tumours derived from head and neck cancer and breast cancer, which appeared on the surface of the body. However, most cancers including primary sites as well as recurrent or metastatic sites are located deep inside the body. This makes hyperthermia alone less effective because it is quite difficult to heat only cancer tissues to more than 42°C using currently available heating devices.[1-2]

Hyperthermia treatment using Remission 1°C device (AdipoLABs, Seoul, Korea) which produced a 0.46-MHz radiofrequency wave that induces strong deep heat has been proposed. It is claimed to increase immunity by increasing the temperature of organs (liver, lung, colorectal and others), thereby destroying the cancer cells. The logic behind its use is that in hyperthermia, the heat increases blood flow to the tumour which does three things; it brings more chemotherapy inside the tumour, it brings oxygen that helps radiation therapy work better, and it induces body's immune system to attack the cancer. Relating to this, Remission 1°C treatment programme (60-90 minutes per session, 2-5 times per week) may varies depending on the patient conditions. [3]

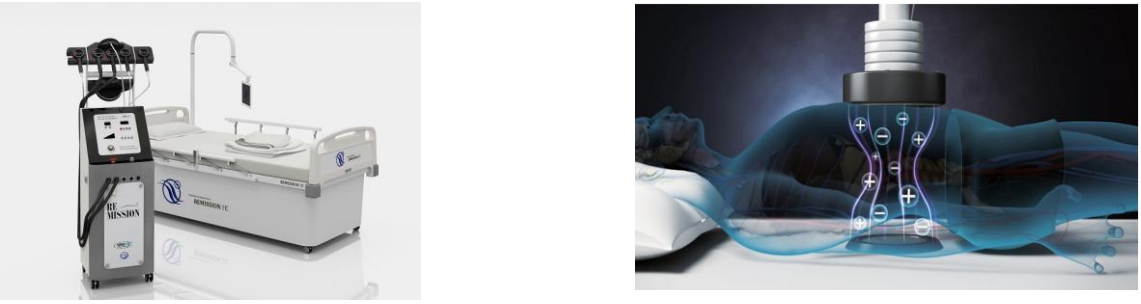

**Figure 1: Remission 1°C hyperthermia system and how it works**

## EVIDENCE SUMMARY

In the earlier 2022 review, a total of 245 titles related to hyperthermia high-frequency device was retrieved from the scientific databases such as Medline, EBM Reviews via OVID, PubMed and from general search engines using the following search terms; *cancer therapy, hyperthermia, radiotherapy, chemotherapy, radiofrequency, combination cancer therapy.* Given this information, nine articles were found to be relevant and finally selected for this review. In addition to the previous review, there were two evidences included in this current review.

## EFFICACY/ EFFECTIVENESS

**Evidence on Remission 1°C:**

**Evidences from previous review:**

Previous assessment by MaHTAS on radiofrequency-[RF-] Hyperthermia ASKIRF-8 (apparently similar technology to Remission 1°C device) recommended its use as an adjunct with chemotherapy, radiotherapy, and surgery for various cancer treatment.[4] Hyperthermia is rarely used as a single cancer treatment modality while there are many combinations with chemotherapy and radiation been used or are currently being studied in clinical trials. Subsequent review in 2022 by MaHTAS concluded that there was no strong evidence on the indication of Remission 1°C high-temperature device in the treatment of cancer, however, there were evidence of its adjunct use alongside standard cancer therapy that resulted in higher response rates, better survival rates, improved tumour control rate and better palliative effects.[16]

A case study in Korea (2016) reported good result on a patient suffering from recurred hepatocellular carcinoma, in which the Remission 1°C device was combined with sorafenib. After the treatment, tumour size was decreased accompanying by reducing the level of tumour markers (AFP, PIVKA-II). Major clinical symptoms were also improved with increasing natural killer (NK) cell activity.[6]

Another case study (2018) also reported the efficacy of Remission 1°C hyperthermia high-frequency device combined with gemcitabine/ cisplatin for the treatment of a 54-year-old man with unresectable extrahepatic bile duct carcinoma (cholangiocarcinoma). Hyperthermia combined with chemotherapy was administered 32 times over a period of four months. The patient experienced no critical complications, and the patient's condition improved with the carbohydrate antigen 19-9 (CA 19-9) and the total bilirubin levels being relatively lowered. In addition, the computed tomography (CT) scan showed that the cholangiocarcinoma had not progressed.[7]

A local clinical trial on the Remission 1°C hyperthermia device was conducted at University Malaya Medical Centre. It was aimed to assess the immune response of locoregional hyperthermia alongside standard cancer treatment for patients with recurrent, metastatic or locally advanced solid malignancies. There were 30 patients involved in this study. The analysis of lymphocytes subsets reported that significant increase in CD8+ central memory T cells (Mean: Baseline 3.854, Week 1A 5.818; p = 0.013) and CD8+ T cell expressing checkpoint inhibitory marker PD-1 (Mean: Baseline 3.854, Week 1A 5.818; p = 0.013 and Mean: Baseline 7.439, Week 1B 9.222; p = 0.033). During the next week-4 of treatment, there was an increase in percentage of CD4+ Effector Memory T Cells (Mean: Baseline 33.60, Week 39.34; p = 0.022). The small study concluded that significant effect in the immune cell profiles of cancer patients (Cd4 + effector memory cells) was observed with the combination of hyperthermia and standard cancer treatment.[12,18]

Updated recent evidence from Lee YK et al. (2025) involved 40 patients with metastatic abdominal lymph nodes who were either receiving combined hyperthermia radiotherapy (HTRT) and radiotherapy alone in South Korea. This study examined the radiological changes such as Hounsfield units (HU) in patients receiving either HTRT or RT. There were no statistically significant changes in clinical characteristics between two groups. However, low biological dose of therapeutic radiation was reported in HTRT group. The median value of the average HU in HTRT and RT groups after treatment were 58.95 HU (range: 15.02 to 136.57 HU) and 71.42 HU (range: 37.53 to 144.41 HU), respectively. Furthermore, HTRT group has shown 9.05% reduction in the average change in HU value (range: -80.30% ± 29.94%; median value of -8.47%), meanwhile, only 0.57% reduction (range: -80.30% ± 29.94%; median value of -8.47%) in RT group. The degree of reduction was noticeable in HTRT group with 80% patients showed reduction in HU values, compared to 50% in RT group. The study concluded that HTRT leads to more pronounced reduction in HU values leads to enhanced changes in necrotic compared to RT alone for patients with metastatic abdominal lymph nodes. However, it should be noted that the sample size of the study was small.[17]

**Evidence on thermal therapy:**

**Combination with chemotherapy**

In an open-label, phase three randomised controlled trial (RCT) across nine centres in Europe and the US, Issels RD et al. (2018) evaluated the efficacy and toxic effects of neoadjuvant chemotherapy plus regional hyperthermia among 341 adult patients with localized soft tissue sarcoma. Compared with neoadjuvant chemotherapy alone, adding regional hyperthermia improved local progression-free survival (hazard ratio [HR] 0.65; 95% confident interval [CI] 0.49 to 0.86; p=0.002). Patients randomised to chemotherapy plus hyperthermia had prolonged survival rates compared with those randomised to neoadjuvant chemotherapy alone (HR 0.73; 95% CI 0.54 to 0.98; p=0.04) with 5-year survival of 62.7%

(95% CI 55.2% to 70.1%) versus 51.3% (95% CI 43.7% to 59.0%), respectively, and 10-year survival of 52.6% (95% CI 44.7% to 60.6%) versus 42.7% (95% CI 35.0% to 50.4%).[5]

**Combination with radiotherapy**

Hyperthermia in combination with radiation may be particularly helpful in some settings. A systematic review and meta-analysis by Datta NR et al. (2015) evaluated the outcome of controlled clinical trials in head and neck cancers using hyperthermia and radiotherapy versus radiotherapy alone. The overall complete response with radiotherapy alone was 39.6% (92/232) and varied between 31.3% and 46.9% across the six trials. With thermoradiotherapy, the overall complete response reported was 62.5% (137/219; range 33.9-83.3%). The odds ratio was 2.92 (95% CI 1.58 to 5.42, p=0.001); the risk ratio was 1.61 (95% CI 1.32 to 1.97, p<0.0001) and the risk difference was 0.25 (95% CI 0.12 to 0.39, p<0.0001), all in favour of combined treatment with hyperthermia and radiotherapy over radiotherapy alone.[8]

A 2019 review of studies looking at the use of hyperthermia combined with radiation therapy for recurrent breast cancer found that the combination appeared to influence the complete response, the duration of responses, and overall survival compared with the use of radiation therapy alone. Similar benefits have been noted in studies looking at melanoma, sarcoma, and cervical cancer.[9]

A phase three RCT by Chi SM et al. (2018) compared the use of radiation therapy alone to treat bone metastases with that of radiation therapy plus hyperthermia (hyperthermia applied within an hour of the radiation). The study demonstrated that the addition of hyperthermia to radiation therapy significantly increased the pain control rate (p<0.01) and extends treatment response duration (p=0.04).[10]

**Combination with chemotherapy and/or radiotherapy**

A systematic review with conventional and network meta-analyses (NMA) was conducted to examine the outcomes of loco-regional hyperthermia with radiotherapy and/or chemotherapy in locally advanced cervix cancer, IIB–IVA (LACC). Eight articles were finally retained while six randomised trials with hyperthermia + radiotherapy (n=215) versus radiotherapy (n=212) were subjected to meta-analysis. The risk difference for achieving complete response and long-term loco-regional control was greater by 22% (p<0.001) and 23% (p<0.001), respectively. The only hyperthermia + chemotherapy + radiotherapy versus radiotherapy trial documented a complete response of 83.3% versus 46.7% (risk difference: 36.7%; p=0.001). Bayesian NMA, incorporating 13 studies (n=1,000) for complete response and 12 studies for patients alive (n=807), comparing hyperthermia + chemotherapy + radiotherapy, hyperthermia + radiotherapy, chemotherapy + radiotherapy, and radiotherapy alone was performed. The pairwise comparison of various groups showed that hyperthermia + chemotherapy + radiotherapy was the best option for both complete response and patient

survival. This was also evident on ranking treatment modalities based on the "surface under cumulative ranking" values.[11]

**Combination with other treatments**

A retrospective record based observational study of 54 cancer patients treated with chemotherapy or radiation therapy was undertaken by Hyeong Joon Jun et al. (2020) to monitor the effect of hyperthermia together with Korean herbal medicine, *Gun-Chil-Jung* capsule for the treatment of various cancer types. It was evident from the data that combination of hyperthermia 1 to 2 times a week with *Gun-Chil-Jung* treatment may improve event-free survival and overall survival of cancer patients treated or being treated with conventional cancer therapies.[13]

Ou J et al. (2020) conducted a randomised phase II trial to evaluate the effect of best supportive care (with or without intravenous vitamin C) combined with simultaneous modulated electrohyperthermia (three times weekly for 25 sessions) on tumour response, progression free survival, and overall survival in previously treated patients with refractory advanced (stage IIIb or IV) non-small-cell lung cancer (NSCLC). After a median follow-up of 24 months, progression-free survival and overall survival were significantly prolonged by combination therapy compared to best supportive care alone (progression-free survival: 3 months versus 1.85 months, $p<0.05$; overall survival: 9.4 months versus 5.6 months, $p<0.05$). Quality of life was significantly increased in the intervention arm despite the advanced stage of disease. The 3-month disease control rate after treatment was 42.9% in the intervention arm and 16.7% in the control arm ($p<0.05$). Overall, intravenous vitamin C and modulated electrohyperthermia may have the ability to improve the prognosis of patients with advanced NSCLC.[14]

## SAFETY

No adverse events (AEs) or complications related to Remission 1°C hyperthermia high-frequency device for cancer treatment were reported. In general, hyperthermia treatments are well tolerated by patients. The risks and side effects of hyperthermia depend on what part of the body is treated (how high the temperature is raised) and tend to be relatively mild, especially compared with the side effects of many other cancer treatments. In terms of combination therapies with hyperthermia, the toxicities were generally mild and acceptable, and there were no grade 3 AEs documented. The most common treatment related AEs were radiotherapy related, such as grade 1 skin reaction, nausea/ vomiting, and diarrhoea.[5-14] Recent evidence reported Grade 1 to 2 skin burn, fat necrosis and pain by patients receiving the combination of hyperthermia and standard cancer treatment.[18]

Regarding safety, the FDA has approved hyperthermia in combination with radiation therapy for the palliative management of certain solid surface and subsurface malignant tumours (i.e.,

melanoma, squamous or basal cell tumours, adenocarcinoma, or sarcoma) that are progressive or recurrent despite conventional radiation therapy.[15] Remission 1°C hyperthermia high-frequency device was registered with Medical Device Authority (MDA) Malaysia and has been certified as Class B Medical Device.[12]

## COST-EFFECTIVENESS

There was no retrievable evidence on the cost-effectiveness of Remission 1°C hyperthermia high-frequency device for cancer treatment.

## CONCLUSION

Based on the above updated review, there was no incidence retrieved on Remission 1°C use as stand-alone cancer therapy. There was limited evidence retrieved demonstrating the use of Remission 1°C as an adjunct with the standard cancer treatment such as chemotherapy, radiotherapy or in combination, in patients with cancer.

## REFERENCE


1. Hyperthermia therapy. Available at https://en.wikipedia.org/wiki/Hyperthermia_therapy Accessed on 31st May.2022
2. Yagawa Y, Tanigawa K, Kobayashi Y et al. Cancer immunity and therapy using hyperthermia with immunotherapy, radiotherapy, chemotherapy, and surgery. J Cancer Metastasis Treat. 2017; 3: 218-230
3. Adipolabs Healthcare Malaysia. Available at https://adipolabs-msia.com/clinical-reference-papers Accessed on 2nd June 2022
4. Ros Aziah MR and Izzuna MMG. Radiofrequency hyperthermia ASKIRF-8 for cancer treatment. Information Brief. Ministry of Health Malaysia: Malaysian Health Technology Assessment Section (MaHTAS); 2018. 9 p. Report No.: 004/2018
5. Issels RD, Lindner LH, Verweij J et al. Effect of neoadjuvant chemotherapy plus regional hyperthermia on long-term outcomes among patients with localized high-risk soft tissue sarcoma: the EORTC 62961-ESHO 95 randomized clinical trial. JAMA Oncol. 2018; 4(4): 483
6. Kim JH, Lee JH, Joo JC et al. A case report of recurred hepatocellular carcinoma patient treated with radio-frequency hyperthermia in conjunction with sorafenib. J Korean Tradit Oncol. 2016; 21: 63-74
7. Ryu J, Lee K, Joe C et al. Patient with unresectable cholangiocarcinoma treated with radiofrequency hyperthermia in combination with chemotherapy: A case report. Integr Cancer Ther. 2018; 17(2): 558-561
8. Datta NR, Rogers S, Ordóñez SG et al. Hyperthermia and radiotherapy in the management of head and neck cancers: A systematic review and meta-analysis. Int J Hyperthermia. 2016; 32(1): 31-40
9. Bakker A, van der Zee J, van Tienhoven G et al. Temperature and thermal dose during radiotherapy and hyperthermia for recurrent breast cancer are related to clinical outcome and thermal toxicity: a systematic review. Int J Hyperthermia. 2019; 36(1): 1024-1039
10. Chi MS, Yang KL, Chang YC et al. Comparing the effectiveness of combined external beam radiation and hyperthermia versus external beam radiation alone in treating patients with painful bony metastases: A phase 3 prospective, randomized, controlled trial. Int J Radiat Oncol Biol Phys. 2018; 100(1): 78-87
11. Datta NR, Rogers S, Klingbiel D et al. Hyperthermia and radiotherapy with or without chemotherapy in locally advanced cervical cancer: a systematic review with conventional and network meta-analyses. Int J Hyperthermia. 2016; 32: 7: 809-821
12. Proposal letter from Sai Development Sdn. Bhd. to Minister of Health Malaysia on Remission 1°C hyperthermia high-frequency device.
13. Ju HJ, Park SJ, Kang HJ et al. The survival benefit of combination therapy with mild temperature hyperthermia and an herbal prescription of Gun-Chil-Jung in 54 cancer patients treated with chemotherapy or radiation therapy: A retrospective study. Integr Cancer Ther. 2018, 19: 1-12

14. Ou J, Zhu X, Chen P et al. A randomized phase II trial of best supportive care with or without hyperthermia and vitamin C for heavily pretreated, advanced, refractory non-small-cell lung cancer. J Adv Res. 2020; 24: 175-182
15. U.S. Food and Drug Administration: Medical Devices: BSD-2000 Hyperthermia System - H090002. Available at www.fda.gov. Accessed on 16th June 2022
16. Syful Azlie MF and Izzuna MMG. Remission 1°C hyperthermia high-frequency device for cancer treatment. Information Brief. Ministry of Health Malaysia: Malaysian Health Technology Assessment Section (MaHTAS); 2022. 9 p. Report No.: 007/2022
17. Lee YK, Choi KH, Cheon W, et al. Hounsfield unit change in metastatic abdominal lymph nodes treated with combined hyperthermia and radiotherapy. PLoS One. 2025 Mar 25;20(3):e0318330.
18. Ho GF, Yong CJ, Rajasuriar R, et al. Immune modulatory effect of hyperthermia during treatment of recurrent, metastatic or locally advanced solid organ malignancies. JUMMEC. 2024;27(2):74–82.

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