Clinical experience of two cases with HIFU and WBH - A. Takeuchi et al.

Case Report

Thermal Combination Therapy with HIFU Ablation and Whole Body Hyperthermia

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Abstract: A new high intensity focused ultrasound (HIFU) apparatus (Sonic CZ901: Mianyang Sonic Electronic Ltd, China) was installed in our hospital last December. The device has been used 20 times in 12 advanced cancer patients, and some results concerning the use of HIFU ablation and Whole body hyperthermia (WBH) via far-infrared equipment (RHS 7500: Enthermics Medical Systems, USA) can be reported. The first patient had pharyngeal cancer (20y.o, F) with lung and multiple liver metastases. The lung tumor shrank after WBH (weekly treatments, for a total of 4 treatments) and the liver tumor was clearly reduced by HIFU treatment. A second patient who received the combined treatment had a neck tumor with bone metastasis (65y.o, M). The patient received WBH after HIFU treatment for a 7th rib bone metastasis. After 10 days, the neck tumor developed internal necrosis, and ruptured. CT imaging showed necrotic changes focused in the neck tumor and also the rib bone metastasis.

These results may be a positive indication for HIFU treatment, but there are other positive indications for the primary organ tumor. This new thermal combination therapy appears to have great promise.

Key Words: high intensity focused ultrasound (HIFU), whole body hyperthermia (WBH), far-infrared, Sonic CZ901, tumor ablation

Introduction

Recently, numerous methods for the use of thermal medicine have been under development for the treatment of cancer, and among these is whole body hyperthermia (WBH) using far-infrared radiation1). Whole body hyperthermia is a treatment mimicking natural conditions because the body is heated within natural fever temperature ranges. The effects are mild and non-invasive for the patient, and no physical trauma is apparent in the heated tissues after frequent treatments. However, these effects are not sufficient for a patient with an advanced cancer who needs local treatment to control a tumor. In these

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cases, a more effective and targeted combination therapy is required.

High intensity focused ultrasound (HIFU) or Focused Ultrasound Surgery (FUS) has the potential to become a future treatment of choice for cancer therapy. Currently, some HIFU equipment has been developed in China and in other countries. The Sonic CZ901 machine was developed by Mianyang sonic electronics Ltd in China. This apparatus, the Sonic CZ901, was installed in our institute last December and described in the 5th International Symposium on Therapeutic Ultrasound held at Harvard University\(^2\). This was the first installation of this apparatus in Japan. Combination therapy involving HIFU and WBH was used without severe side effects, and preliminary results with this therapeutic regime are reported here.

**Equipment**

**WBH equipment**

WBH using far-infrared radiation has been used since 1991 in patients with advanced cancer over 5000 times. Previously, this method of treatment was accomplished by using extracorporeal circulation. However, there were pronounced adverse events, and the current equipment using far-infrared radiation was developed to avoid these effects. In this clinic, USA manufactured equipment using far-infrared radiation was used (RHS 7500: Enthermics Medical Systems, USA).

**HIFU equipment**

The Sonic CZ901 installed in our clinic is shown in Fig. 1. Some intravenous anesthetic agents are used to suppress the stimulation of the HIFU treatment used for ablation as well as for WBH. The Sonic CZ901 has the following characteristic features. It is compact, occupying a volume 3×2.3×1.7 cubic meters, and weighs 800 kg. Moreover, the control unit can be installed in a separate location or room. The ultrasound imaging system can also be installed in a separate location and upgraded to a more advanced regular ultrasound unit like the Sonosite or Toshiba, permitting real-time color Doppler or 3D image evaluation. An underwater skin surface camera can enable real-time monitoring for precise focusing and skin burn lesions. The therapeutic ultrasound head can be equipped with a focus depth of either 11 cm or 15 cm, and easily replaced, and a tumor as large as 9×7×9 cm can be treated (Fig. 2). The ultrasound head is 17 cm in diameter. Therefore, liver lesions can be reached through a wider area of intercostal space. It has a special mode of operation (Duty cycle, with 1 Hz pulse, of 40-50% duration) to minimize the

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*Fig. 1. Thermal therapy room at Luke clinic.*

Left side: The RHS 7500 for WBH. Right side: The CZ 901 for HIFU.
accumulation of heat on rib surfaces. These features permit the treatment of liver tumors without removing any ribs during the procedure. This apparatus permits ultrasound treatment with separate multi-layer step-by-step applications. The initial programming automatically controls the output of ultrasound energy with three axial movements.

Materials and Methods

*WBH treatment*

The entire body of the patient, except the head, is heated until a rectal temperature about 41-42 degrees centigrade is obtained. Intravenous anesthetic agents are used to suppress any over-reaction of the body's thermal regulation mechanisms. Hyperthermia is scheduled weekly for 4 applications a month, and the patient is evaluated before and after treatment.

*HIFU treatment*

Treatment is administered as follows; patients are properly positioned on the treatment bed and anesthetized intravenously. Next, high intensity ultrasound is focused on the target area over the tumor, and radiation is emitted from the probe which is located under the treatment bed (Fig. 3). The treatment duration is approximately 90 minutes, and the patient remains for 3-5 hours in the hospital after treatment, is examined, and allowed to return home without an overnight hospital stay.

*Patients*

WBH and HIFU were performed on cancer patients with advanced cancer without any heart failure, or severe respiratory, liver dysfunction or other problems. All treatments were administered with informed consent, and with approval by the ethics committee of the hospital.

**Results**

*Case 1*

A female patient was 20 years old and had relapsed with lung and multiple liver metastases from naso-pharyngeal Ca. last April. She was treated four times with WBH in August to treat metastatic tumors and embolization of the liver. After treatment, the size of lung tumors and tumor markers appeared to be reduced. However, the treatments were not enough to destroy the metastatic liver tumor.
On December 1, HIFU was applied to the liver. The liver mass was clearly reduced after 25 days (Fig. 4), and the severe abdominal pain was eliminated.

**Case 2. A designed combination treatment for a patient with malignant neck tumors.**

The 65 years old male patient’s neck tumor was diagnosed as a malignant schwannoma from peripheral nerves in 2000. He received a total tumor resection and irradiation with chemotherapy for post adjuvant therapy. Unfortunately, the neck tumor recurred and spread into the bone and lung last April. For the neck tumor and lung, whole body hyperthermia was planned. The neck tumor showed good thermal sensitivity with internal necrotic changes 10 days after the first hyperthermia treatment (Fig. 5a-b). After 4 treatments, the tumor ruptured and produced a massive necrotic tissue discharge (Fig. 5c). HIFU was used for treatment and focused on the 7th rib bone tumor. The bone tumor showed mild internal necrotic changes (Fig. 6) and there was an improvement in serum tumor marker displays.

**Discussion and Conclusions**

Hyperthermia is a non-invasive mode of treatment for the cancer patient which produces no severe side effects. The results are toxic to cancer cells, and concurrent studies with this treatment are examining systemic reactions to heat shock. This combination system of hyperthermia is an attempt to extend and improve the effects of hyperthermia treatment by combining local and systemic hyperthermia. Systemic hyperthermia is not a sufficient treatment for some patients where there is a need.

Fig. 4. (a) MRI T1W1 before HIFU ablation. (b) MRI T1W1 25 days after HIFU ablation.

Fig. 5. (a) Enhanced CT image before HIFU. (b) Enhanced CT image 10 days after the first HIFU treatment. (c) Enhanced CT image after 4 treatments with WBH.
to control a regional or local tumor. Thus it is necessary to develop hyperthermia treatments to produce strong systemic effects as well as strong local effects, and this is what was attempted here. The combination of HIFU and WBH is designed to produce an effective non-invasive therapy. The use of HIFU is needed to extend the efficacy of hyperthermia cancer treatments. The goal was to develop a combination therapy using HIFU ablation of local tumors in conjunction with systemic WBH. Currently, there are several MRI-guided FUS systems use in several locations in Japan and two Ultrasound-guided HIFU systems in use near Tokyo. The new HIFU apparatus described here was obtained from Mianyang, China and has been used to treat several patients. The new equipment described here and the Chongqing Model JC apparatus are related designs. The Model JC has been used by many medical facilities internationally. In contrast, the Sonic CZ901 has been mainly developed in China by ultrasound engineering specialists. This HIFU system has been approved for use in China since November, 2004, and currently 3 systems are working there. Its first introduction and use in other areas outside of China is the instrument now installed in Japan in the department of thermo-therapy (Luke Clinic) last December. Good results in response to this combination therapy with HIFU and WBH have been obtained in patients who have multiple metastases, and without severe adverse reactions. Further work should enhance this type of combined hyperthermia therapy, and this method appears promising for use in patients with advanced localized cancers in specific organs.

References


集束超音波焼灼療法 (HIFU) と
全身ハイパーサーマリアによる高体温療法

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要 旨：我々は全身対応の高密度集束超音波焼灼療法：HIFU (ソニック CZ901：綿陽ソニックエレクトロニック：中国) を昨年の12月に導入し、その可能性や我々の症例における適応について評価を試みている。以来、全身ハイパーサーマリア外来に来院した12例の進行がん症例に対して、20回のHIFUを施行し、全身ハイパーサーマリア：WBH (RHS 7500：エンサーサーマスメディカルシステムス：米国) との併用や単独治療で良好な結果を得た。最初の1例目は上腕頭がん再発の多発性の肺、肝臓転移の20歳女性であった。週1回計4回のWBHで腫瘍マーカーの改善と共に肺転移は縮小し、その後、肝臓に対して施行したHIFUにより著明な縮小効果を得られた。2例目は頭部神経鞘腫の再発、肋骨転移の65歳の男性であった。HIFU 施行が不可能な頭部に対してはWBHの効果に期待し、肋骨転移に対してはHIFUを行った。WBHの10日後に頭部腫瘤は縮小し、その後自然に破壊、縮小した。造影CTにおける評価ではHIFUを施行した第7肋骨腫瘍及び頭部腫瘍は著明な内部壊死に伴いサイズの縮小が認められた。今後のHIFUの適応には、この様々な治療法との併用による緩和治療や、より根治を目的とした原発腫瘍への治療効果が期待される。