ISSN 1882-2576

Vol. 30
Supplement, 2014

Thermal Medicine

The 6th Asian Congress of Hyperthermic Oncology (ACHO) & The 31st Japanese Congress of Thermal Medicine (JCTM) at Fukui City, Japan

Thermal Medicine: The Key Modality of Cancer Therapy

September 5 (Fri.) — 6 (Sat.), 2014

Program and Abstracts

President of the 6th ACHO and the 31st JCTM:
Kanji Katayama M.D., Ph.D.

Director and Prof., Cancer Care Promotion Center,
Medical School Hospital, University of Fukui, Japan

Venue: AOSSA (Fukui City, Japan)

Japanese Society for Thermal Medicine

Invitation

Dear Colleagues:

It is our great honor to invite you from Asian countries to the 6th Asian Congress of Hyperthermic Oncology (ACHO) and the 31st Japanese Congress of Thermal Medicine (JCTM) to be held in Fukui, from Thursday, September 4 to Saturday, September 6 of 2014.

A main theme of the conference is "Thermal Medicine: The Key Modality of Cancer Therapy". By holding out this theme, we would host and organize an exciting program on the latest hyperthermic oncology research to show how hyperthermia is effective and plays an important role in cancer therapy now.

Hyperthermia is now one of the key modalities in the multidisciplinary approach for cancer and is a latest evidence-based treatment supported by research on biology, medical engineering, basic and clinical medicines. Hyperthermia is not meant to be the modality next to surgery, radiotherapy or chemotherapy but is a standard adjunct modality to promote effect of these treatments by using concurrently with them.

However, the efficacy and needs of hyperthermia is not well known among physicians and other medical professionals yet. The general public is not familiar with hyperthermia treatment and it is often regarded as a kind of alternative medicine.

The name of the venue, "AOSSA" comes from the Japanese word but a dialect of Fukui which mean "Let's get together".

Please enjoy fascinating culture and foods of Fukui with your colleagues and family.

We are cordially welcome for your coming to Fukui and hope that acquiring new information and heartily discussion in these Congresses will inspire you to attain future advanced development and global collaboration in the field of hyperthermic oncology.

So, my fellow Colleagues, AOSSA in Fukui!!

We would trust you could find the 6th ACHO & the 31st JCTM most scientifically rewarding.

The 6th Asian Congress of Hyperthermic Oncology
The 31st Japanese Congress of Thermal Medeicine
President
Kanji Katayama, M.D., Ph.D.
Director and Prof., Cancer Care Promotion Center,
Medical School Hospital, University of Fukui

Organization

Organized by

Asian Society of Hyperthermic Oncology (ASHO)
Japanese Society of Thermal Medicine (JSTM)

Co-organized by

Nonprofit Organization to support Peritoneal Dissemination Treatment (NPO PDT)

Supported by

General Incorporated Association Fukui Medical Association

Local Organizing Committee

President of the 6th ACHO & the 31st JCTM

Kanji Katayama — Professor, Cancer Care Promotion Center, Medical School Hospital, University of Fukui, Japan

Secretary General of the 6th ACHO & the 31st JCTM

Hideki Matsumoto — Associate Professor, Biomedical Imaging Research Center, University of Fukui, Japan

Scientific Program Committee of the 6th ACHO & the 31st JCTM

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Koichi Ito, Chiba University
Hirokazu Kato, Okayama University
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Yoko Harima, Kansai Medical University
Masahiro Kuroda, Okayama University
Kosuke Ueda, Hachiya Orthopaedic Hospital
Yutaka Yonemura, NPO Organization to support Peritoneal Dissemination Treatment
Kanji Katayama, University of Fukui

General Information

Dates

September 5 (Fri.) and 6 (Sat.), 2014.

Venue

AOSSA(1-4-1 Teyose, Fukui City, Fukui 910-0858, Japan)

- Fukui Prefectural Citizens' Hall (8F)
  Phone: +81-776-87-0003; Fax: +81-776-87-0303
- Fukui City Communication Plaza (6F)
  Phone: +81-776-20-1535; Fax: +81-776-20-1536

Official Language

The official language of the Congresses is mainly English.
Japanese is available in a portion of JCTM specific sessions.

Executive Office

Cancer Care Promotion Center, Medical School Hospital, University of Fukui
Phone: +81-776-61-8857
Fax: +81-776-61-8196
E-mail: eternal@u-fukui.ac.jp

Secretariat

c/o Nippon Travel Agency Co., Ltd.
EPC Team, Public Sector & Corporate Sales Department Nippon Travel Agency Co., Ltd.
Toranomon Marine Bldg. 11F, 3-18-19 Toranomon, Minato-ku, Tokyo 105-0001, Japan
Phone: +81-3-5402-6401
Fax: +81-3-3437-3955
E-mail: jstm_31@nta.co.jp

Congress Website

http://web.apollon.nta.co.jp/jstm31/eng/index.html

Social Events

Excursion

Date & Time:	September 5 (Fri.) 13:00 ~ 17:00
Traffic:	Chartered bus will start out from Bus Terminal in front of AOSSA at 13:00 (See "Hall Guide", p10)
Destination:	Fukui Prefectural Dinosaur Museum (One of big three dinosaur museums in the world) (http://www.dinosaur.pref.fukui.jp/en/)

*Foreign participants and their accompanying persons are welcome, free of charge.

Congress Banquet

Venue:	Yours Hotel Fukui (http://www.yours-hotel.co.jp/) 1-4-8 Chuou, Fukui City, Fukui 910-0006, Japan Phone, +81-776-25-3200
Date:	September 5 (Fri.)
Time:	18:00 (doors open), 18:30 (opening curtain)
Due:	Charge-free
Style:	Buffet
Dress Code:	Casual

Business Meeting

ASHO Council Meeting	September 4 (Thu.)	14:00 ~ 15:00	602 (6F)
JSTM Commission Meeting	September 4 (Thu.)	15:15 ~ 16:15	602 (6F)
JSTM Council Meeting	September 4 (Thu.)	16:30 ~ 17:30	Room 2 (6F)
JSTM General Meeting	September 5 (Fri.)	13:15 ~ 14:00	Room 1 (8F)

Registration

Registration Desk

Foyer of Fukui Prefectural Citizens' Hall (8F)

Registration Hour

September 5 (Fri.) 08:30 ~ 17:00
September 6 (Sat.) 08:30 ~ 16:00

※ Registration Desk is available at 601A (6F) at 13:00 ~ 17:00 on September 4 (Thu.)

Registration Fee

Members: 10,000 JPY
Non-Members: 15,000 JPY
Students: 5,000 JPY (※ Please show your student identification card.)
*including admissions to the scientific programs, congress materials, luncheon seminars and coffee breaks.
Accompanying Persons: 5,000 JPY
*including admissions to the opening & closing ceremony and coffee breaks.

Name Card

You will be given Name Card in exchange for payment of Registration Fee. Please drape Name Card after writing down your name and affiliation during the course of the Congress sessions.

Program and Abstract Book

The ASHO members or the participants from abroad: You will be given the Program and Abstract Book in exchange for payment of Registration Fee.
The JSTM members: Please bring the Program and Abstract Book.
*The Program and Abstract Book is available at 2,000 JPY on the General Information Desk, when you hope another one, or you may forget it.

Other Information

Scientific Luncheon Seminars

Date & Time: September 5 (Fri.) 12:00 ~ 13:00 Room 1 (8F)
September 6 (Sat.) 12:15 ~ 13:15 Room 1 (8F)
Numbered Ticket: You can pick up a numbered ticket at General Information Desk from 8:30 on the day. It will be closed as soon as the numbered ticket has run out.

JSTM Educational Lecture

The Educational Lecture will be held as the Hyperthermia Training Course to get credit in the recognition system of JSTM.

Displays of Companies related to Hyperthermic Oncology

The Displays of Companies will be opened throughout the Congresses. Please visit there.
Place: Foyer of Fukui Prefectural Citizens' Hall (8F)

Free Soft Drink

You can get a free soft drink at Poster Presentation Room (Rehearsal Room) (8F)

Cloak Room

Cloak room (beside General Reception) will be available during the Congresses.

Date & Time: September 5 (Fri.) 08:30 ~ 18:30
September 6 (Sat.) 08:30 ~ 18:30

Others

- Paging Service
  In principle, Paging Service is not available in the Conference Venue. The Massage Board is available beside General Reception.
- Taking photographs etc.
  In principle, prohibit you from taking photographs and recording images and sounds.
- Smoking
  No smoking in AOSSA. Smoking in designated areas only (outside of AOSSA).

Information for the Presentation

For Chairpersons

- Please come by **General Information Desk** without fail, when you arrive the Conference Venue.
- Please take a seat at least 20 min. prior to the start of your session. The seat for the next Chairpersons is in store ahead of the Conference Room on the right.
- The proceedings for the Symposium Session is up to the Chairpersons, but please make sure to keep to the allotted time according to the Time Table.
- The allotted presentation time of the Workshop Session is 12 min. including the discussion time of 4 min. Please make sure to keep to the allotted time according to the Time Table.
- Please order questioners and discussers to self-introduce their name and affiliation in order to facilitate discussions.

For Questioners and Discussers

- Welcome to questions, discussions and comments.
- Please self-introduce your name and affiliation in order to facilitate discussions.

For Presenters

1. For oral speakers

- For oral speakers, only the PC presentations using the Microsoft PowerPoint data are available. Photo-Slides are not available.
- At the podium, speakers should operate themselves the PC.
- The allotted presentation time in the Symposium Session varies from the session to session. Please see the Program.
- The allotted presentation time in the Workshop Session is 12 min. including the discussion time of 4 min.
- The short oral presentation time of the Poster Presentation is 3 min. In the presentation, there is no discussion time. The speakers should be strict with the presentation time limitation. The speakers should register their PowerPoint data on PC Desk. The speakers cannot use their own PC.
- Please consider privacy protection in relation to the personal information of patients.

2. Registration of the presentation data

Registration Place: **PC Desk (Foyer of Fukui Prefectural Citizens' Hall) (8F)**
Registration Hour: **September 5 (Fri.) 08:30 ~ 17:00**
September 6 (Sat.) 08:30 ~ 16:00

- The speakers who bring their PowerPoint data using USB memory drive or CD-R should preview their presentation, complete a run-through of the operation on the PC at PC Desk and enregister their data at least 60 minutes before their session and 30 minutes before the first session are scheduled to begin. Even if your session is scheduled on September 6 (Sat.), you can preview and enregister your PowerPoint data on September 5 (Fri.) at PC Desk.

- The speakers who bring their own PC should preview their presentation and complete a run-through of the operation at PC Desk at least 60 minutes before their session and 30 minutes before the first session are scheduled to begin. Please remember to bring together power adaptor and cable.
- The speakers who play the video imagery on their presentation should bring their own PC. In this case, the speakers should confirm the D-sub15 pin cable is available in their own PC. Please remember to bring together power adaptor and cable.
- The speakers who use Macintosh PC on their presentation should bring their own PC. Please remember to bring together the D-sub15 pin cable adaptor, power adaptor and cable.
- In any case, the audio system is not available.

For the speakers bringing their PowerPoint data

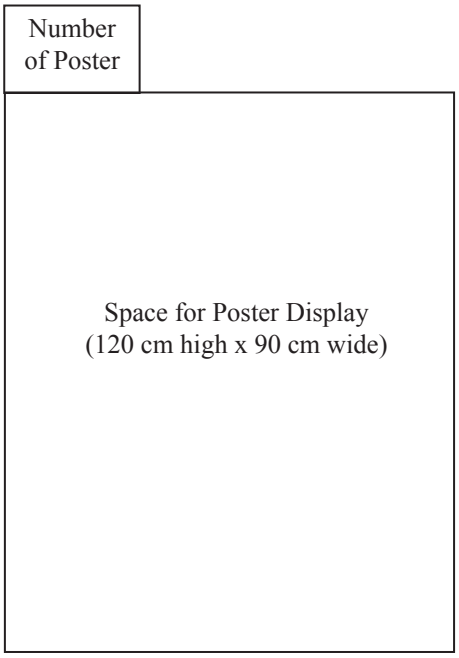
- The OS, Windows 7 only is available.
- The Microsoft PowerPoint 2003, 2007, 2010 and 2013 are available. Only the fonts supplied with Microsoft Windows 7 is available. We recommend using 'MSP Gothic', 'MSP Mincho', 'Times New Roman', 'Century' and 'Arial' in consideration of the layout and balance on screen.
- The PowerPoint data of your presentation should be saved in the USB memory drive or CD-R.
- When you saved your presentation data on CD-R, you should finalize the disc. If you did not finalize the disc, you cannot perform your presentation. Packet write CD-R is not available.
- You cannot revise your presentation data on PC Desk.
- You should perform virus scanning in advance in your drive.
- You should save only the final version of your presentation in your drive.
- Please write down your name, affiliation, the name of session and the number of presentation on your CD-R. The display resolution is XGA (1024 x 768 pixels, only 60 Hz). Please spare to use any other resolution.
- The registered data for your presentation should be surely erased by Secretariat after the Congresses.

For the speakers bringing their own PC

- The OS, Windows XP and new one and also Mac OS 9 and new one are available.
- The Microsoft PowerPoint 2003 and new one (including Keynote for Macintosh) are available.
- Only D-sub15 pin cable is available for the connection with the projector.
- Please remember to bring together the D-sub15 pin cable adaptor, power adaptor and cable.
- You cannot revise your presentation data on PC Desk.
- The display resolution is XGA (1024 x 768 pixels, only 60 Hz). Please spare to use any other resolution.
- Screen saver and energy-saving should be awaked.
- Please bring the backup data of the USB memory drive or CD-R just in case. Please refer to the information 'For the speakers bringing their PowerPoint data'.
- If the speaker will play the video imagery, please preview their presentation and complete a run-through of the operation at PC Desk.

Set up a Poster Presentation

- Place: AOSSA 8F Poster Presentation Room (Rehearsal Room)
- Poster panels will be prepared in the format indicated to the right.
- Maximum dimensions for Posters are 120 cm high x 90 cm wide. Do not exceed these dimensions. Number of Poster and double-stick tape will be prepared by Secretariat.
- Poster should include the presentation title, the authors' names, affiliations and the presentation contents.
- You can confirm your poster number on the Congress Website, http://web.apollon.nta.co.jp/jstm31/eng/event.html.
- Poster presentation will be displayed for the second successive day.



- **Poster Set-Up Time:** **September 5 (Fri.) 08:30 ~ 10:00**
  Poster Tear-Down Time: **September 6 (Sat.) 15:45 ~ 16:45**
  *The poster displaying will be cleaned up by Secretariat after September 6 (Sat.) at 16:45.

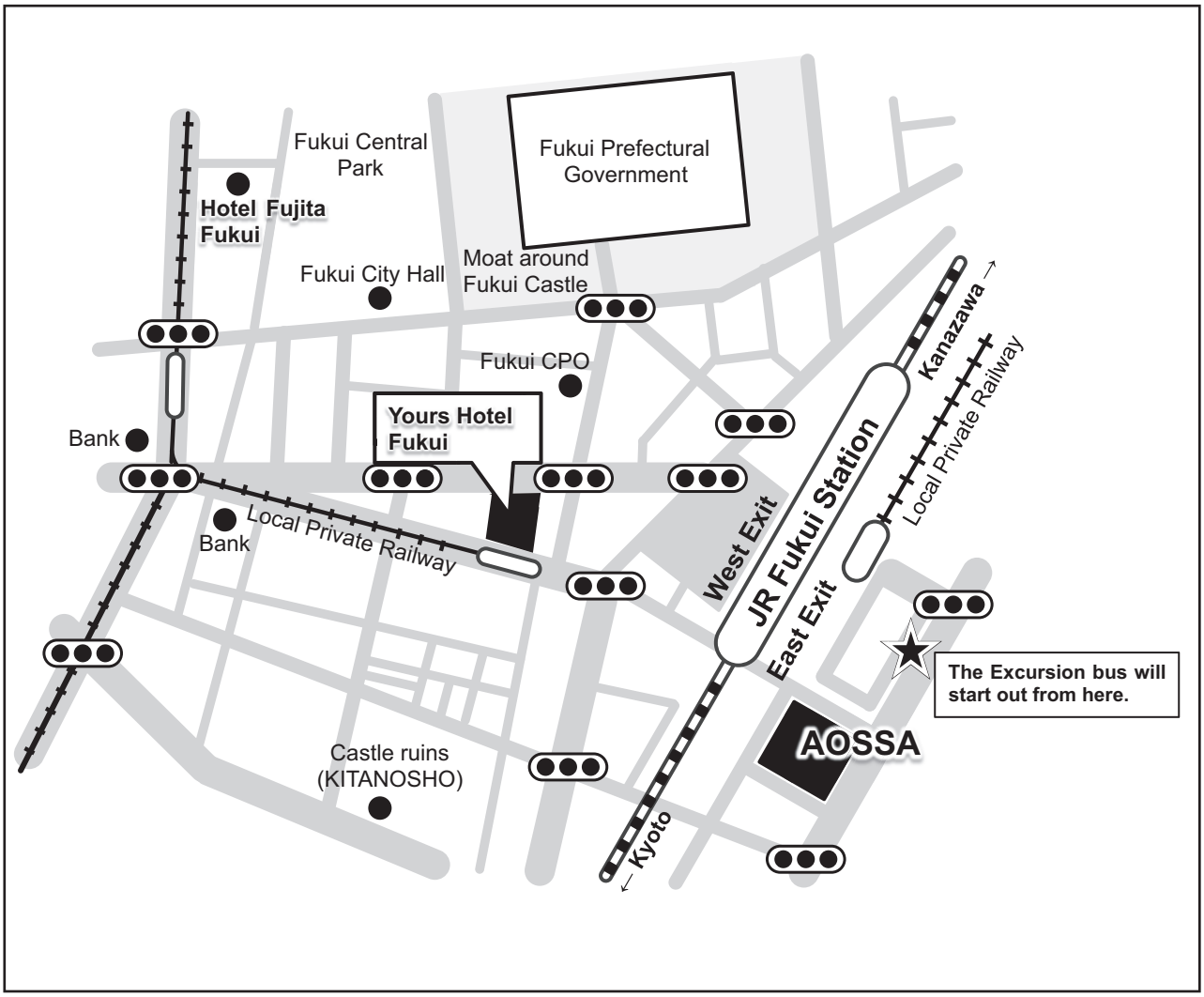
Viewing of Poster Presentation

- If you may have any questions when you are viewing the Poster Presentation, would you please write down your question on 'Post-it' with your E-mail address and paste the 'Post-it' on the poster.
- If you have your name card, you can put it on the 'Post-it' using double-stick tape.

Hall Guide

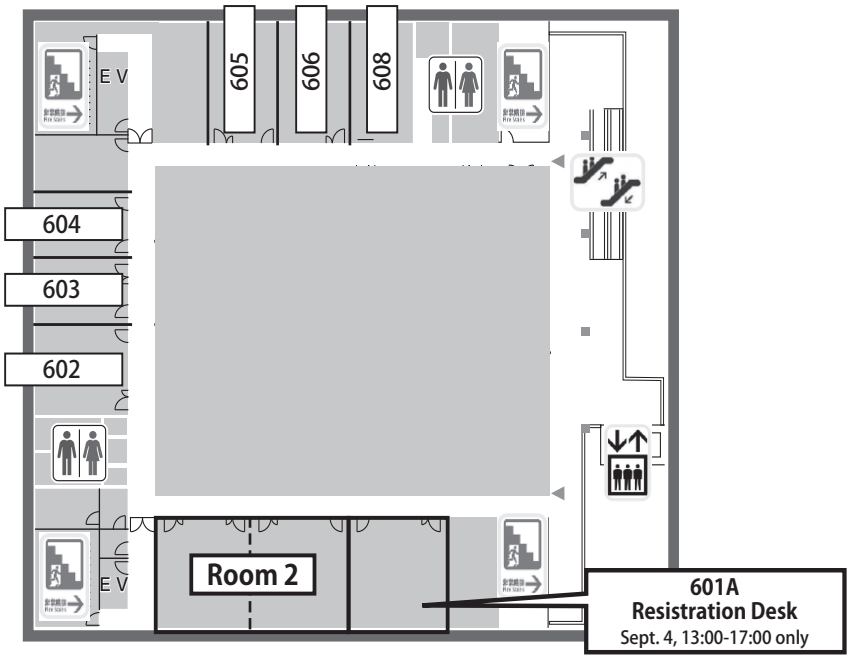
Venue: **AOSSA**

- **Fukui Prefectural Citizens' Hall (8F)**
- **Fukui City Communication Plaza (6F)**

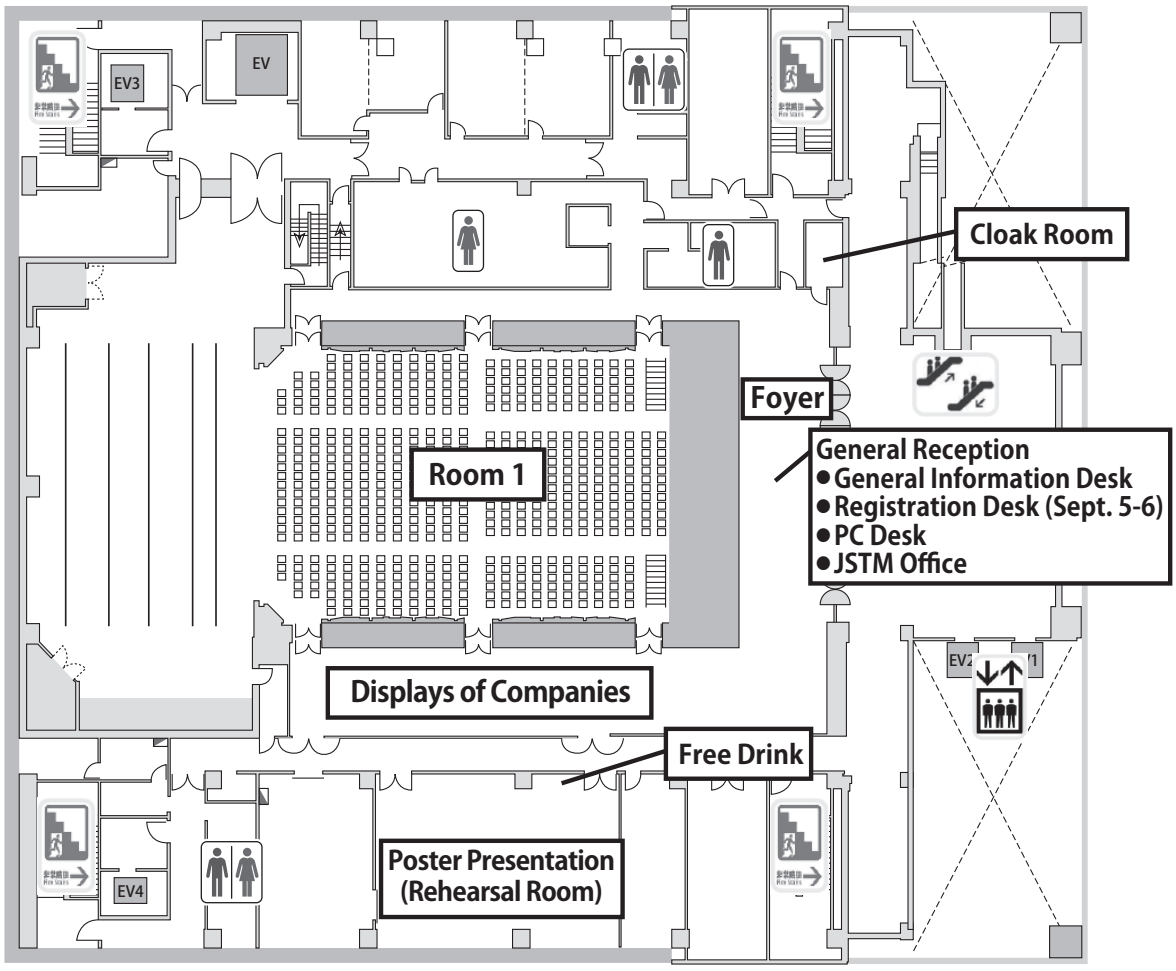


AOSSA Floor Guide

6F Fukui City Communication Plaza



8F Fukui Prefectural Citizens' Hall



Program at a Glance

September 5 (Fri.), 2014

	Room1 AOSSA 8F Fukui Prefetural Citizens' Hall	Room2 AOSSA 6F 601B-C	Poster AOSSA 8F Rehearsal Room	
8:45	Opening Remarks		8:30 – 10:00 **Setting of Poster**	
9:00	9:00 – 11:00 **Symposium 2** Impact of HSPs – Revisit & Perspective – Chairs: Kenzo Ohtsuka, S.V. Chiplunkar			
10:00			10:00 – 17:00 **Poster Viewing**	
11:00	11:00 – 12:00 **Congress Lecture** Chair: Takeo Ohnishi (YAMAMOTO VINITA CO., LTD.)			
12:00	12:00 – 13:00 **Luncheon 1** Oncothermia Chair: Andras Szasz (TATEYAMA MACHINE CO., LTD.)	12:00 – 14:00 **Thermotron Users' Meeting** (Japanese) Chair: Hajime Imada (YAMAMOTO VINITA CO., LTD.)		
13:00	13:15 – 14:00 **JSTM General Meeting** (Japanese)			13:00 – 17:00 **Excursion for Foreign Researchers and their Accompanying Persons**
14:00	14:00 – 15:00 **JSTM Educational Lecture** (Japanese) Chair: Hirokazu Kato			
15:00	15:00 – 17:00 **Workshop 2** Development of the New Modality in Hyperthermic Cancer Therapy Chairs: Kagayaki Kuroda Tzyy-Leng Horng	15:00 – 17:00 **Workshop 3** Future Activities regarding NHI Point of Hyperthermia (Japanese) Chair: Yoshiaki Tanaka		
16:00				
17:00	17:00 – 18:15 **Award Lecture** (English) **The ASHO Award** Satoshi Kokura Chair: Hiroyuki Kuwano **The JSTM Award** Iwai Tohnai Chair: Koichi Ito **The Young Investigator Award of JSTM** Kazuyuki Saito Chair: Koichi Ito **Excellent Paper Award** Ryo Suzuki Chair: Akihisa Takahashi			
18:00				
18:30 –	**Congress Banquet** (Yours Hotel Fukui)			
19:00				

September 6 (Sat.), 2014

	Room1 AOSSA 8F Fukui Prefetural Citizens' Hall	Room2 AOSSA 6F 601B-C	Poster AOSSA 8F Rehearsal Room
8:45			
9:00	9:00 – 10:00 **Workshop 1-1** Hyperthermia: Up to Date in Asia – Oncothermia – Chairs: Takashi Kondo, Taesig Jeung	9:00 – 12:14 **Poster/Short-Oral Presentation** GSE1 - GSE43 GSJ1 - GSJ6 (Japanese)	9:00 - 15:30 **Poster Viewing**
10:00	10:00 – 12:00 **Workshop 1-2** Hyperthermia: Up to Date in Asia – Clinical Case Reports and Biology – Chairs: Hideyuki Sakurai Takayuki Asao		
11:00			
12:00			
	12:15 - 13:15 **Luncheon 2** The Latest Therapy for Peritoneal Metastasis Chairs: Kanji Katayama (SEIREN CO., LTD.)		
13:00			
	13:30 – 15:30 **Symposium 1** Hyperthermic Effects of HIPEC on Peritoneal Surface Malignancies Chairs : Yutaka Yonemura, Yan LI, Mao-Chih Hsieh (SEIREN CO., LTD.)	13:30 – 15:26 **Poster/Short-Oral Presentation** GSJ: 7 - 35 (Japanese)	
14:00			
15:00			
	15:30 – 15:45 **Closing Ceremony**		
		15:45 – 17 : 45 **HIPEC Training Course** (Japanese)	15:45 – 16:45 **Removal of Poster**
16:00	16:00 – 17:30 **Extension Course of Hyperthermia for the General Public** (Japanese) Chair: Mitsuyuki Abe		
17:00			
18:00			
19:00			

Acknowledgments

The 6th Asian Congress of Hyperthermic Oncology (ACHO) & The 31st Japanese Congress of Thermal Medicine (JCTM) gratefully acknowledges the generous help of the following companies and organizations. Without their sponsorship and support, the 6th ACHO & the 31st JCTM could not have been organized.

President of the 6th ACHO & the 31st JCTM
Kanji Katayama, M.D., Ph.D.

Sponsors

Organizing Scientific Sessions

YAMAMOTO VINITA CO., LTD.
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TATEYAMA MACHINE CO., LTD. / Oncotherm kft.

Organizations

Public Interest Incorporated Foundation Fukui Convention & Visitors Bureau
The 1st Department of Surgery, School of Medicine, University of Fukui
Medical Corporation Senjukai Medical Welfare Group, Tsukushino Hospital
General Foundation Fukuwakai

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Program

September 5 (Fri.) Room 1

8:45 **Opening Remarks**

President of the 6th ACHO & the 31st JCTM
Kanji Katayama

9:00 — 11:00 **Symposium 2**

Impact of HSPs — Revisit & Perspective —

Chairs: Kenzo Ohtsuka, S.V. Chiplunkar

S2-1

Different cytotoxic effect from different hyperthermia devices. Comparison of the oncotherm-labehy and the thermotron RF-8 in an *in vitro* model

Yu-Shan Wang

S2-2

Heat shock proteins and gamma delta T cell immunity in oral cancer

S. V. Chiplunkar

S2-3

Inhibiting heat shock transcription factor 1 and its related genes for novel hyperthermia therapy

Yoshiaki Tabuchi

S2-4

Pifithrin-μ, an inhibitor of HSP70, can increase the antitumor effects of hyperthermia against human prostate cancer cells

Mamoru Harada

S2-5

Constitutively active stress-responsive signals and stress proteins are novel targets for cancer stem cell/cancer-initiating cell-targeted therapy

Toshihiko Torigoe

11:00 — 12:00 **Congress Lecture**

Chair: Takeo Ohnishi

Past, present and future of hyperthermia in the war against cancer

Chang W. Song

Sponsored by YAMAMOTO VINITA CO., LTD.

12:00 — 13:00 **Luncheon Seminar 1**

Clinical Practice and Studies on Oncothermia Therapy

Chairs: Andras Szasz, Yasunori Akutsu

LS1-1

Oncothermia in clinical practice

Andras Szasz

LS1-2 (no abstract)

A phase I / II study of EHY-2000 oncothermia therapy for advanced esophageal cancer

Yasunori Akutsu

LS1-3 (no abstract)

Preliminary report of the prospective randomized controlled trials: Evaluating a new modality of locally advanced breast cancers treatment and advanced stage hepatocellular carcinoma (HCC) by loco-regional hyperthermia

Thanasitthichai Somchai

LS1-4 (no abstract)

Current status of oncothermia therapy in Korea

Joon H. Kim

Sponsored by TATEYAMA MACHIE CO., LTD. / ONCOTHERM CO., LTD.

13:15 － 14:00 **JSTM General Meeting with Award Ceremony** *(Japanese)*

日本ハイパーサーミア学会　活動報告会および授賞式

14:00 － 15:00 **JSTM Educational Lecture** *(Japanese)*

日本ハイパーサーミア学会　教育講演　　座長：加藤　博和

EL-1

子宮頸癌の放射線温熱療法の臨床

播磨　洋子

EL-2

ハイパーサーミアの生物作用：温熱誘導分子損傷

高橋 昭久

EL-3

ハイパーサーミアにおける物理・工学の基礎

伊藤 公一

15:00 － 17:00 **Workshop 2**

Development of the New Modality in Hyperthermic Cancer Therapy

Chairs: Kagayaki Kuroda, Tzyy-Leng Horng

WS2-1

Combination therapy with low dose chemotherapy and regional hyperthermia for the treatment of progressive renal pelvis carcinoma

Kosuke Ueda

WS2-2

rAd-p53 hepatic arterial infusion (HAI) with thermo-chemotherapy for unresectable liver carcinoma

Shan-wen Zhang

WS2-3

Spiruchoustatin-B, a novel histone deacetylase inhibitor enhanced apoptosis induced by hyperthermia

Mati Ur Rehman

WS2-4

Enhancement of hyperthermia-induced cancer cell killing by withaferin A, — Implication for cancer therapy —

Zheng-Guo Cui

WS2-5

Effect of administering bevacizumab combined with mild temperature hyperthermia in neutron capture therapy on local tumor control and lung metastasis

Shin-ichiro Masunaga

WS2-6

Magnetically-engineered superparamagnetic nano-theranostic agents with exceptially high AC heat induction and r2-relaxivity

Bae Seongtae

WS2-7

Investigations towards the role of controllable therapeutic parameters for nanoparticle assisted thermal therapy for cancer

Sanjeev Soni

WS2-8

Signal processing for noninvasive temperature imaging of fat using spin-lattice relaxation time of proton magnetic resonance

Shuhei Morita

WS2-9

Numerical analysis of coupled effects of pulsatile blood flow and thermal relaxation time during thermal therapy

Tzyy-Leng Horng

WS2-10

Effects of effective tissue thermal conductivity and pulsatile blood flow in large vessels on thermal dose distributions during thermal therapy

Tzu-Ching Shih

17:00 — 18:15 **Award Lecture**

The ASHO Award Chair: Hiroyuki Kuwano

The present state of hyperthermia in Japan, and by what kind of way should we progress from now on?

Satoshi Kokura

The JSTM Award Chair: Koichi Ito

Hyperthermia for oral cancer — Basic principles and clinical applications —

Iwai Tohnai

The Young Investigator Award of JSTM Chair: Koichi Ito

Study on practical application of microwave antenna for treatment of bile duct carcinoma

Kazuyuki Saito

Excellent Paper Award Chair: Akihisa Takahashi

Novel strategy for ultrasound diagnostics and therapeutics using micro/nanobubbles
— Development of hyperthermia for cancer with liposomal nanobubbles —

Ryo Suzuki

September 5 (Fri.) Room 2

12:00 — 14:00 **Thermotron Users' Meeting** *(Japanese)*
サーモトロンユーザーズミーティング

座長 : 今田 肇

りんくう出島クリニックでの温熱療法ハイパーサーミアの取組みと工夫

大木 幸治

温熱療法室における取り組み及び技術的工夫

佐藤 光幸

ハイパーサーミア治療における心理学的側面の応用について

森 信二

新札幌恵愛会病院におけるハイパーサーミアの現状

諸澤 英之

戸畑共立病院のハイパーサーミアについて

大田 真

Sponsored by YAMAMOTO VINITA CO., LTD.

15:00 — 17:00 **Workshop 3**
Future Activities regarding NHI Point of Hyperthermia *(Japanese)*
ハイアパーサーミア診療報酬の現状と問題点
－その改定に関する経緯と今後の活動について－

座長 : 田中 良明

WS3-1
社会医療診療行為別調査からみる日本のハイパーサーミアの現状

黒崎 弘正

WS3-2
我が国のハイパーサーミアと診療報酬の現状

寺嶋 廣美

WS3-3
保険適応後に蓄積されたハイパーサーミアの臨床試験から得られたエビデンス

大栗 隆行

WS3-4
松山西病院における温熱療法治療の現状

俊野 昭彦

WS3-5
術中温熱腹膜還流 hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC) の有効性のエビデンスと世界の保険支払いの状況

米村 豊

September 6 (Sat.) Room 1

9:00 － 10:00 **Workshop 1-1**

Hyperthermia: Up to Date in Asia － Oncothermia －

Chairs: Takashi Kondo, Taesig Jeung

WS1-1-1
Modulated electro-hyperthermia applied as monotherapy for various cases having no other options

Taesig Jeung

WS1-1-2
Modulated electro-hyperthermia therapy combined with gold-standard therapies for primary, recurrent and metastatic sarcomas

Ji Hoon Choi

WS1-1-3
Can modulated electro-hyperthermia (mEHT) elicit immune reaction? － From basic and clinical research －

Yasunori Akutsu

WS1-1-4
Dialectics of hyperthermia and oncothermia: development through negation

Sergey Roussakow

WS1-1-5
Suppression of human cancer cell growth in *vitro* by oncothermia

Hee Bum Yang

10:00 － 12:00 **Workshop 1-2**

Hyperthermia: Up to Date in Asia － Clinical Case Reports and Biology －

Chairs: Hideyuki Sakurai, Takayuki Asao

WS1-2-1
Multidisciplinary treatment for border line unresectable pancreatic body cancer

Makoto Murakami

WS1-2-2
Hyperthermia in locally advanced head & Neck Cancer – A retrospective analysis

Nagraj G. Huilgol

WS1-2-3
Long-term results of second-look operation following radio-hyperthermo-chemotherapy for unplanned excision of soft tissue sarcoma

Katsuhiro Hayashi

WS1-2-4
Impact on histologic effect of neo-thermo-chemoradiotherapy for rectal cancer

Hisanori Shoji

WS1-2-5

A phase III clinical trial: combination of radiotherapy and chemotherapy with vs. without hyperthermia for patients with advanced cervical cancer

Yoko Harima

WS1-2-6

Gastric cancer surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) for scirrhous gastric cancer

Satoshi Murata

WS1-2-7

Usefulness of an operation under laparoscopy as neoadjuvant chemotherapy to appendix origin pseudomyxoma peritonei

Kousuke Noguchi

WS1-2-8

Clinical study of intraperitoneal hyperthermic perfusion chemotherapy in combination with intravenous chemotherapy for the treatment of advanced-stage gastric carcinoma

Shenglin Ma

WS1-2-9

The immunologic hyperthermia to the advanced gastric cancer patient who refused the standard chemotherapy

Satoshi Kokura

WS1-2-10

Heat-sensitization of human cancer cells by HR inhibitor B02 but not NHEJ inhibitor NU7026

Akihisa Takahashi

12:15 — 13:15 **Luncheon Seminar 2**

The Latest Therapy for Peritoneal Metastasis

Chair: Kanji Katayama

LS-2

The latest therapy for peritoneal metastasis

Yutaka Yonemura

Sponsored by SEIREN CO., LTD.

13:30 — 15:30 **Symposium 1**

Hyperthermic Effects of HIPEC on Peritoneal Surface Malignancies

Chairs: Yutaka Yonemura, Yan Li, Mao-Chih Hsieh

S1-1

Cytoreductive surgery and hipec experience for peritoneal metastases in Turkey after education for peritoneal malignancies in Japan

Emel Canbay

S1-2

Laparoscopic hyperthermic intraperitoneal chemotherapy for advanced gastric cancer with peritoneal carcinomatosis

Masumi Ichinose

S1-3

Laparoscopic hyperthermic intraperitoneal chemotherapy (LHIPEC) for stomach cancer patients with peritoneal carcinomatosis

Chai Young Lee

S1-4

CRS + HIPEC improves survival for patients with colorectal peritoneal carcinomatosis: A phase II study from a Chinese center

Chao-Qun Huang

S1-5

HIPEC is effective for peritoneal dissemination of colon cancer and MUC2 protein expression status is a useful indicator

Takanori Goi

S1-6

Cytoreductive surgery combined hyperthermic intraperitoneal chemotherapy for pseudomyxoma peritonei treatment- experience in Taiwan

Chang-Yun Lu

S1-7

Hyperthermic intraperitoneal chemotherapy for patients with pseudomyxoma peritonei undergoing incomplete cytoreductive surgery

Yang Liu

S1-8

Cytoreductive surgery combined hyperthermic intraperitoneal chemotherapy for peritoneal superficial malignancy- experience in Thailand.

Thawatchai Akaraviputh

Sponsored by SEIREN CO., LTD.

15:30 — 15:45 **Closing Ceremony**

16:00 — 17:30 **Extension Course of Hyperthermia for General Public** *(Japanese)*

市民公開講座

「温熱療法（ハイーパーサーミア）は、がん治療の鍵」

司会：阿部 光幸

1. 残されたがんの治療　—安心・安全なハイパーサーミアの応用

寺嶋 廣美

2. ハイパーサーミアがん治療法のしくみ

大西 武雄

3. 福井県におけるがん温熱療法の実際

片山 寛次

September 6 (Sat.) Room 2

9:00 — 12:15 **Poster/Short-Oral Presentation**

GSE1-43 *(English)* **and GSJ1-6** *(Japanese)*

GSE1

Mechanism of hyperthermia in magnetic nanoparticles

G. Vallejo-Fernandez

GSE2

Development of combination therapy with cisplatin and hyperthermia generated with ferucarbotran (Resovist) in an alternating magnetic field for oral cancer

Itaru Sato

GSE3

A Combination therapy with hyperthermia and IL-13 cytotoxin for human oral cancer cells

Makiko Okubo

GSE4

Carcinostatic activities of L-ascorbic acid and its derivatives combined with a capacitive-resistive electric transfer (CRet) hyperthermic apparatus

Ryoko Asada

GSE5

Molecular mechanisms of hyperthermia-induced apoptosis enhanced by romidepsin (FK228)

Paras Jawaid

GSE6

Short-time focused ultrasound hyperthermia enhances liposomal doxorubicin delivery and anti-tumor efficacy for brain metastasis of breast cancer

Sheng-Kai Wu

GSE7

Heating properties of coaxial needle applicator made of SMA for brain tumor hyperthermia treatment with 3-D anatomical human head model

Kazutoshi Shibafuji

GSE8

Resonant cavity applicator with ultrasound monitoring system

Keito Nakamura

GSE9

Heating properties of resonant cavity applicator for treating osteoarthritis

Takuma Matsushita

GSE10

Does the success of hyperthermia depend on the heating-method?

Andras Szasz

GSE11

Thermal lesion deflection of blood vessel on the thermal lesion formation during radio-frequency ablation for liver tumors

Huang-Wen Huang

GSE12

A fast adaptive power scheme using Sentinel Convergence Value, based on temperature and convergence value for optimal hyperthermia treatment

Huang-Wen Huang

GSE13

Pulsed RF heating using MRI

Yoshio Nikawa

GSE14

Microwave focusing using metamaterials

Yoshio Nikawa

GSE15

Temperature distributions with blood perfusion inside artery and vein during hyperthermia treatment

Junichi Nagasawa

GSE16

MRI-compatible testing of dual-curvature high-intensity focused ultrasound phased array transducer

Gin-Shin Chen

GSE17

Oncothermia treatment induced immunogenic cancer cell death - New possibilities for therapeutic cancer vaccine

Gabor Andocs

GSE18

In what kind of advanced or recurrent cancer do immunotherapy and/or hyperthermia show effect?

Tsutomu Takeda

GSE19

The systemic efficacy of combined immunotherapy with oncothermia and intratumoral injection of dendritic cells

Yu-Shan Wang

GSE20

Challenges and perspectives of hyperthermia in oncology

Oliver Szasz

GSE21

Effect of local hypothermia combined with highly active anti-retroviral therapy on the immunologic function of patients with AIDS

Daoke Yang

GSE22

Enhancement of heat sensitivity by depression of homologous recombination repair

Atsuhisa Kajihara

GSE23

Hyperthermia enhances the therapeutic efficacy of cetuximab in human oral squamous cell carcinoma

Tomohiro Iisaka

GSE24

Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy: a case report

Masato Okigami

GSE25

Definitive radiotherapy plus regional hyperthermia for high-risk and very high-risk prostate carcinoma: Thermal parameters correlated with biochemical relapse-free survival

Takayuki Ohguri

GSE26

Peritoneal perfusion of rAd-p53 combined with thermo-chemotherapy for peritoneal carcinomatosis model of advanced cancer (a report of forty-one cases)

Yong-heng Li

GSE27

Effect of hyperthermic intraperitoneal perfusion chemotherapy in combination with intravenous chemotherapy as postoperative adjuvant therapy for advanced gastric cancer

Zhibing Wu

GSE28

Seven cases of pancreatic cancer treated with chemo proton beam therapy and hyperthermia

Takashi Saito

GSE29

A case of long-term survival after intrathoracic perfusion hyperthermo-chemotherapy for pleural dissemination of non-small cell lung cancer

Akitoshi Okada

GSE30

The outcomes of oncothermia with chemotherapy for far advanced lung cancer

Doo Yun Lee

GSE31

Clinical evaluation of thermochemoradiotherapy using retrograde superselective intra-arterial infusion for advanced oral squamous cell carcinoma with cervical lymph node metastases

Masaki Iida

GSE32

Thermochemoradiotherapy using superselective intra-arterial infusion for N3 cervical lymph node metastases of tongue squamous cell cancer

Kenji Mitsudo

GSE33

Successful treatment of N3 cervical lymph node recurrence from oropharyngeal cancer with thermochemoradiotherapy: A case report

Yuta Sekino

GSE34

Preoperative thermochemoradiotherapy using retrograde superselective intra-arterial infusion for locally advanced oral cancer with cervical lymph node metastases

Toshiyuki Koizumi

GSE35

Locally advanced unresected uterine leiomyosarcoma with triple;modality treatment combining radiotherapy, chemotherapy and hyperthermia

Akiko Shinagawa

GSE36

Conversion of chemo-sensitivity by adding electro-hyperthermiain recurrent endometrial cancer: A case report

Yun Hwan Kim

GSE37

Clinical effectiveness of recombinant adenovirus-p53 combined with hyperthermia in advanced soft tissue sarcoma (a report of 30 cases)

Shao-wen Xiao

GSE38

Effects of a shower bathing or whole body bathing on HSP70 induction of the bathing after that

Youko Itoh

GSE39

Mixed response to TS-1 and oncothermia in an esophageal cancer patient with lung metastases: Case report

Joon H Kim

GSE40

Analysis of respiratory-induced deformation and translation of liver using branching structure of portal vein observed by MR imaging for HIFU

Tatsuhiko Matsumoto

GSE41

Feasibility of noninvasive magnetic resonance thermometry of the knee joint under thermal therapy

Atsushi Shiina

GSE42

Enhancement of hyperthermia-induced apoptosis by isofraxidin in human lymphoma U937 cells

Peng Li

GSE43

P53 gene therapy combined with whole body hyperthermia and local hyperthermia

Akira Takeuchi

GSJ1

Anti-tumor and anti-invasive effects of diverse delta- and gamma-lactones and the combined hyperthermia

Kazuki Hara

GSJ2

Trial of treatment-standardization; similar quality of treatment of hyperthermia by "Thermotron RF-8"

Koji Sugawara

GSJ3

Correlation between complications induced by [Thermotron RF-8] and physical status

Kazuki Jinbo

GSJ4

Trial of prevention for complications induced during "Thermotron RF-8" treatment

Satoshi Suda

GSJ5

Evaluation on heating characteristics of multiple coaxial-slot antenna as a feeding probe of metallic stent for bile duct carcinoma

Erika Yashima

GSJ6

Effects of laser radiation on HeLa cells using diode laser (ADL-20)

Kouki Tadai

13:30 — 15:30 **Poster/Short-Oral Presentation**

GSJ7-35 *(Japanese)*

GSJ7

Capacitive coupling-type hyperthermia treatment method combined with wireless energy transmission system; Measurement of temperature with transmission power of 1 W

Kenji Shiba

GSJ8

Hyperthermia-induced tumor-specific T-cell immunity and its role in the therapeutic efficacy of hyperthermia

Ken Ando

GSJ9

Treatment of advanced castration resistant prostate cancer with multiple metastases by regional hyperthermia under thermosensitization with Parthenolide: A case report

Hisaya Shiozaki

GSJ10

Retrospective analysis of hyperthermia therapy in 47 case of unresectable pancreatic cancer

Yoshiyuki Yanai

GSJ11

The effect and benefit of hyperthermia therapy combined with chemotherapy and/or hormonal therapy for breast cancer patients with liver metastasis

Rika Fukui

GSJ12

Treatment with hyperthermic intraperitoneal chemotherapy for pseudomyxoma peritonei arising from appendix, Report of 3 cases

Tsuyoshi Yamaguchi

GSJ13

Colon cancer with peritoneal dissemination and lung metastasis, survived for 22months received multidisciplinary treatment: A case report

Mitsuhiro Morikawa

GSJ14

Two cases of rectal cancer with urinary bladder invasion treated with chemo-hyperthermia and radiotherapy surviving with complete response (CR)

Yuko Higuchi

GSJ15

Chemo-hyperthermia with hyperbaric oxygen therapy for stage IVb pancreatic cancer

Tomoaki Morioka

GSJ16

Preliminary result of hyperthermochemoradiotherapy using IMRT and capecitabine for advanced low-rectal cancer

Yosuke Takakusagi

GSJ17

Combination therapy combining low dose chemotherapy and regional hyperthermia for the treatment of castration-resistant prostate carcinoma

Kosuke Ueda

GSJ18

Two cases of small cell lung cancer (SCLC) treated with multidisciplinary treatment surviving with good disease control

Shin Ohta

GSJ19

Long-term outcomes of hyperthermic treatment combined with chemotherapy for patients with residual or recurrent esophageal cancer after definitive chemoradiotherapy

Sho Nishimura

GSJ20

Sequential boost HCRT using IMRT after conventional 3DCRT for cervical esophageal squamous cell carcinoma: Pilot experience in 6 patients

Makoto Sakai

GSJ21

Re-irradiation with hyperthermia in patients with recurrent tumor

Hiromasa Kurosaki

GSJ22

Two cases of myxofibrosarcoma treated with radiohyperthermochemotherapy (RHC)

Satoshi Yamada

GSJ23

Chemoradiotherapy combined with hyperthermia and hyperbaric oxygen therapy for three cases of malignant fibrous histiocytoma (MFH)

Yoshinori Tomoda

GSJ24

A fundamental study for the mechanism of cell death by special effects of microwave

Mamiko Asano

GSJ25

Change of QOL and stage of cancer progression for patients getting long-term hyperthermia treatment

Hideyuki Morosawa

GSJ26

Usefulness of pat and jelly in hyperthermia

Mai Ito

GSJ27

Hyperthermia as an effective alternative treatment for advanced cancers refractory to conventional therapies

Hiroshi Terunuma

GSJ28

Numerical evaluation on heating characteristics of microwave forceps with cutting blade

Yuta Endo

GSJ29

Evaluation on heating performances of microwave forceps for biological tissue coagulation

Kazuyuki Saito

GSJ30

Hyperthermia and team medical treatment

Keishi Takeda

GSJ31

Improvement of heating methods of hyperthermia under daily clinical practice by team medical care

Rumiko Yamada

GSJ32

Investigation of thermal efficiency in measures of hot spot with hyperthermia

Kaname Oka

GSJ33

Noninvasive temperature measurement during acupuncture treatment using MRI

Suguru Nakamura

GSJ34

BAG3 acts protectively against hyperthermia-induced apoptosis through modulation of nuclear factor kappa B activity in human retinoblastoma Y79 cells

Tatsuya Yunoki

GSJ35

Effects of whole-body heat treatment on T cell-mediated immune response in cancer patients

Yusuke Ito

15:45 － 17:45 **HIPEC Training Course** *(Japanese)*
HIPEC トレーニングコース

1. Thermal Dose と輸液管理
片山 寛次
2. 腹腔鏡の役割
平野 正満
3. LHIPEC の方法
一瀬 真澄
4. 術後合併症十対策
水本 明良
5. 温熱療法の適応
米村 豊
6. 腹膜播種に対する包括的治療を立ち上げる際の要点
鍛 利幸
7. HIPEC と CRS に有用な手術機器
寺下 義一

Memo

Abstracts

ASHO Congress Lecture

Past, present and future of hyperthermia in the war against cancer

September 5 (Fri.) 11:00 — 12:00
Room 1

Chang W. Song
Radiobiology Laboratory, Department of Radiation Oncology,
University of Minnesota, USA

Chair
Takeo Ohnishi
Nara Medical University, Japan

CL Congress Lecture

Past, Present and Future of Hyperthermia in the War against Cancer

Chang W. Song, Ph.D.[1], Heon Joo Park, M.D., Ph.D.[2] and Jae-Hoon Jeong, Ph.D.[3]

[1]*Radiobiology Laboratory, Department of Radiation Oncology, University of Minnesota, Minneapolis, Minnesota, U.S.A.*

[2]*Department of Microbiology, Medical College, Inha University, Inchon, Korea*

[3]*Research Center for Radiotherapy, Korea Institute of Radiological & Medical Sciences, Seoul, Korea*

Hyperthermia has been used from ancient time for treatment of various diseases particular cancer. Egyptian used hot blade and sticks to treat breast cancers more than 5000 years ago. Likewise, heat was used to treat various diseases in ancient China and India. Greek philosopher Parmenides (540-470 BC) stated "I will cure all diseases if I am given the power to produce fever" and Hippocrates (460-370 BC), a Greek physician who is considered to be the father of western medicine, wrote "The disease must be incurable, if it cannot be cured with heat". However, treating diseases with heat or fever remained mostly as a folk medicine or even as unproven quackery until late 1800s. Busch reported in 1866 that application of facial sarcoma with erysipelas produced high fever and led to disappearance of the tumor. Subsequently, Coley and others observed in 1890s that raising body temperature to fever range, e.g. 39-40°C, by injecting bacteria toxins was effective to cause regression of various inoperable tumors. In 1898, F. Westmark reported that heating inoperable cervical carcinoma with a metal coil circulated with 42-44°C water resulted in regression of the tumors. This observation was probably the landmark evidence in modern era that local hyperthermia treatment is effective for controlling solid tumors. The potential value of hyperthermia as an anti-cancer treatment modality was further confirmed in 1970s when cell death by heating at 42-45°C range was found to be closely related to the temperature and the length of heating. It was soon found that hyperthermia is able to markedly increase the response of cancer cells to radiotherapy and chemotherapy. It was also demonstrated in 1970s-1980s that, because the newly formed tumor vascular bed is more vulnerable than that of normal tissues to heat, tumors can be preferentially damaged relative to normal tissue by hyperthermia. These attractive biological features that malignant tumor cells can be killed, radiosensitized and chemosensitized by heating led to conduction of numerous clinical trials for efficacy of hyperthermia in combination with conventional cancer treatment modalities such as radiotherapy, chemotherapy or surgery. Concomitantly, a variety of techniques and approaches have been developed for local and regional heating. External coupling of microwave and radiofrequency (RF) either with a single electrode or phased array and capacitive application of RF have been the most popular methods for heating superficial or deep-seated tumors up to the present time. Perfusion of cavity or isolated limb with heated chemotherapeutic drug solution is utilized to achieve regional hyperthermia. Whole- body hyperthermia at fever range temperatures, e.g. 39-41°C, using various means such as radiant heaters with long infrared rays are used to enhance the effect of chemotherapy drugs and also to stimulate anti-tumor immune response. Deep-seated tumors are ablated by heating to >50°C with microwave or RF using needle-type applicator inserted into tumors or with laser light though laser fibers placed in tumors. High-intensity focused ultrasound (IHIFU) is another approach for ablative heating of tumors. There have been increasing interest in heating tumors by depositing various nanoparticles or nanotubes in target tumors and then heating them with microwaves, RF, magnetic or laser beam.

It is an undeniable fact that, unfortunately, the clinical outcomes of hyperthermia failed to meet the initial enthusiastic expectations mainly because heating human tumors to cytotoxic temperatures, i.e.> 42-43°C, is technically difficult with the use of previously available heating devices. Consequently, interest for the use of hyperthermia for controlling human cancer has considerably diminished in recent years. However, indications

are that the interest in hyperthermia is reviving in many countries owing to realizations that hyperthermia at relatively mild temperatures, i.e. 39-42°C is able to enhance the efficacy of radiotherapy and chemotherapy although the mild heating may not directly kill tumor cells. There is increasing evidence that mild heating at 39-42°C improves tumor blood circulation, thereby elevating tumor oxygenation and the response of tumors to radiotherapy. Likewise, mild heating increases drug delivery to tumors by increasing blood perfusion, increases cellular uptake of drugs and potentiated the interaction of drugs with target molecules in the tumor cells. In this regard, combination of mild heating with heat-sensitive liposomes has been shown to be potentially useful for increasing drug delivery to target tumor volume. Recent investigations have shown that mild heating upregulates expression of certain enzymes which are involved in killing tumor cells by certain drugs. Furthermore, mild heating may enhance the conversion of pro-drugs to cytotoxic drugs. Cancer stem cells have been known to be resistant to radiotherapy and ordinary chemotherapy drugs. Intriguingly, however, hyperthermia alone or with certain chemotherapy drugs has been demonstrated to be able to preferentially kill cancer stem cells relative to non-stem cancer cells. The biological response to heat stress is temperature dependent. Rational combination of hyperthermia at different temperatures with relevant biological responses would make a significant leap and advance in our war against cancer.

Chang Won Song, Ph.D

Professor of Radiation Biology, Department of Therapeutic Radiology-Radiation Oncology, University of Minnesota, Minneapolis, MN, USA (1978 – present)

Degrees

- BSc in Chemistry, Seoul National University, 1957
- MS in Biochemistry, Korea University, 1959
- Ph.D. in Radiation Biology, University of Iowa, 1964

Professional Society Memberships

- Radiation Research Society
- American Association for Cancer Research
- North American Hyperthermia Society
- Cell Kinetics Society
- American Association for the Advancement of Science
- Korean Scientists and Engineers
- Association of America
- American Society for Therapeutic Radiology and Oncology

Research Interests

- Role of blood flow, pO2 and pH in tumor treatment
- Effect of radiation and hyperthermia on tumor physiology, e.g. blood flow, pH, pO2 and glucose metabolism
- Chemical radiosensitization and radioprotection Molecular mechanism of apoptosis caused by radiation, drugs, and heat shock

Award Lecture

September 5 (Fri.) 17:00 — 18:15
Room 1

The ASHO Award

Chair: Hiroyuki Kuwano
Gunma University, Japan

Satoshi Kokura
Kyoto Prefectural University of Medicine, Japan
Kyoto Gakuen University, Japan

The JSTM Award

Chair: Koichi Ito
Chiba University, Japan

Iwai Tohnai
Yokohama City University Graduate School of Medicine, Japan

The Young Investigator Award

Chair: Koichi Ito
Chiba University, Japan

Kazuyuki Saito
Chiba University, Japan

The Young Investigator Award

Chair: Akihisa Takahashi
Gunma University, Japan

Ryo Suzuki
Teikyo University, Japan

The ASHO Award

The present state of hyperthermia in Japan, and By what kind of way should we progress from now on?

Satoshi Kokura[1,2]

[1]*Dept. of Cancer Immuno Regulation, Kyoto Pref. Univ. of Med., Japan*

[2]*Center for Educational Research and Development, Kyoto Gakuen Univ., Japan*

The clinical trial of hyperthermia that was started in the 1980s, has been a significant contribution to the cancer therapy in Japan. In addition, hyperthermia also has been addressed actively in basic research for many years, and it has been revealed the mechanism of the combined effect of the anti-cancer agents and the role of free radical reactions in the anti-cancer mechanism of hyperthermia. Since the combination with hyperthermia and chemotherapy is useful, we should use them together as much as possible. Recently, it was clearly showed the enhanced effect of hyperthermia for immunotherapy, and showed the mechanisms by which cancer vaccine and immune-cell therapy were enhanced by hyperthermia. Moreover, hyperthermia itself can cancel cancer tissue produced immunosuppressive status, and can inhibit EMT. Hyperthermia plus immunotherapy are also expectable. Moreover, we are also performing translational research of immunotherapy.

Now I expect the combination therapy of hyperthermia plus immunotherapy. The basic study and clinical trial proving it are on going.

The JSTM Award

Hyperthermia for oral cancer —Basic principles and clinical applications—

Iwai Tohnai

Department of Oral and Maxillofacial Surgery

Yokohama City University Graduate School of Medicine Yokohama, Japan

Standard of care for oral cancer is surgery at the present time. However, the dysfunction such as dysarthria, dysphagia and dysmasesis appears after surgery of oral cancer. Especially, cosmetic disturbance is major problem after surgery. There is a great difference between oral cancer and other cancer such as gastric cancer in cosmetic disturbance. Therefore, noninvasive therapy is greatly desired for oral cancer. Then, hyperthermia was focused as one of the strategy in noninvasive therapy.

Basic research

Thermotolerance: The relationship between Hsp40/Hsp70 synthesis and the development of thermotolerance was investigated *in vitro* and *in vivo*. The extent of thermotolerance was well correlated with the relative amount of Hsp40/Hsp70. These results obtained *in vivo* were very similar to those *in vitro*. These findings suggest that Hsp40 could be a useful indicator of the degree of thermotolerance in addition to Hsp70 *in vivo* and *in vitro*.

Interstitial hyperthermia: Heating device of interstitial hyperthermia consists of ferromagnetic implant, induction coil and generator to produce high frequency magnetic field. The ferromagnetic implant is composed of Fe-Pt alloy in content ratio of iron and platinum is 73%, and 27%, and Curie temperature of 68°C. The generator has maximum power of 2.5 kw and yield a maximum magnetic power of 16 Gauss at the center of induction coil with frequency of 250 kHz. The needle-shaped implant is inserted into the tumor. The rationale for this system is that the implant is heated by eddy current under the high frequency magnetic field. Antitumor effect was observed in VX7 rabbit tumor model using interstitial hyperthermia. However, the long axes of the implant must be parallel to the direction of the magnetic field for maximal heat production. Therefore, magnetite particle covered cationic liposomes (MCL) was developed instead of ferromagnetic implant for interstitial hyperthermia. The effect of interstitial hyperthermia using MCL on primary lesion and cervical lymph node (LN) metastasis in VX7 rabbit tumor model were investigated. The head and neck region was irradiated after MCL injected into the tongue tumor only without cervical LN metastasis. The tumor decreased significantly not only the primary lesion, but also cervical LN metastasis.

Clinical research

Interstitial hyperthermia: Eight patients with oral cancer of early stage were treated by thermochemoradiotherapy (CDDP: 100mg/m^2, PEP: 25mg/m^2, iv) using magnetic induction hyperthermia without radiotherapy before surgery. Clinical and pathological responses were excellent results.

Thermochemoradiotherapy: The patients with N3 cervical LN metastases of oral cancer underwent thermochemoradiothrerapy (CDDP: 100mg/m^2, RT: 40Gy) using RF hyperthermia before surgery. Pathological CR rate was low as 12.5% (1/8). Therefore, chemotherapy was exchanged to superselective intra-arterial infusion from intravenous infusion. This superselective intra-arterial infusion is a new method that the catheter is not through common carotid artery, because of retrograde catheterizations from superficial temporal artery and occipital artery. Nine patients with N3 cervical LN metastases of oral cancer underwent thermochemoradiotherapy using superselective intra-arterial infusion with docetaxel (DOC) and cisplatin (CDDP). Treatment consisted of hyperthermia (2-8 sessions), superselective intra-arterial infusions (DOC, total 40-60 mg/m^2; CDDP, total 100-150 mg/m^2) and daily concurrent radiation therapy (total, 40-60 Gy) for 4-6 weeks. Six of 9 patients underwent neck dissection 5-8 weeks after treatment. In four of these 6 patients, all metastatic lymph nodes, including those at N3, were grade 3 (non-viable tumor cells present) or grade 4. Thermochemoradiotherapy using superselective intra-arterial infusion provided good histopathologic effects and locoregional control rates in patients with N3 metastatic lymph nodes.

The Young Investigator Award of JSTM

Study on practical application of microwave antenna for treatment of bile duct carcinoma

Kazuyuki Saito

Center for Frontier Medical Engineering, Chiba University, Japan

Microwave thermal therapy is one of the modalities for cancer treatment. Here, there are several schemes of microwave heating. The authors have been studying thin coaxial antenna for intracavitary microwave heating aiming at the treatment of bile duct carcinoma. In this treatment, an endoscope is first inserted into the duodenum and a long and flexible thin antenna is then inserted into the forceps channel of the endoscope, which is used to insert the tool for surgical treatment. Finally, the antenna is guided to the bile duct through the papilla of Vater, which is located in the duodenum, and is inserted into the bile duct. Up to now, the heating characteristics of the antenna are investigated by numerical simulation and experiment for finding a possibility of the treatment. In this study, in order to consider practical situations of the treatment, heating characteristics of the antenna are calculated by use of some different models. For example, they include a stenosis, a metallic stent, etc. As the results of investigations, possibilities of microwave heating by use of thin coaxial antenna could be confirmed under some practical situations. As a further study, results of the calculations should be confirmed by phantom and animal experiments.

Excellent Papar Award

Novel strategy for ultrasound diagnostics and therapeutics using micro/nanobubbles -Development of hyperthermia for cancer with liposomal nanobubbles-

Ryo Suzuki[1], Yusuke Oda[1], Daiki Omata[1], Yoshikazu Sawaguchi[2], Mutsumi Seki[1], Hitoshi Uruga[1], Johan Unga[1], Tomoyuki Naoi[1], Yoichi Negishi[3], Kazuo Maruyama[1]

[1]*Faculty of Pharma-Sciences, Teikyo University, Japan*

[2]*Nihon Pharmaceutical University, Japan*

[3]*School of Pharmacy, Tokyo University of Pharmacy and Life Sciences, Japan*

Theranostics is a novel concept that combines diagnostics and therapeutics. For diagnostics, there are various medical equipments such as X ray computed tomography (CT), Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET) and Sonography. In physical energy with these equipments, ultrasound is a useful tool for theranostics due to having potential both in diagnostics with sonography and in therapeutics with hyperthermia for cancer. Recently, microbubbles have been utilized as an effective imaging agent for blood flow in tumor. Sonazoid, which is a commercially available microbubble is applied for detection of hepatic tumor. In addition, microbubbles are also useful tools for theranostics due to be able to utilize as not only ultrasound contrast imaging agent but also enhancer in drug/gene delivery and hyperthermia with therapeutic ultrasound. To improve accessibility of microbubbles into deep tissue, some researchers are developing various types of smaller bubbles such as submicron sized nanobubbles. We also developed novel liposomal bubbles (Bubble liposomes), which are entrapping perfluoropropane gas in inner aqueous phase of liposome. Bubble liposomes are easy to modify with targeting molecules and it is easy to load genes on their surface. In addition, Bubble liposomes are sensitive to ultrasound which can induce oscillation/collapse of the bubbles. This behavior of Bubble liposomes can be utilized for ultrasound theranostics and we have applied them as ultrasound imaging agent, enhancer of drug/gene delivery and hyperthermia with therapeutic ultrasound. Here, we would like to introduce our recent research about hyperthermia for cancer by the combination of Bubble liposomes and ultrasound.

The phenomenon in which Bubble liposomes collapse is known as cavitation, induces jet streams and heat under ultrasound irradiation, thereby damaging nearby cells. In this study, we examined the anti-tumor effects of intra-tumoral injection of Bubble liposomes and ultrasound exposure. With this therapy, the temperature in tumor tissues increased and a necrosis area in a part of tumor tissues was observed. Surprisingly, priming of cellular immune system also occurred and contributed to tumor growth suppression. Therefore, the combination of Bubble liposomes and ultrasound would be an effective method to cause hyperthermia for cancer that by various mechanisms could be successful in tumor growth suppression.

[Acknowledgements] This work was supported by JSPS KAKENHI (Grant Number 21700511, 23300192, 24650299, and 23500567), the MEXT-Supported Program for the Strategic Research Foundation at Private Universities 2013-2017, the Programs for Promotion of Fundamental Studies in Health Sciences of the National Institute of Biomedical Innovation (NIBIO).

Symposium 1

Hyperthermic Effects of HIPEC on Peritoneal Surface Malignancies

September 6 (Sat.) 13:30 — 15:30
Room 1

Chairs

Yutaka Yonemura
Nonprofit Organization to support Peritoneal Dissemination Treatment (NPO PDT), Japan

Yan Li
Zhongnan Hospital of Wuhan University, China

Mao-Chih Hsieh
Taipei Medical University, Wanfang Hospital, Taiwan

S1-1 Symposium 1

CYTOREDUCTIVE SURGERY AND HIPEC EXPERIENCE FOR PERITONEAL METASTASES IN TURKEY AFTER EDUCATION FOR PERITONEAL MALIGNANCIES IN JAPAN

Emel Canbay[1], Suleyman Temiz[2], Ozcan Yildiz[3], Bahar Canbay Torun[4], Celalettin Peru[1], Amira Baker[1], Yutaka Yonemura[1,5,6,7]

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AIM:

The present study reports our experience concerning with the advanced cancer treatment using cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in patients with peritoneal metastases.

METHODS:

In a period of May 2013 to June 2014, we evaluated 12 patients with peritoneal metastases (PM) (2 patients with ovarian serous cancer, 5 with stomach cancer, and 5 with colorectal cancer). All patients underwent CRS and HIPEC procedures. Peritoneal involvement was quantified according to the Peritoneal Cancer Index (PCI) and the remaining postoperative disease according to the Completeness of Cytoreduction score (CC). HIPEC was always performed with closed technique for 60 min, with an average inflow temperature of 42.5°C. The drugs were administered in combination according to two schemes: 1) 40 mg/m^2 of cisplatin and 2) 40 mg/m^2 of taxotere®. Morbidity and mortality were evaluated in accordance with the NCI CTCAE v. 3.0 (USA).

RESULTS:

The average age was 57 years (range 30-72). Patients were afflicted by PM of intraabdominal cancers. From this group, 3 (25%) were subjected to neoadjuvant bidirectional chemotherapy and 2 (12%) to surgery as a first intervention; 7 (58%) patients had recurrence of primary cancers and all of them had previously undergone surgery and adjuvant chemotherapy. The average PCI was 21.25 (range 3-39). In 6 patients (50%), cytoreduction was considered total or almost total (CC-0/CC-1); in 6 patients (50%), it had not been optimal (CC-2/CC-3). In all patients with PCI less than 12, it was possible to achieve an optimal cytoreduction, and this was not possible in patients who had a PCI greater than 12. The average operative time, including HIPEC, was 612 min (range 425-840). In 9 patients (75%), the postoperative course was uncomplicated, in 2 patients (16%) complications were minor (G1-G2) and in 1 patient (8%) morbidity was severe (G4). Mortality occurred in one patient due to sepsis developed due to previous incomplete surgery.

CONCLUSION:

Although CRS and HIPEC in the treatment of advanced or recurrent PM represents a reliable method with encouraging results both in terms of morbidity and outcomes, there are still many controversial aspects that need to be clarified with further and prospective randomized phase III studies.

S1-2 Symposium 1

Laparoscopic hyperthermic intraperitoneal chemotherapy for advanced gastric cancer with peritoneal carcinomatosis

Masumi Ichinose, Yutaka Yonemura, Masamitsu Hirano, Akiyoshi Mizumoto,
Yutaka Morikochi, Nobuyuki Takao, Kosuke Noguchi

Department of General Surgery, Kusatsu General Hospital, Japan

Background:

There is no standard treatment for peritoneal dissemination from gastric cancer (GC). Laparoscopy assisted hyperthermic intraperitoneal chemotherapy (LHIPEC) was introduced as a new approach. The aims of LHIPEC are control for malignant ascites, stage reduction and an increased incidence of complete cytoreduction for peritoneal carcinomatosis (PC).

Methods:

LHIPEC were performed on 102 GC patients with PC from July 2008 to February 2014. The chemotherapy solutions used were docetaxel 40mg and cisplatin 100mg in 4000ml of normal saline at 42-43 degree. Complete cytoreduction including peritonectomy was achieved in 17 (17.2%) of the 102 patients after LHIPEC.

Results:

Median survival of patients performed LHIPEC after diagnosis of PC from GC was 21 months. LHIPEC is effective for eighteen (51.0%) of the 35 patients who had malignant ascites. No treatment-related mortality was observed. Postoperative complications included one injury of urinary bladder, one renal failure, one ileus and one injury of small bowel.

Conclusion:

LHIPEC is a safe and effective method for palliating malignant ascites. LHIPEC and complete cytoreduction for PC may improve the survival of patients with PC from gastric cancer.

S1-3 Symposium 1

Laparoscopic Hyperthermic Intraperitoneal Chemotherapy (LHIPEC) for Stomach Cancer Patients with Peritoneal Carcinomatosis

Chai Young Lee[1], Se Jong Park[2], Hong Ki Lee[1], Eun Kyung Kim[2], Ji Yeon Lee[2] and Dae Hee Lee[2]

[1]*Department of Oncologic Surgery, Sam Integrative Cancer Center, G-Sam Hospital, Gunpo 435-010, Korea*

[2]*Department of Hematology and Oncology, Sam Integrative Cancer Center, G-Sam Hospital, Gunpo 435-010, Korea*

Background: Peritoneal carcinomatosis and malignant ascites are common problems in patients with cancers of gastrointestinal origin. The standard treatment for peritoneal carcinomatosis is currently limited to systemic chemotherapy. Recently cytoreductive surgery with Hyperthermic intraperitoneal chemotherapy (HIPEC) has been introduced with promising results. This is a retrospective study of the clinical outcomes of laparoscopic hyperthermic intraperitoneal chemotherapy (LHIPEC) in stomach cancer patients diagnosed with peritoneal carcinomatosis.

Materials and Methods: One hundred twenty-three stomach cancer patients with diagnosed peritoneal carcinomatosis underwent single or multiple LHIPEC from November 2008 to May 2014. The patients underwent LHIPEC with mitomycin C (12.5mg/m^2) and cisplatin (50mg/m^2) for the perfusion solution. The temperature of the inflow fluid was maintained at 42~43°C during the intraperitoneal circulation for 60 minutes. The patients were analyzed for overall survival (OS), efficacy of local control and safety profile. Also, the amount of ascites and the PCI (peritoneal cancer index) of the patients were analyzed.

Results: The median OS of 123 enrolled patients was 12.3 months. The median OS of 13 patients who underwent cytoreductive surgery (CRS) and HIPEC after a few of sessions of LHIPEC was 15.8 months. The median OS of the other 110 patients without CRS and HIPEC was 12.2 months. The median OS in the group of patients who underwent repeated sessions of LHIPEC was better than the group with single session of LHIPEC (14.1 vs.10.9 months). Significant benefit of local control was noted with majority of patients showing reduction of ascites compared with the ascites measured in previous session of LHIPEC. Also, reduction in PCIs was observed in laparoscopic examination in patients who underwent multiple LHIPEC. LHIPEC was feasible to most patients with low toxicity profile.

Conclusion: Based on our experience, LHIPEC is an effective and feasible method of controlling peritoneal carcinomatosis in stomach cancer patients with possible survival benefit. Also, this study suggests that LHIPEC may be more effective when it can be performed in repeated sessions.

Key words: Laparoscopy, Peritoneal carcinomatosis, Hyperthermic intraperitoneal chemotherapy, malignant ascites

S1-4 Symposium 1

CRS + HIPEC Improves Survival for Patients with Colorectal Peritoneal Carcinomatosis: A Phase II Study from a Chinese Center

Chao-Qun Huang, MD[*, 1], Xiao-Jun Yang, MD, PhD[*, 1], Yang Yu, MD[1], Hai-Tao Wu, MD[1], Yang Liu[1, 2], MD, Yutaka Yonemura[2], MD, PhD, Yan Li, MD, PhD[1]

**These authors contributed equally*

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ABSTRACT

Background: Peritoneal carcinomatosis (PC) is a difficult clinical challenge in colorectal cancer (CRC) because conventional treatment modalities could not produce significant survival benefit, which highlights the acute need for new treatment strategies. Increasing studies on this problem has gradually resulted in revolutions in both the basic pathological sciences and clinical approaches to CRC PC. Our previous case-control study demonstrated the potential survival advantage of cytoreductive surgery (CRS) plus hyperthermic intraperitoneal chemotherapy (HIPEC) over CRS alone (the OS was 8.5 months in Control group versus 13.7 months in Study group, $P = 0.02$). This phase II study was to further investigate the efficacy and adverse events of CRS+HIPEC for Chinese patients with CRC PC.

Methods: A total of 60 consecutive CRC PC patients underwent 63 procedures consisting of CRS+HIPEC and postoperative chemotherapy, all by a designated team focusing on this combined treatment modality. All the clinico-pathological information was systematically integrated into a prospective database. The primary end point was disease-specific overall survival (OS), and the secondary end points were perioperative safety profiles. The OS was defined as the time interval from the first surgery to death due to the disease for synchronous PC, and from CRS+HIPEC to death due to the disease for metachronous PC.

Results: By the most recent database update, the median follow-up was 29.9 (range 3.5 – 108.9) months. The peritoneal cancer index (PCI) ≤20 was in 47.0% of patients, complete cytoreductive surgery (CC0-1) was performed in 53.0% of patients. The median OS was 16.0 (95% confidence interval [CI] 12.2–19.8) months, and the 1-, 2-, 3-, and 5-year survival rates were 70.5%, 34.2%, 22.0% and 22.0%, respectively. The median OS in subgroup were 21.7 months in PCI ≤20 and 14.8 months in PCI >20 ($P = 0.04$); 22.1 months in CC0-1 and 14.5 months in CC2-3 ($P = 0.01$); 22.1 months in adjuvant chemotherapy ≥6 and 8.5 months in adjuvant chemotherapy <6 ($P < 0.001$). Mortality and grades 3 to 5 morbidity rates in postoperative 30 days were 0.0% and 30.2%, respectively. Univariate analysis identified 3 parameters with significant effects on OS: PCI ≤20, CC0-1 and adjuvant chemotherapy over 6 cycles. On multivariate analysis, however, only CC0-1 and adjuvant chemotherapy ≥6 cycles were found to be independent factors for OS benefit.

Discussion: CRS+HIPEC at a specialized treatment center could improve OS for selected CRC PC patients from China, with acceptable perioperative safety.

KEY WORDS: colorectal cancer; peritoneal carcinomatosis; cytoreductive surgery; hyperthermic intraperitoneal chemotherapy; phase II clinical research

S1-5 Symposium 1

HIPEC is effective for peritoneal dissemination of colon cancer and MUC2 protein expression status is a useful indicator

Takanori Goi, Kanji Katayama, Youhei Kimura, Daisuke Fujimoto, Mitsuhiro Morikawa, Kenji Koneri, Makoto Murakami, Yasuo Hirono, Atsushi Iida, Akio Yamaguchi

The First Department of Surgery, University of Fukui, Fukui, Japan

The prevalence and mortality of colon cancer are the highest among malignant tumors in all countries. The incidence of peritoneal dissemination is 7% of initial colon cancers and 4-19% of recurrent colon cancers, but no effective treatment modalities for this peritoneal dissemination have been established. We present the effectiveness of HIPEC and whether expression of mucin family proteins plays some type of role.Methods:Patients:The subjects were 94 colon cancer patients with synchronous/metachronous peritoneal dissemination at the First Department of Surgery, University of Fukui, Japan, between 1994 and 2011. Surgical specimens of the peritoneal dissemination were obtained from 37 primary colon cancer patients. HIPEC was performed in 30 patients with peritoneal dissemination. HIPEC procedure:This procedure allowed the abdominal cavity to be extended widely enough to allow perfusate to spread throughout the peritoneal cavity. Four litres of saline contained cisplatin, mitomycin C, and etoposide. Abdominal temperatures were measured at the serosal surface in the subphrenic space and the cavity of Douglas, and the temperature of the infusate was also measured in the inflow tube, outflow tube, and water bath. The thermal dose (TD) obtained during the treatment was calculated simultaneously during HIPEC and expressed in terms of equivalent time at 43C. HIPEC was performed until the TD reached 40 minutes. Immunohistostaining:Surgical specimens were analyzed for MUC-2 protein expression by the streptavidin-biotin peroxidase methodResults:(1)The survival rate of P1 and P2 cases: In the non-HIPEC group, the 5-year survival rate was 28%, whereas in the HIPEC group the 3-year survival rate was 39.2%. The HIPEC group had significantly better outcomes. (2)The survival rate of P3 cases:In the non-HIPEC group, the median survival time was 4 months, whereas in the HIPEC group the median survival time was 20 months.(3)When MUC2 expression was investigated in the HIPEC group, in patients positive for MUC2 expression, the 3-year survival rate was 0%, while in patients negative for MUC2 expression, the 3-year survival rate was 40%. Conclusions:HIPEC therapy is effective in prolonging survival in colon cancer patients with peritoneal dissemination, and MUC2 expression is useful as an indicator.

S1-6 Symposium 1

Cytoreductive surgery combined Hyperthermic intraperitoneal chemotherapy for pseudomyxoma peritonei treatment- Experience in Taiwan

Chang-Yun Lu, Mao-Chih Hsieh

Department of Surgery, Division of General Surgery,

Taipei medical university affiliated Wanfang Hospital, Taipei, Taiwan

From Feb 2002 to Feb 2014, 31 patients histologically proven appendiceal neoplasm with pseudomyxoma peritonei were treated at Taipei medical university affiliated Wanfang hospital. Among them 23 patients underwent previous surgeries in other institutes. All patients underwent laparotomy for aggressive cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). Thirty-one patients underwent 48 procedures in total, 13 patients underwent more than one procedures for staged residual tumor debulking, or recurrent disease. The peritoneal cancer index (PCI) and completeness of cytoreduction score (CC s) reported by Jacquet and Sugarbaker were used for quantitative assessment of peritoneal tumor, and for recording residual tumors after cytoreduction. The average PCI score is 27, 58% (18/31) patients underwent optimal cytoreduction (CCs:0-1) at first operation. There were 5 events of grade III-IV complication, and three mortality during hospitalization. The survival of pseudomyxoma peritonei patient treated by CRS/HIPEC is related to Extent of intraperitoneal tumor loading (PCI) and completeness of cytoreduction (CCs).

S1-7 Symposium 1

Hyperthermic Intraperitoneal Chemotherapy for Patients with Pseudomyxoma Peritonei Undergoing Incomplete Cytoreductive Surgery

Yang Liu[1], Haruaki Ishibashi[1], Shouzou Sako[1], Kazuyoshi Takeshita[2], Akiyoshi Mizumoto[2], Masamitsu Hirano[2], Masumi Ichinose[2], Yutaka Yonemura[1,2]

[1]*Peritoneal Dissemination Center, Kishiwada Tokushukai Hospital, Kishiwada, Japan*

[2]*Department of Surgery, Kusatsu General Hospital, Shiga, Japan*

Abstract

Background: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) have been accepted as the standard treatment for patients with pseudomyxoma peritonei. Complete cytoreduction is an independent factor influencing patients' prognosis. However, complete CRS cannot be achieved on some patients. For these patients, the role of HIPEC is not confirmed. In this study, we are going to investigate the role of HIPEC on patients undergoing incomplete CRS.

Methods: A total of 225 patients with PMP received incomplete CRS with residual tumor > 2.5mm in diameter in our institution during January 2006 and January 2014. After CRS, HIPEC was performed with mitomycin C (MMC) at a dose of 15 mg/m^2 and cisplatin at a dose of 60 mg/m^2 at 42.9-43.5 centigrade in 4L of saline. The HIPEC procedure lasted for 60mintues. Patients were closely monitored after surgery.

Results: A total of 225 patients received incomplete CRS. The median age was 62 years (range 21-85 years). Seventy-two patients were male, and 153 patients were female. Sixty-two patients received a cytoreduction of CC-2, and other 163 patients received a cytoreduction of CC-3. Fifty-four patients received HIPEC after CRS. The median survival of patients who did not receive HIPEC was 21 months (95% CI 15.0-27.0 months). Patients undergoing HIPEC had an estimated median survival of 40 months (P=0.022). Postoperative complications did not differ between two groups.

Conclusion: HIPEC was helpful in improving patients' survival and prognosis even when complete cytoreduction cannot be achieved without more adverse events.

S1-8 Symposium 1

Cytoreductive surgery combined Hyperthermic intraperitoneal chemotherapy for peritoneal superficial malignancy- Experience in Thailand

Thawatchai Akaraviputh

Thailand

Symposium 2

Impact of HSPs — Revisit & Perspective —

September 5 (Fri.) 09:00 — 11:00
Room 1

Chairs

Kenzo Ohtsuka
Chubu University, Japan

S. V. Chiplunkar
Advanced Center for Treatment, Research & Education in Cancer, India

S2-1 Symposium 2

DIFFERENT CYTOTOXIC EFFECT FROM DIFFERENT HYPERTHERMIA DEVICES. COMPARISON OF THE ONCOTHERM-LABEHY AND THE THERMOTRON RF-8 IN AN IN VITRO MODEL

Yu-Shan Wang[1], Chao-Chun Chang[1], Yi-Chun Huang[1], Yi-Ying Huang[1], Ren-Hong Wu[1], Gabor Andocs[2], Yuk-Wah Tsang[3] , Kwan-Hwa Chi[1,4]

[1]Department of Radiation Therapy and Oncology, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan, [2]Department of Veterinary Clinical Medicine, Tottori University, Tottori, Japan, [3]Department of Radiation Oncology, Chiayi Christian Hospital, Chiayi, Taiwan, [4]Institute of Radiation Science and School of Medicine, National Yang-Ming University, Taipei, Taiwan.

Purpose: Deep heating electro-hypertermia methods are a promising cancer treatment modalities used to enhance conventional treatment. This could be achieved through radiofrequency field on 8 and 13.56 MHz by Thermotron RF-8 and Oncotherm-Labehy, respectively. However, the difference cytotoxic effect between different hyperthermia devices has never been evaluated.

Materials and Methods: HepG2, a human hepatoma cell line was treated by water bath, Oncotherm-Labehy or RF-8 for 30 min at 42°C. Cell proliferation, apoptotic cell and cell cycle distribution were assayed at 24, 48 and 72 hours after treatment. The membrane expression of adherens junction proteins on cell membrane, E-cadherin and β -catenin, were investigated by immunocytochemistry. The expression and releasing of heat-shock proteins (HSPs) after various treatments were evaluated. We further analyzed the effect of 5-Aminolevulinic acid hydrochloride (ALA) as thermosensitizer on different hyperthermia devices.

Result: Both of Oncotherm-Labehy and RF-8 inhibited cell proliferation on HepG2 cells. Oncothermia could significantly induce apoptosis on HepG2 48h after treatment. Both effects were not observed by water bath control. The expression of E-cadherin and β -catenin on cell membrane were increased after Oncothermia treatment but not with RF-8 and water bath. The expression and releasing of HSP70 were significantly increased after Oncothermia treatment. On the other hand, RF-8 significantly increased the intracellular expression of HSPs. ALA could sensitize both Oncothermia and RF-8 effect on the inhibition of cell proliferation and releasing of HSP70.

Conclusion: In this report, we found that different hyperthermia devices may induce different mechanisms on their cytotoxic effects and cell responses to heat. These results may provide significant insight on future clinical application of electro-hyperthermia on different type of cancers.

Key words: Hyperthermia, Oncotherm, Thermotron RF-8

S2-2 Symposium 2

Heat shock proteins and gamma delta T cell immunity in oral cancer

S. V. Chiplunkar

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Heat shock proteins are molecular chaperones with a central role in protein folding and homeostasis. They also play major roles in the development of cancer and in recent years have emerged as promising therapeutic targets. Heat shock proteins (hsp) and phosphoantigens have gained importance as ligands that induce oligoclonal stimulation of γδ T cells. γδ T lymphocytes expressing the γδ T cell receptor constitute a minor population in the peripheral blood (<10%). Studies from our laboratory have demonstrated that γδ T cells expressing Vγ9 and Vδ2 receptor recognize hsp60 expressed on oral tumor cells and have the ability to lyse autologous and allogenic oral tumors. Tumor cells treated with aminobisphosphonates (Zoledronate) upregulate intracellular levels of isopentyl pyrophosphate (phosphoantigen) and are actively killed by γδ T cells. The aim of the present study was to investigate the mechanism of lysis of oral tumor cells by γδ T cells upon treatment with aminobisphosphonates. Proteomic profiling of Zoledronate treated tumor cells showed increased expression of hsp60/70. Time kinetics experiments exhibited that membrane expression of hsp60 increased after treatment of tumor cells with Zoledronate. γδ T cells incubated with monoclonal antibody recognising hsp60 could lyse oral tumor cells by antibody dependent cellular cytotoxicity (ADCC) mechanism . Treatment of oral tumor cells with Zoledronate further increased the ADCC mediated by γδ T cells . To monitor the involvement of additional costimulatory signals, in hsp recognition by gd T cells, the role of notch signal was investigated. Purified gd T cells were cultured in the presence of rIL2 and hsp60 in the presence and absence of g-secretase inhibitor. It was demonstrated that Notch signaling is involved in hsp60 induced proliferation and IFN□ secretion by gd T cells. In conclusion, the study demonstrates that heat shock proteins expressed on oral tumor cells can serve as therapeutic targets for γδ T cell based immunotherapy in oral cancer patients.

S2-3 Symposium 2

Inhibiting heat shock transcription factor 1 and its related genes for novel hyperthermia therapy

Yoshiaki Tabuchi[1], Tatsuya Yunoki[2], Takashi Kondo[2]

[1]*Life Science Research Center, University of Toyama, Toyama 930-0194, Japan*

[2]*Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Toyama 930-0194, Japan*

Hyperthermia (HT) induced by heat stress in the range of 40 to 45˚C is a well-established treatment modality that is used alone or in combination with other therapies, such as radiotherapy and chemotherapy, for the treatment of a variety of tumors. One of the problems with HT therapy is the acquisition of thermoresistance against heat stress. Heat shock proteins (HSPs), molecular chaperons, are induced by a variety of physiological insults, particularly heat stress. Therefore, it has been considered that HSPs play a role in the acquisition of thermoresistance in cells. The expression of HSPs is mainly regulated by heat shock transcription factor 1 (HSF1). Previous findings indicated that HSF1 regulates many other targets in addition to HSPs. In these, BAG3 (Bcl-2 associated athanogene 3), a co-chaperone of HSP70, is shown to be a target gene regulated, at least in part, by HSF1. HSF1 and BAG3 have been reported to be abundantly expressed in a wide variety of tumors in humans, and participate in the proliferation and maintenance of tumors. In human oral squamous cell carcinoma HSC-3 cells, an increase in the protein expressions of HSP70, HSP40 and BAG3 was observed in HT-treated cells, whereas expressions of these proteins were remarkably decreased in HSF1-silencing cells. Interestingly, silencing of HSF1 or BAG3 significantly enhanced sensitivity to HT in HSC-3 cells (1, 2). Several studies also demonstrated that the inhibition of functions of HSF1 was shown to reduce the acquisition of thermoresistance and sensitize tumors to HT-induced cell death (3-5). Taken together, inhibiting either HSF1 or its related genes including BAG3 in combination with HT may be a promising approach for the treatment of cancer.

References: 1. Tabuchi Y. et al., Thermal Med. 27, 99-108 (2011); 2. Yunoki T. et al., Cancer Lett. 335, 52-57 (2013); 3. Wang J.H. et al., Biochem. Biophys. Res. Commun. 290, 1454-1461 (2002); 4. Rossi A. et al., Cancer Res. 66, 7678-7685 (2006); 5. Nakamura Y. et al., J. Dermatol. Sci. 60, 187-192 (2010)

S2-4 Symposium 2

Pifithrin-μ, an inhibitor of HSP70, can increase the antitumor effects of hyperthermia against human prostate cancer cells

Mamoru Harada

Department of Immunology, Shimane University Faculty of Medicine, Shimane, Japan

Hyperthermia (HT) is an effective therapy that has low toxicity, mild side-effects, and has been shown to be synergistic with other types of anti-cancer therapies. Numerous in vitro and in vivo studies have revealed that HT effectively improves the efficacy of radiotherapy and chemotherapy against various types of cancers. Additionally, many clinical trials have shown that adding HT to radiotherapy or chemotherapy can yield a more complete response. However, HT is inevitably associated with heat-shock proteins (HSPs) that protect cells by limiting the effects of protein-damaging agents through protein chap¬eroning and refolding and by directly blocking cell death pathways. Among the HSPs, HSP70 is a stress-inducible HSP that has been reported to play a role in therapy-resistance. Importantly, increased expression of HSP70 in cancer cells has been reported to be associated with malignant features and poorer prognosis of cancer patients, suggesting that HSP70 is a promising target in cancer treatment.

Pifithrin (PFT)-μ (2-phenylethynesulfonamide) was initially identified as a small-molecule inhibitor of binding of p53 to mitochondria. Thereafter, this molecule was found to selectively interact with HSP70 and to inhibit its functions. This information led us to test the hypothesis that PFT-μ could enhance HT-induced antitumor effects against human prostate cancer. After confirming that HSP70 is constitutively expressed and/or enhanced by HT and plays a pro-survival role in human prostate cancer cell lines (LNCaP, PC-3, and DU-145), we revealed that the combination of suboptimal doses of PFT-μ can efficiently enhance HT-induced antitumor effects, i.e. cell death and growth arrest, against human prostate cancer in vitro, and that the combination therapy inhibited PC-3 tumor growth in a xenograft mouse model. These findings suggest that PFT-μ can effectively enhance HT-induced antitumor effects via inhibition of HSP70 functions, and that PFT-μ is a promising agent for use in combination with HT to treat prostate cancer.

S2-5 Symposium 2

Constitutively active stress-responsive signals and stress proteins are novel targets for cancer stem cell/cancer-initiating cell-targeted therapy.

Toshihiko Torigoe[1], Yoshihiko Hirohashi[1], Kazuyo Yasuda[1], Hiroki Kusumoto[1, 2], Satoshi Nishizawa[2], Hiroko Asanuma[1], Isao Hara[2], Noriyuki Sato[1]

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Cancer stem cell/cancer-initiating cells (CSC/CICs) are thought to be responsible for cancer recurrence and metastasis, since they have highly tumorigenic capacity and resistance to various stress stimuli, including chemotherapy and radiotherapy. However, molecular mechanisms for the stress-resistance of CSC/CICs have not been clarified very well. In this presentation, we show unique properties of CSC/CICs, especially constitutive expression and activation of stress-responsive genes, and their roles in the cancer-initiating capacity.

We isolated CSC/CICs from a variety of solid cancer cell lines such as ovarian and endometrial cancer lines by using Hoechst33342 staining assay, ALDH1 assay, and spheroid formation. Comparative gene expression analysis revealed that a number of stress-responsive genes were preferentially expressed in CSC/CICs, such as genes encoding heat shock proteins (HSPs), stress-activated protein kinases, and oxidoreductases. Remarkably, some of them were testis-specific stress-responsive genes that might be involved in the spermatogenesis. In addition, we found that master transcriptional factors for stress responses such as HSF-1 and Foxo3a were constitutively expressed and activated in CSC/CICs. siRNA-mediated knockdown of HSF-1 or Foxo3a could lead to decreased sphere-forming capacity of CSC/CICs, whereas stress stimuli could induce a transformation of non-CSCs to CSC/CICs, thus enhancing the tumorigenic capacity. Immunostaining of clinical tumor tissues revealed that phospho-HSF1 could be a marker for worse prognosis of ovarian cancer patients.

Our findings account for the molecular basis of stress-resistance and plasticity of CSC/CICs, and highlight the stress-responsive genes as novel molecular targets for CSC/CIC-targeted therapy.

Workshop 1-1

Hyperthermia: Up to Date in Asia
— Oncothermia —

September 6 (Sat.) 09:00 — 10:00
Room 1

Chairs

Takashi Kondo
University of Toyama, Japan

Taesig Jeng
Kosin University Gospel Hospital, Korea

WS1-1-1 Workshop 1-1

Modulated electro-hyperthermia applied as monotherapy for various cases having no other options

Taesig Jeung[1], Sun Young Ma[1], Ji Hoon Choi[1], Jae Sang Yu[1], Sangwook Lim[1], Oliver Szasz[2]

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Introduction: Cancer has limited curative possibilities in high-line treatments. Our objective study modulated electro-hyperthermia (mEHT) [2], as monotherapy, treating patients in advanced stages, when other possibilities was not applicable.Methods: This study reports 16 patients, treated by mEHT (EHY2000+ device).3 pancreas, 3 lung adenocarcinoma, 2 gastric, 2 colorectal and 1-1 synovial, bladder, hepatocellular, ovary, renal and cystic cases. mEHT was applied like chronic treatment numerous times (4-82 sessions) for a long time (months), 2-3 times a week. Sessions were 60 min. each12 sessions in one cycle. The average number of sessions was 33. In most of the cases both the primary and metastatic lesions were treated in independent sessions, or when the metastasis was near than covered both by the large electrode. Control of the cases was made by regular imaging and by the appropriate tumor-markers. Results: All patients had benefit from the treatments. Although complete remission was not achieved due to the advanced stages, but good partial remission was very common. Despite of the generally short expected survival in these cases, the long mEHT treatment processes were available, well improving the survival time compare to the historical expectations. Definite reducing of pain (improved quality of life) and no remarkable mEHT related side effect was observed, despite the definite dose escalation. In some cases skin erythema appeared, handled with appropriate cream. It did not terminate any further treatments. In some cases ascites made complications of the treatments, but could it be controlled by appropriate medication. Conclusion: mEHT was successfully applied as monotherapy in various far advanced cases. [1] Issels R, et.al, Lancet Oncology, 11:561-570, (2010) [2] Szasz A, et.al, Oncothermia-Principles and Practices, Springer, (2010)

WS1-1-2 Workshop 1-1

Modulated electro-hyperthermia therapy combined with gold-standard therapies for primary, recurrent and metastatic sarcomas

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Introduction: After surgery sarcoma has high incidence of local recurrence and distant metastases. It is mostly resistant on radiotherapy and shows only limited response to chemotherapy. Presently a study showed the efficacy of conventional hyperthermia for sarcoma cases [1]. Our objective study modulated electro-hyperthermia (mEHT) [2], combined with conventional therapies for various sarcomas.Methods: 13 sarcoma patients were treated by mEHT (EHY2000+ device). Patients aged between 18~73 years. Histologic type is 2 rhabdomyosarcoma, 2 synovial sarcoma, 2 chondrosarcoma, 1 osteosarcoma, 3 leiomyosarcoma, 1 malignant peripheral nerve sheath tumor, 1 spindle sell sarcoma and 1 malignant fibrous histiocytoma (MFH). Treatment modality was 5 postoperative radiation therapy (RT) and mEHT, 2 combined RT and mEHT for primary lesion, 2 combined RT and mEHT for recurrent sarcoma at original region and 4 combined RT and mEHT for metastatic lesion. mEHT was applied 2~3 times a week. Post-operative RT was applied 50.4 Gy in 28 fractions and other RT was applied 30~39 Gy in 10~13 fractions. Results: 5 patients who received post-operative RT and mEHT didn't show local recurrence. One MFH patient received RT 50.4 Gy and 27 times of mEHT and showed good partial remission (PR). Patient with peripheral nerve sheath tumor received RT 30 Gy and tumor mass regressed continuously by 108 sessions of mEHT. One recurrence rhabodomyosarcoma patient received RT 30 Gy and 12 times of mEHT in neck for 1 month with PR. The chondrosarcoma patient who had recurrence at pelvic bone replacement region after surgery, received RT 30 Gy and 50 times of mEHT with PR. 1 patient received RT 30 Gy in 2 weeks and 48 times of mEHT in metastatic lung lesion and showed good PR. Patient with chondrosarcoma had chest-wall metastasis received RT 30 Gy in 10 fractions and 47 times of mEHT showed partial regression. A patient had cervical spine metastasis and received RT 30 Gy and 5 times of mEHT. Patient with osteosarcoma had multiple lung metastasis received chemotherapy and 84 times of mEHT. Metastatic cancer almost disappeared but one lesion that was out of the range of electrode is progressed. Conclusion: Primary, recurrent, and metastatic sarcomas were well responded to mEHT treatment. Furthermore mEHT effectively controlled pain and reduced the side effects of the combined therapies.[1] Issels R, et.al, Lancet Oncology, 11:561-570, (2010) [2] Szasz A, et.al, Oncothermia-Principles and Practices, Springer, (2010)

WS1-1-3 Workshop 1-1

Can modulated electro-hyperthermia (mEHT) elicit immune reaction? - From basic and clinical research -

Yasunori Akutsu[1], Yutaka Tamura[2], Kentaro Murakami[1], Wei Qin[1], Xin Hu[1], Akiko Suganami[2], Hiroshi Suito[1], Hisahiro Matsubara[1]

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[Background] Previously, we investigated whether radiotherapy can elicit immunoreaction which, we think, is mediated by abscopal effect. On the other hand, modulated electro-hyperthermia (mEHT) was developed and it is still unknown whether mEHT can elicit immunoreaction or not. Therefore, we conducted a basic and clinical research.

[Methods] For basic research, we used intratumorally dendritic cells injection and mEHT to treat C3H/He mice inoculated with SCCVII cells in the left leg. Tumors were examined every two days in order to assess growth inhibition. The tumor-draining lymph nodes were removed to enable FACS analysis of CD4+, and CD8+ cells, whereas immunohistochemistry was used to assess CD8, S100, and Foxp3 expression in the tumors. For clinical research, we performed monotherapy with hyperthermia using EHY-2000 for esophageal squamous cancer and evaluated immunoreaction and survivals.

[Results] In basic research, the mean tumor volume was larger than that in other groups. A larger number of CD4+, and CD8+ cells were detected by FACS analysis in the DC plus mEHT treatment group. Tumor tissue immunostaining showed that CD8 and S100 were more strongly expressed in the DCs plus mEHT treatment group, although Foxp3 expression was much higher in the control group. We performed clinical treatment with EHY-2000 for 5 patients. All patients were in their stage of IV or failed standard therapies (surgery, chemotherapy and radiotherapy). There were no cases in that the target lesions shrunk but long SD was observed in some cases. The markers of immunoresponse (IFN-gamma, IL-12, TNF-alpha, TH1/2 balance, Treg, CTL) were measured and they were enhanced after the treatment of EHY-2000. 4 cases are still live in good quality of live and the estimated median survival time of all cases was 305.8 days (95% C.I., 213.7-397.8 days).

[Conclusion] mEHY is useful to prolong survival in good quality of life even in the terminal stage of cancers.

WS1-1-4 Workshop 1-1

Dialectics of hyperthermia and oncothermia: development through negation

Sergey Roussakow

Galenic Research Institute, Moscow, Russia

Electromagnetic therapy in terms of biological effect is initially 'a unity of opposites', namely of the specific, non-thermal effect of alternating electromagnetic fields and inevitable nonspecific heating, each having its own efficiency. First, 'the struggle of the opposites' led to negation of any role of non-thermal effects and absolutisation of the thermal component, resulted in the formation of so-called 'thermal dogma' in 30s. Temperature oncological hyperthermia based on the 'thermal dogma' failed in terms of implementation after 50 years of development. At the same time, theory and practice of non-thermal effects of alternating electromagnetic fields were developing. Oncothermia (modulated electro-hyperthermia) originated around 1996 from the negation of the central role of temperature in oncological electromagnetic therapy. This was a 'transformation of quantity into a quality', namely transformations of quantity of knowledge about non-thermal effects of alternating electromagnetic fields into a new quality of treatment. Thus, oncothermia is a natural dialectical development of oncological hyperthermia and qualitatively new electromagnetic treatment based on non-thermal effects and hyperthermic heating.

WS1-1-5 Workshop 1-1

Suppression of Human Cancer Cell Growth In Vitro by Oncothermia

Hee Bum Yang, Mi Young Shin, Yun Han Lee, Chang Geol Lee

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PURPOSE In the present study, we investigated the potential of oncothermia (electro-hyperthermia) for an alternative therapeutic option of pan-human cancer. MATERIALS AND METHODS To address this issue, we applied oncothermic heating (42 centigrade 1 hour, three times with a two- or three-day interval) to various human cancer cell lines such as A549 (lung cancer), HepG2 (liver cancer), MDA-MB231 (breast cancer) and A172 & U-87MG (brain cancer), and then examined for cancer cell phenotypic changes. Cell growth was analyzed by an MTT assay or microscopic observation in 3 days of the third oncothermic heating, and apoptosis was estimated in 24h of the third treatment by ELISA for the detection of denatured ssDNA only formed during apoptotic progression. In addition, the changes in apoptotic cell population was assessed by flow cytometry. The expression of heat shock protein 70 (HSP70), which is known for a typical marker of heat resistance, was determined by quantitative real-time PCR.RESULTS As results, oncothermia effectively inhibited the growth of A549, HepG2, MDA-MB231, A172 and U-87MG cells by about 45%, 70%, 47%, 44% and 75%, respectively, accompanying with remarkable morphological changes in cellular level. We also proved that inhibition of U-87MG cell growth was due to increased rate of apoptotic cell death which was about 2-fold higher than in unheated control cells. FACS analysis showed that oncothermic heating (three times with a three-day interval) to U-87MG and A172 glioma cells retards cell cycle progression and increases the apoptotic cell population by about 17% and 7%, respectively. Meanwhile, we observed that the treatment conditions of oncothermia still upregulatethe expression of HSP70 by about 84-fold higher in both U-87MG and A172 cells, in 24h of the third treatment. It may imply that multiple heating could overcome heat-resistance to drive therapeutic outcome in terms of cancer phenotypic changes. CONCLUSION Taken together, these results indicate that oncothermia maybe an attractive alternative for pan-cancer treatment. Further studies should be warranted to investigate the molecular mechanisms underlying the cancer phenotypic changes induced by oncothermia. KEY WORDS Oncothermia, lung cancer, liver cancer, breast cancer, brain cancer, growth inhibition, apoptosis, molecular mechanism

Workshop 1-2

Hyperthermia: Up to Date in Asia
— Clinical Case Reports and Biology —

September 6 (Sat.) 10:00 — 12:00
Room 1

Chairs

Hideyuki Sakurai
University of Tsukuba, Japan

Takayuki Asao
Gunma University, Japan

WS1-2-1 Workshop 1-2

Multidisciplinary treatment for border line unresectable pancreatic body cancer.

Makoto Murakami[2], Kanji Katayama[1], Mitsuhiro Morikawa[2], Kenji Koneri[2], Yasuo Hirono[2], Takanori Goi[2], Atsushi Iida[2], Akio Yamaguchi[2]

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[2]*1st Dept. of Surgery, University of Fukui, Japan*

The prognosis of the locally advanced pancreatic cancer is poor, because not only radical excision is difficult, but also early distant metastasis is frequently caused after resection. Also, insufficient resection will reduce the quality of life of the patients and may promote peritoneal dissemination and liver metastasis.
In the unresectable pancreatic cancer, the controls of such as a gastrointestinal passage disorder, cancer pain, and obstructive jaundice become important, too.
This time, we report treatment strategy and the results of our multidisciplinary treatment (MDT) for the locally advanced pancreatic body~head cancer .

Method:

Since 1988, we have performed multidisciplinary treatment (MDT) including an operation (Distal partial gastrectomy, Gstro and Choledocho –jejunostomy), intra-operative irradiation (IOR; 20-25Gy), RF-Hyperthermia (RF-HT), and chemotherapy for locally advanced cases.

RF-Hyperthermia (RF-HT) and chemotherapy:

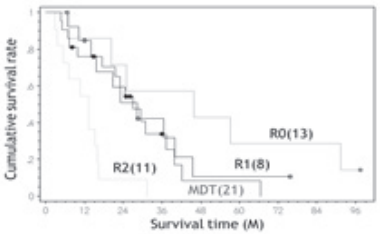
One week after the operation, we intravenously administrate 5FU continuously, and begin extra corporeal radiation on days 1 to 5.
On the 5th day, we do heat the tumor with use of Thermotoron RF-8 after radiation and simultaneously give CDDP and MMC.

Result:

21 cases received MDT and 32 cases received resection and adjuvant chemotherapy were compared.
There were patients of more advanced Stage in MDT group rather than resection group.
Resection method was PD; 6, DP; 23, and TP; 3, as result, R0; 13, R1; 8, and R2; 11.
Total exposure dose was 58.5Gy (range 30 to 71Gy) and the mean number of hyperthermia was 4.2 times.
We could achieve the tumor reduction in 64% of patients. And could relief pain of most patients complained. Tumor marker decreased in 79% and normalized in 41% of the patients.

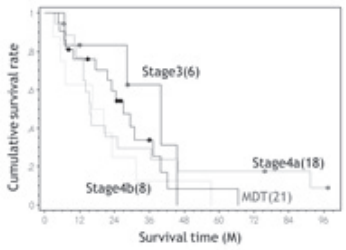
MDT (no resection) vs Resection according to resection(R) degree

	No.	MST(m)	3Y	P value
R0	13	45.9	57.1%	
R1	8	28.3	31.7%	
R2	11	13.4	0%	0.0018
MDT	21	27.1	33.9%	



MDT (no resection) vs Resection according to Stage

	No.	MST(m)	3Y	P value
Srage3	6	40.0	62.5%	
Stage4a	18	16.7	23.6%	0.9808
Stage4b	8	16.5	12.5%	0.2653
MDT	21	27.1	33.9%	



Conclusion:

Multidisciplinary treatment could control local disease and prolong survival of locally advanced pancreatic cancer.
In terms of clinical benefit, it may be no worth performing non-curative resection but carrying out our multidisciplinary treatment.

WS1-2-2 Workshop 1-2

Hyperthermia in locally advanced head & Neck Cancer – A retrospective analysis.

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Head and Neck cancer is the leading cancer in men in India. Hyperthermia with radiation has shown to be effective in a randomized trial. This is an analysis of 545 patients with head & Neck cancer treated with hyperthermia and radiation. A total of 320 patients received HT + RT while 195 received Chemo-radiation with Hyperthermia. Hyperthermia was delivered on modified Thermatron, operating at 8 - 2 MHz Seventy four percent showed complete response with an overall response of 98.3. The presentation will include in analysis of patients treated with various modalities with hyperthermia, radiation or Chemo-radiation. Both initial response and survival data for various sub groups will be discussed. Hyperthermia in addition to other modalities has shown to enhance response. It is an interim analysis.

WS1-2-3 Workshop 1-2

Long-Term Results of Second-Look Operation following Radio-Hyperthermo-Chemotherapy for Unplanned Excision of Soft Tissue Sarcoma

Katsuhiro Hayashi[1, 2], Satoshi Yamada[2], Hiroaki Kimura[1, 2], Hiroyuki Inatani[1, 2], Hideki Okamoto[2], Hiroyuki Tsuchiya[1], Takanobu Otsuka[2]

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Background: Soft tissue tumors of limbs can sometimes be resected relatively easily by general surgeons. However, in some cases, the tumor is determined to be malignant after surgery. Tumor cell contamination of the initial surgical field requires wider excision that can result in the sacrificing of neurovascular bundles and/or unexpected amputation. We have established a "second-look operation" protocol that consists of whole biopsy of surgical scar tissue following radio-hyperthermo-chemotherapy (RHC) after unplanned excision of soft tissue sarcoma and report the long-term results of second-look operation.

Method: A total of 30 patients underwent RHC for soft tissue sarcoma at our institution between 1995 and 2004. Of these 30 patients, 6 were enrolled into this study to undergo second-look operation for unplanned excision. Radiotherapy involved for a total dose of 32 Gy. Hyperthermia was conducted once a week, for a total of five sessions. Chemotherapy was performed at weekly intervals. Surgery was performed to excise the scar tissue that was enhanced on preoperative MRI. Resected specimens were examined postoperatively under a microscope. If any residual tumors were present in the specimen, wide excision was planned.

Results: In all 6 cases, no residual tumors were identified in resected scar tissue; thus, no additional wide excision was performed. No major complications occurred during preoperative RHC, except for mild pain and minor burns. Postoperative function was 100% by Enneking's score in all patients. The average follow-up period was 10.9 years. There were no local recurrences, and all patients were alive at final follow-up. Thus, RHC and second-look operation produced excellent clinical results.

Conclusion: Second-look operation following RHC were performed for unplanned excisions of soft tissue sarcoma. These patients have not experienced any recurrence or functional disturbance. Long-term follow-up confirmed that RHC can replace additional wide excision for unplanned excision of soft tissue sarcoma.

WS1-2-4 Workshop 1-2

Impact on histologic effect of Neo-thermo-chemoradiotherapy for rectal cancer.

Hisanori Shoji[1], Masahiko Motegi[1], Kiyotaka Osawa[1], Yousuke Takakusagi,[1] Atsushi Okazaki[1], Kyoji Ogoshi[1], Takeo Takahashi[2], Takayuki Asao[3], Hiroyuki Kuwano[3]

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Purpose: To provide hyperthermia treatment in rectal cancer patients for preventing colostomy based on new conception; treatment-standardization (similar quality of treatment of hyperthermia (Neo-thermia)), we investigated the relationship between Neo-thermia and histologic effect and treatment condition on rectal cancer by preoperative thermochemoradiotherapy (HCR).

Materials and Methods: Rectal cancer patients (n=52, 63-year-old average age (33-89 years, male : female = 40:12)) who underwent preoperative HCR and diagnostic imaging examination had been treated five times with 1 time/week with 50 min irradiation by Thermotron RF-8 in December 2011 to January 2014. Nineteen patients received operation and evaluated histological examination and 4 could not receive operation because progressive disease (PD). Chemoradiotherapy was consisted with IMRT five times weekly dosing 50Gy/25 times, capecitabine 1700mg/m^2/day, 2x/week 5 times. Thirty-one patients received Neo-thermia.

Results: Histological effect grade 3+clinical CR, grade 2 +1b + 1a+PR + MR + SD and PD were 18 (34.6%), 30 (57.7%), and 4 (7.7%), respectively. Average irradiation output Watts of patients with histological effect grade 3+clinical CR, grade 2 +1b + 1a+PR + MR + SD and PD were 775.2 Watt, 668.7 Watt, and 613.4 Watt, respectively.In the case of resection (n=30), histological effect grade 3, 2, 1b, and 1a were 8 (26.7%), 9 (30.0%), 7 (23.3%), and 6 (20.0%), respectively. Patients treated with chemo-radiation and receiving RF treatment same day, next day, or three days showed higher histological effect grade 3+clinical CR than two days later.

Conclusion: To evaluate the contribution of hyperthermia to cancer treatment, treatment-standardization is essential. We now try to fumble higher power output treatment without complication of RF eradiation.

WS1-2-5 Workshop 1-2

A phase III clinical trial: combination of radiotherapy and chemotherapy with vs. without hyperthermia for patients with advanced cervical cancer

Yoko Harima[1], Takayuki Ohguri[2], Hajime Imada[3], Hideyuki Sakurai[4], Tatsuya Ohno[5], Yoshiyuki Hiraki[6], Koh Tuji[7], Masahiro Tanaka[8], Hiromi Terashima[9]

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Cervical cancer is one of the most common gynecological cancers, both in high incidence and mortality worldwide. For many years, the standard treatment of locally advanced cervical carcinoma (LACC) had been radiotherapy (RT). However, locoregional failure rate of RT for LACC was 41-72%. Standard treatment of LACC at present is concurrent platinum-based chemoradiation, showing a 5-year survival of 66%. Meanwhile, since 1987, papers on six randomized trials for LACC comparing treatment outcomes of RT alone with RT and hyperthermia (RHT) have been published. Recently, Lutgens et al reviewed combined use of hyperthermia (HT) and RT for treating LACC in Cochrane Database Syst Rev. As a result, using complete tumor response at the end of treatment as endpoint yielded a significantly better treatment outcome following RHT than RT (RR 0.56; $p<0.001$). In addition, using overall survival as endpoint yielded a significantly better survival for RHT than RT (HR 0.67; $p = 0.05$). Using acute and late toxicity as endpoint showed no difference between both treatment groups ($p = 0.99$, $p = 0.98$). These results of international multicenter Phase I/II trials for LACC suggested that a combination of RT with both CT and HT treatments was feasible. From this viewpoint, to improve treatment outcomes in patients with LACC, a randomized multicenter Phase III trial comparing RT plus CT with combination of RT with both CT and HT started in Japan on 3rd September, 2001, and closed on 31th October, 2013. A total of 101 eligible patients were enrolled in this Phase III trial. The eligible criteria were: informed consent; previously untreated with radiotherapy, chemotherapy, or surgery; histologically confirmed invasive cancer of the uterine cervix FIGO stage IB larger than 4 cm, IIA, IIB, IIIA, IIIB, or IVA; para-aortic lymph-nodes negative; no double cancer; no pacemaker; chemotherapy possible; and hyperthermia possible. The number of patients was 50 in the RT plus CT group, and 51 in the RT with both CT and HT group. There were no difference between two groups in age, tumor size, FIGO stage, radiation dose, and chemotherapy dose. Hyperthermia was delivered via a radiofrequency capacitive heating device (Thermotron RF-8, Yamamoto Vinita Co.), which uses 8 MHz radiofrequency electromagnetic waves as a source of heat. We will analyze the result of this Phase III trial from 31th October 2014. In the future, we may be able to find out the exact role of hyperthermia for LACC.

WS1-2-6 Workshop 1-2

Gastric cancer surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) for scirrhous gastric cancer

Satoshi Murata, Tsuyoshi Yamaguchi, Hiroshi Yamamoto, Sachiko Kaida, Tomoharu Shimizu, Hisanori Shiomi, Shigeyuki Naka, Hiromichi Sonoda, Hiroyuki Ohta, Tohru Tani

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Background: Scirrhous gastric cancer (SGC) is biologically aggressive, and the prognosis is poor even with curative gastric surgery. Although recent advances in therapeutic strategies against GC, using effective anticancer drugs, have prolonged the survival of patients with advanced GC, therapeutic outcome of SGC is not enough to be satisfied. Here we show the improved outcome of SGC patients with gastric surgery and hyperthermic intraperitoneal chemotherapy (HIPEC), and introduce a new treatment protocol for SGC.

Patients and Methods: In the patients of SGC with pSS, pSE, or pSI tumor invasion, who were treated with gastric cancer surgery (gastrectomy with D2 lymph node dissection) and HIPEC (n = 23), overall survival (OS), recurrence pattern, and safety were evaluated comparing with those of patients with non-SGC (n = 67). SGC (n = 19) and non-SGC (n = 116) patients with gastric cancer surgery but without HIPEC were also analyzed as control groups. HIPEC was performed with open method using 5L of warm saline with 3 anticancer drugs: MMC, CDDP, and 5FU. This solution was strictly maintained at 42-43 degree Celsius in the peritoneal cavity and perfused for 30 minutes. All of patients underwent standard chemotherapies after surgery.

Results: In patients with R0 surgery without HIPEC (n = 110), 3-year and 5-year OS rate were 28.6%, 28.6% in SGC (n = 7), 50.8%, 36.3% in non-SGC (n = 103), respectively. In patients with R0 surgery and HIPEC (n = 57), 3-year and 5-year OS rate were 100%, 85.7% in SGC (n = 10), 94.9%, 88.3% in non-SGC (n = 47). In patients with CY1 or P1, who underwent gastrectomy without HIPEC, 1-year and 3-year OS rate were 33%, 0% in SGC (n = 12), 35.2%, 17.6% in non-SGC (n = 13), respectively. In patients with CY1 or P1, who underwent gastrectomy and HIPEC, 1-year and 3-year OS rate were 69.2%, 23.1% in SGC (n = 13), 80%, 40% in non-SGC (n = 20), respectively. Patients with gastric cancer surgery and HIPEC did not have severe complications, and were dramatically reduced peritoneal relapse.

Conclusion: Gastric cancer surgery with HIPEC greatly improves the prognosis of SGC patients with an acceptable morbidity.

WS1-2-7 Workshop 1-2

Usefulness of an operation under laparoscopy as neoadjuvant chemotherapy to appendix origin pseudomyxoma peritonei

Kousuke Noguchi[1], Masumi Ichinose[1], Nobuyuki Takao[1], Akiyosi Mizumoto[1],
Masamitsu Hirano,[1] Yutaka Yonemura[2]

[1]*Kusatsu general hospital, Japan,*

[2]*Nonprofit Organization to support Peritoneal Dissemination Treatment (NPO PDT), Japan*

It says that cytoreduction surgery including peritoneum resection and internal-organs resection is first needed for the medical treatment of the appendix origin pseudomyxoma peritonei. On the other hand, even if diagnosis of the appendix origin pseudomyxoma peritonei is difficult and diagnosis is obtained, it has trouble to a treatment policy in many cases. We have treated the hyperthermic intraperitoneal chemotherapy (HIPEC) and the appendectomy (total biopsy) as initial treatment for providing definitive diagnosis to appendix origin pseudomyxoma peritonei. By carrying out by an operation under laparoscopy with little invasion, it was regarded as the neoadjuvant therapy before radical surgery, and has included in the medical treatment strategy of pseudomyxoma peritonei. We reported 25 cases in which it was suspected for appendix origin pseudomyxoma peritonei.

WS1-2-8 Workshop 1-2

Clinical Study of Intraperitoneal Hyperthermic Perfusion Chemotherapy in Combination with Intravenous Chemotherapy for the Treatment of Advanced-Stage Gastric Carcinoma

Shenglin Ma, Zhibing Wu, Qinghua Deng, Saisai Jing, Yabo Gao, Zhishuang Zheng, Kan Wu, Juan Li, Rongjun Tang, Xiadong Li

Department of Radiation Oncology,Nanjing Medical University Affiliated Hangzhou Hospital (Hangzhou First People's Hospital),Hangzhou China

To observe and compare the preliminary efficacy and side effects of docetaxel, 5-fluorouracil and leucovorin intravenous chemotherapy in combination with cisplatin intraperitoneal hyperthermic perfusion chemotherapy for the treatment of advanced gastric cancer. Retrospectively analyzed 101 patients with advanced gastric cancer receiving docetaxel, 5-fluorouracil, leucovorin and cisplatin intravenous chemotherapy or intravenous administration of docetaxel, 5-fluorouracil and leucovorin combined with cisplatin intraperitoneal hyperthermic perfusion chemotherapy, 49 patients in intravenous chemotherapy (VC) group, 52 patients in hyperthermic intraperitoneal perfusion chemotherapy (HIPEC) group. The effective rate was 44.9% (22/49) in VC group and 65.4% (34/52) in HIPEC group, among which there was 1 case of CR, and the difference was statistically significant (p= 0.038); for CBR evaluation, the effective rate was 65.3% (32/49) in VC group and 82.7% (43/52) in HIPEC group, and the difference was statistically significant (p= 0.0458); the median progress free survival time (PFS) was 3.4 months in VC group and 4.6 months in HIPEC group, the difference was statistically significant (p= 0.045); the median overall survival time (OS) was 6.7 months in VC group and 7.5 months in HIPEC group, the difference was not statistically significant (p= 0.201); the main side effects in two groups were bone marrow suppression, gastrointestinal reactions, neurotoxicity and so on, and there was no statistically significant difference. The short-term efficacy and PFS of weekly administration regimen of docetaxel, 5-FU and leucovorin combined with cisplatin intraperitoneal hyperthermic perfusion chemotherapy in the treatment of advanced gastric cancer were better than single intravenous chemotherapy, and there was no significant improvement in OS, the side effects were similar in two groups with good tolerability.

WS1-2-9 Workshop 1-2

The immunologic hyperthermia to the advanced gastric cancer patient who refused the standard chemotherapy

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[2]Dept. of Cancer Immuno Regulation, Kyoto Pref. Univ. of Med., Japan,

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[4]Center for Cell and Gene Therapy, Takara Bio Inc., Japan

Background: Adoptive immunotherapy is one of expecting approaches against cancer. However, in an immunotherapy independent, the curative effect is restrictive. Recently it is reported hyperthermia cancels the immunologic escape mechanism of a cancer. Therefore hyperthermia is often used with immunotherapy. In this study, we report the case of gastric cancer patient with peritonitis carcinomatosa. A subject and a course: The male in his 60's of the advanced gastric cancer with peritonitis carcinomatosa received 1 course of S-1+CDDP. However, since the side effects were very severe, he refused further chemotherapy. Therefore he received adoptive immune cell therapy (naive T cell) combined with hyperthermia for eight months. As a result, the peritonitis carcinomatosa disappeared and the primary focus also disappeared endoscopically. He maintained good QOL. Although this case in which I succeeded extremely is rare so far, we have experienced several CR cases or cases, which are carrying out the long term survive. Conclusion: The naive T cell is a main transfusion cells, and the phase I study of naive T cell adoptive therapy showed also CR. I consider the usefulness of introducing this naive T cell. Moreover, I also consider usefulness of naive T cell adoptive therapy with hyperthermia.

WS1-2-10 Workshop 1-2

Heat-sensitization of human cancer cells by HR inhibitor B02 but not NHEJ inhibitor NU7026

Akihisa Takahashi[1], Hongyu Ma[2], Akiko Nakagawa[2], Mayumi Komachi[2], Mayu Isono[3], Yukari Yoshida[3], Atsuhisa Kajihara[4], Eiichiro Mori[5], Takeo Ohnishi[5]

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Background: Recent work has revealed that DNA double-strand breaks (DSBs) play an important role in heat-induced cell killing. The cell can respond to the presence of DSBs through two major repair pathways: Homologous recombination (HR) and non-homologous end-joining (NHEJ). This study examined the effect of the inhibitor of HR repair or NHEJ repair for DSBs on heat sensitivity.

Methods: We used the H1299 (*p53* deficient human non-small cell lung cancer) cells. Sixteen hours after seeding, cells were exposed to the inhibitor of HR-related Rad51 (B02, Calbiochem) or inhibitor of NHEJ-related DNA-PK (NU7026, Calbiochem) for 24 h. Cells were heat-treated at 44°C with a water bath (Thermominder EX, TAITEC Co., Ltd) at 6 h after exposure to inhibitor. The heat sensitivity was measured by colony forming assays.

Results: Heat sensitivity was not affected by NU7026. On the other hand, B02 was able to enhance heat sensitivity.

Conclusions: These results suggest that the heat sensitivity may be enhanced by the suppression of HR repair. In addition, these findings provide support for the concept that heat may lead to the induction of DSBs.

Workshop 2

Developement of the New Modality in Hyperthermic Cancer Therapy

September 5 (Fri.) 15:00 — 17:00
Room 1

Chairs

Kagayaki Kuroda
Tokai University, Japan

Tzyy-Leng Horng
Feng Chia University, Taiwan

WS2-1 Workshop 2

Combination therapy with low dose chemotherapy and regional hyperthermia for the treatment of progressive renal pelvis carcinoma

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Introduction Progressive renal pelvis carcinoma is difficult to be treated with surgery and radiation therapy. Therefore, systemic chemotherapy with cisplatin (M-VAC) is usually performed. However, side effects of chemotherapy are severe and these clinical effects are difficult to obtain a complete response. We conducted the combination therapy with low dose chemotherapy and regional hyperthermia for the treatment of three cases with progressive renal pelvis carcinomas. Methods and results Cisplatin 5mg/body or Gemcitabin 100mg/body was given intravenously before and after the regional hyperthermia respectively. Regional hyperthermia was performed to heat up the renal pelvis by using 8MHz- radio frequency (Yamamoto Vinitor Co. Japan) for 50 minutes. Through their treatments, tumor weight were decreased more than 50%, and survival duration were increased from 6 months to 5 years, and side effects were revealed minor general fatigue. Conclusion Combination therapy with low dose chemotherapy and regional hyperthermia is safe and obtained good clinical results and long survival.

WS2-2 Workshop 2

rAd-p53 Hepatic Arterial Infusion (HAI) with Thermo-chemotherapy for Unresectable Liver Carcinoma

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Objective To evaluate the efficacy and safety of recombinant adenovirus- p53 (rAdp53) with thermo-chemotherapy for unresectable liver carcinoma.

Basic study demonstrated that tumor suppressor gene p53 plays a key role in the cellular response to DNA damage induced by irradiation, or hyperthermia and that racombinant adenovirus p53 gene (rAd-p53) transfer results in suppression and reversal of the malignant phenotype and induces sensitization to hyperthermia and radiotherapy. The rAd-p53 (trademarked as Gendicine) is an E1 substituted replication-incompetent recombinant adenovirus encoding the human p53 gene.

Previous data indicate that rAd-p53 inhibits VEGF expression and angiogenesis, and promotes tumor necrosis and shrinkage induced by hyperthermia plus or not plus radiotherapy in advanced cancer. rAd-p53 acts as a thermosensitizer for hyperthewmia. The rAd-p53 upgrades hyperthermia to radical cure for patients with cancer.

High p53 mutation rate in hepatocarcinogenesis is related with cellular differentiation and tumor diameter and thermo- or radio-resistant phenotype. Hepatic arterial infusion (HAI) of rAd-p53 in this setting is an attractive approach.

Methods: rAd-p53 is administered through an implantable subcutaneous infusion pump connected to a surgically placed hepatic artery catheter, a dose of up to 2×1012 vp (viral particles) diluted in 100 ml of saline solution, once a week. Every week 2 days after the HAI of rAd-p53, Pirarubicin 20mg and 5-fluorouracil (5-FU) 1G is administered through an HAI pump, concurrently total liver were received hyperthermia using 41MHz radiofraqunce for 1 hour at 41-42°C. Completed above course is considered one cycle. Total 6-8 cycles were competed. More than 3cm lesion size of tumor concurrently were added by irradiation with 50-60Gy doses using three-dimensional conformal techniques.

6 patients with unresectable primary or metastatic liver cancer were enrolled into this clinical trial included 2 patients with hepatocellular carcinoma (HCC) and 4 patients with metastatic liver cancer.

Results. Among 6 cases, the treatment achieved CR in 2 cases (33.2%), PR in 2 cases (33.2%), SD in 1 case (16.6%), and PD in 1 case (16.6%) and with excellent tolerance (individualy case report as follow)

Conclusions: The trial demonstrated that enhancement efficacy of rAd-p53 HAI combined with thermo-chemotherapy with or without radiotherapy showed that obvious tumor necrosis and shrinkage in unresectable liver carcinoma.

WS2-3 Workshop 2

Spiruchoustatin-B, a novel histone deacytylase inhibitor enhanced apoptosis induced by hyperthermia

Mati Ur Rehman[1], Paras Jawaid[2], Qing Li Zhao[2], Koichi Narita[3], Tadashi Katoh[3], Tadamichi Shimizu[1], Takashi Kondo[2]

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Spiruchostatin B (SP-B), a potent histone deactylase inhibitor (HDAC) has been well reported for its HDAC inhibitory activity and the potential for chemotherapy of leukemia. In this study we investigate whether SP-B can enhance hyperthermia induced apoptosis in human leukemia cells *in vitro*. Cells were treated with SP-B at a non-toxic concentration, and then exposed to HT 44 °C for 20 min. Apoptosis was determined by nuclear morphological changes, DNA fragmentation assay, Annexin V-FITC/PI and cell cycle analysis. Detection of intracellular reactive oxygen species (ROS) and mitochondrial membrane potential (MMP) was performed by using flow cytometry. Caspase-8 activity was measured with a FLICE/caspase-8 colorimetric protease assay kit and absorbance was quantified using a spectrophotometer. Furthermore, western blot analysis was performed to determine the expression of caspase-3, and Bcl-2 family proteins. SP-B significantly enhanced the HT induced apoptosis as evidenced by nuclear morphological changes, DNA fragmentation and Annexin V-FITC/PI staining. Loss of mitochondria membrane potential (MMP), activation of caspase-3 were enhanced in the combined treatment. The pre-treatment with SP-B significantly enhanced apoptosis induced by hyperthermia.

WS2-4 Workshop 2

Enhancement of hyperthermia-induced cancer cell killing by withaferin A, -Implication for cancer therapy-

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[Background] Hyperthermia is a good therapeutic tool for non-invasive cancer therapy; however, its cytotoxic effects are not sufficient. In the present study, withaferin A (WA), a steroid lactone derived from the plant Withania somnifera Dunal, has been investigated for its possible enhancing effects on hyperthermia-induced apoptosis and its molecular mechanism.

[Methods] HeLa cells were treated at 44°C for 30 min with or without WA. Apoptosis was examined by DNA fragmentation, externalization of phosphatidylserin. Generation of intracellular reactive oxygen species (ROS) and depletion of GSH monitored by DCFH-DA staining and a Cell Meter Intracellular GSH Assay Kit, respectively. Mitochondrial trans-membrane potential (MMP) were monitored by flow cytometry. The changes in the expression of apoptosis associated proteins were examined by Western blot.

[Results] After combined treatment of 44°C 30 minutes with 1 μM WA for 24hr, HeLa cells were induced significant enhanced apoptosis accompanied with increases of intracellular ROS, reduction of intracellular glutathione and activation of caspase-3, while either of the two treatments alone could only induce minimum apoptosis. The fraction of the cells with decrease of MMP was dramatically increased by the combined treatment, accompanied by increase in pro-apoptotic Bcl-2 family protein Noxa and tBid, decrease in anti-apoptotic Bcl-2 protein Bcl-2 and Mcl-1. In addition, significant phosphorylation of JNK (p-JNK) and decreases in the phosphorylation of ERK (p-ERK) compared with either treatment alone were detected at 3hr and 24hr after the combined treatment, respectively. Phosphorylation of AKT was unchanged.

[Conclusion] In conclusion, WA enhances hyperthermia-induced apoptosis significantly via mitochondria-caspase dependent pathway. The underlying molecular mechanism involved in the elevation of intracellular ROS, mitochondria dysfunction, and dynamic changes in the increased activation of JNK and decreased activation of ERK1/2.

WS2-5 Workshop 2

Effect of Administering Bevacizumab Combined with Mild Temperature Hyperthermia in Neutron Capture Therapy on Local Tumor Control and Lung Metastasis

Shin-ichiro Masunaga, Yoshinori Sakurai, Hiroki Tanaka, Keizo Tano, Minoru Suzuki, Natsuko Kondo, Masaru Narabayashi, Tsubasa Watanabe, Akira Maruhashi, Koji Ono

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Purpose/Objective(s): To evaluate the effect of bevacizumab on local tumor response and lung metastatic potential in boron neutron capture therapy (BNCT), referring to the response of intratumor quiescent (Q) cells.

Materials/Methods: B16-BL6 melanoma tumor-bearing C57BL/6 mice were continuously given 5-bromo-2'-deoxyuridine (BrdU) to label all proliferating (P) tumor cells. The tumors received reactor thermal neutron beams following the administration of a ^{10}B-carrier (*L-para*-boronophenylalanine-^{10}B (BPA) or sodium merc aptoundecahydrododecaborate-^{10}B (BSH)), with or without the administration of bevacizumab, and further in combination with an acute hypoxia-releasing agent (nicotinamide) or mild temperature hyperthermia (MTH, 40 centigrade for 60 minutes). Immediately after the irradiation, cells from some tumors were isolated and incubated with a cytokinesis blocker. The responses of the Q and total (= P + Q) cell populations were assessed based on the frequency of micronuclei using immunofluorescence staining for BrdU. In other tumor-bearing mice, 17 days after irradiation, lung metastases were enumerated.

Results: Three days after bevacizumab administration, the sensitivity of the total tumor cell population after BPA-BNCT had increased more than after BSH-BNCT. The combination with MTH, but not with nicotinamide, further enhanced total tumor cell population. With or without a ^{10}B-carrier, MTH enhanced the sensitivity of the Q cell population. With or without irradiation, the administration of bevacizumab showed some potential to reduce the number of lung metastases to a similar level as nicotinamide, especially in BPA-BNCT compared with BSH-BNCT.

Conclusions: In BNCT, bevacizumab has the potential to sensitize total tumor cells and cause a decrease in the number of lung metastases to a similar level to nicotinamide. It was elucidated that control of the chronic hypoxia-rich Q cell population in the primary solid tumor has the potential to impact the control of local tumors as a whole and that control of the acute hypoxia-rich total tumor cell population in the primary solid tumor has the potential to impact the control of lung metastatic potential. Also in BNCT, administering bevacizumab combined with MTH was thought to be as useful as nicotinamide treatment combined with MTH from the viewpoint of both local tumor control and repressing distant lung metastasis.

WS2-6 Workshop 2

Magnetically-Engineered Superparamagnetic Nano-Theranostic Agents with Exceptially High AC Heat Induction and r2-Relaxivity

Bae Seongtae

Seoul National University, Korea

Accurate control as well as real-time monitoring of temperature evolution and the higher AC magnetic heat induction during hyperthermia are the critical challenges in current magnetic nanofluid hyperthermia for achieving highly efficacious thermal ablation tumor treatment modality. Accordingly, a great deal of research efforts to develop a new powerful magnetic nano-theranostic agent has been made for the past few years. However, despite various research activities, there has been no prominent reports on the development and the clinical trial of promising magnetic nano-theranostic agent, which can exhibit both high thermal induction capability and strong T2 contrast imaging, up to now.

In this work, we present our recently developed quarterly superparamagentic ferrite nano-theranostic agent with exceptionally high AC magnetic heat induction and ultra fast T2-weighted time (high r2-relaxivity). The developed superparamagnetic ferrite nanoparticle (SPN) was magnetically-engineered from conventional Ni1Zn1-xFe2O4 SPNs by chemically and thermally modifying a HTTD (High Temperature Thermal Decomposition) synthesis method. The magnetically-engineered Ni1Zn1-xFe2O4 SPNs (ENZSPNs) (x = 0.6 ~ 0.75) showed the magnetically softest properties (a larger Ms (Saturation magnetization) value, a higher exchange energy, a higher magnetic susceptibility, and a larger AC hysteresis loss) that result in significantly enhancing both AC magnetically-induced heating temperature (or specific loss power) and T2-weighted time for MRI contrast imaging. In addition, the PEG-coated ENZSPN colloidal suspension (nanofluids) prepared by our newly developed coating technique had higher biocompatibility and cell uptake with fetal midbrain human cells and U87MG glioblastoma cell lines. According to the physical and chemical analysis results, the significantly improved magnetic, structral, AC heating, and electrical properties of ENZSPNs were due to the chemcially-induced change of concentration and occupation ratio of Ni2+, Zn2+, and Fe2+ or 3+ cations in the tetrahedral A sites and octahedral B sites of NixZn1-xFe2O4. In addition, it was empirically and theoretically revealed that the significantly enhanced r2-relaxicity was due to the very thin coating layer thickness and the highly improved PDI (Poly Diversity Index) value of nanofluids, which are directly related to the longer spin-spin relaxation time and the enhanced water diffusivity (H+ ion accessibility) to the coating layer. The in-vitro/in-vivo imaging studies with a 3 T (Tesla) MRI and the magnetic nanofluid hyperthermia studies with U87MG cell lines and xenocrafted animal models along with our develped AC hyperthermia magnetic col system strongly demonstrated that ENZSPNs/ENZSPN nanofluids can be a powerful nano-theranostic agent in nanomedicine.

WS2-7 Workshop 2

Investigations towards the role of controllable therapeutic parameters for nanoparticle assisted thermal therapy for cancer

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Nanoparticle assisted thermal therapy is evolving as a promising thermal therapeutic for cancer. Such thermal therapeutic involves irradiation of a nanoparticle embedded tumour for thermal ablation of cancer. Here, the non-ionizing radiation interacts with the nanoparticles. The nanoparticles act as miniature sources of heat within a tumour and generate heat to kill the cancer cells. Bringing this modality to the bedside of a patient requires proper understanding as well as tuning of controllable therapeutic parameters. This will help in confining the thermal treatment specific to a tumour region as well as for treatment planning. Our work aims to optimize the therapeutic parameters to confine the thermal damage specific to tumour region.Experimental and numerical studies have been performed by our group in this direction. This presentation will discuss the role of controllable therapeutic parameters namely, (a) nanoparticle relevant - optical coefficients, dose and distribution, (b) thermal - tumour specific damage, healthy tissue sparing extents and blood flow, (c) irradiation - source type, intensity, shape, size and spectral characteristics. Above parameters significantly influence the thermal ablation temperature achieved within a tumour and surrounding healthy tissue. This will help in quantifying the spatial extents of healthy tissue sparing surrounding a tumour. The minimum dose of nanoparticles required for effective thermal damage is evaluated. The experiments involve agarose gel as a mimic of tissue to evaluate the heat generation. The experiments comprised of a low cost radiation source with suitable optical filters which can be a compact cost effective setup for future clinical use. The discussed developments will help in treatment planning, specific to a patient, for such therapy by tuning the controllable therapeutic parameters. Future challenges and directions will be discussed to implement this evolving therapy to clinical practice. Further work involves incorporation of Monte Carlo simulation to understand the distribution and absorption of radiation in a nanoparticle embedded tumour, especially for the case of non uniform distribution of nanoparticles. For clinical practice, real time temperature monitoring is necessary and MRI seems a promising method for this. Our work shows that through proper control of the therapeutic parameters, it is possible to confine the thermal treatment specific to a tumour and avoid damage to healthy tissue beyond 2 mm from the tumour boundary.

WS2-8 Workshop 2

Signal Processing for Noninvasive Temperature Imaging of Fat using Spin-Lattice relaxation time of Proton Magnetic Resonance

Shuhei Morita[1], Mie Kee Lam[2], Wilbert Bartels[2], Yutaka Imai[3], Kagayaki Kuroda[1]

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[Purpose] High intensity focused ultrasound (HIFU) therapy under MR guidance requires temperature distribution images around the target tissue. For tissues with high water content, resonance frequency shift of water proton signal is available. On the other hand, this approach is not applicable to a voxel containing only fat. For solving this issue, we have proposed a novel technique using multiple flip angle and multipoint Dixon methods to use spin lattice relaxation time (T_1) of methylene or terminal methyl proton for fat thermometry [1, 2]. In the present work, we have examined the usefulness of the prior information about the signal intensity and T_1's of the fatty acid proton components in reducing the complexity of the signal processing.

[Method] Proton spectra of bovine fat tissue were observed with a 11T MR spectrometer at various temperature points to obtain the ratios of signal intensities as well as T_1's between the different fat proton components. Temperature was raised from room temperature to 60 degrees Celsius and lowered to the room temperature again. The ratios of the signal intensities and relaxation times were determined by using simple linear regression. Then the resultant rations were used to estimate the T_1 values. The effect of using the prior knowledge was evaluated by using a 9-compoonent numerical phantom with signal to noise ratio (SNR) of 10 for the total signal.

[Result] The errors in estimating T_1's of H_2O, CH_2 and CH_3 using a 3-component model with the prior ration information were 1.2%, 1.2% and 0.9%, while those with 9-component model were 0.02%, 0.0% and 0.3%.

[Conclusion] The prior knowledge markedly reduced the T_1 estimation error. Between the 3- and 9-component models, the latter yielded better results. The error level of both models were sufficient for evaluating fat tissue temperature. The use of the prior knowledge seemed to be effective for fat temperature imaging.

[1]Kuroda K, Iwabuchi T, Obara M et al. Magn Reson Med Sci 2011;10(3):177-183.

[2]Kuroda K, Morita S, Lam MK et al. Thermal Medicine 2012;28(4):87-96.

WS2-9 Workshop 2

Numerical analysis of coupled effects of pulsatile blood flow and thermal relaxation time during thermal therapy

Tzyy-Leng Horng[1], Tzu-Ching Shih[2], Huang-Wen Huang[3], Kuen-Cheng Ju[4], Tzung-Chi Huang[2], Po-Yuan Chen[5], Yung-Jen Ho[2], Win-Li Lin[6]

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The main purpose of this study is to investigate the coupled effects of the pulsatile blood flow in thermally significant blood vessels and the thermal relaxation time in living tissues on temperature distributions during thermal treatments. Considering the fact that propagation speed of heat transfer in solid tissues is actually finite according to experiments, the traditional Pennes bioheat transfer equation (PBTE) was modified to a wave bioheat transfer equation (WBTE) that contains both wave transportation and diffusion competing with each other and characterized by the thermal relaxation time. The wave behavior will be more dominant when the relaxation time is large. WBTE together with a coupled energy transport equation for blood vessel flow was used to describe the temperature evolution of our current tumor-blood vessel system, and the equations were numerically solved by the highly accurate multi-block Chebyshev pseudospectral method. Numerical results showed that temperature evolution from WBTE was quite different from their counterparts from PBTE due to the dominant wave feature under large relaxation time. For example, larger relaxation time would preserve high temperature longer and this effect is even more pronounced when heating is fast. It further implies that heat is drained more slowly when relaxation time is large, and would make thermal lesion region cover the tumor tissue, the heating target, better. This phenomenon would therefore hint that the traditional PBTE simulations might under-estimate the thermal dose exerted on tumor. As to the pulsation frequency of blood flow from heart beat which was originally predicted to be important here, it turned out that the thermal behavior is quite insensitive to pulsation frequency in the current study.

WS2-10 Workshop 2

Effects of Effective Tissue Thermal Conductivity and Pulsatile Blood Flow in Large Vessels on Thermal Dose Distributions during Thermal Therapy

Tzu-Ching Shih

Department of Biomedical Imaging and Radiological Science, China Medical University, Taiwan

The purpose of this study is to investigate the effects of pulsatile blood flow in a thermally significant blood vessel, the effective thermal conductivity of blood perfused solid tissue, and the thermal relaxation time of solid tissue on thermal dose distributions during thermal therapies. Numerical results show that the total velocity profiles of pulsatile blood flow at different phases for diameters of 1, 1.4, and 2 mm, with the maximum velocities about 25, 32, and 60 mm/s, respectively. It is obvious that larger blood vessel has higher velocity. The maximum velocity of pulsatile blood flow was about three times of the average blood flow velocity. For pulsatile blood flow with diameter of 1 mm, the velocity of pulsatile blood flow increased as the phase increasing from 0 to $\pi/4$, decreased to a minimum value at phase of $3\pi/4$, and then continually increased until $9\pi/4$. For example, the maximum velocities of the oscillation part of total velocity for diameters of 1, 1.4, and 2 mm were approximately ±8, ±10, and ±18 mm/s, respectively. The oscillation amplitude of pulsatile flow in blood vessels became lager while the diameter was larger. Furthermore, for a 2-mm diameter blood vessel the velocity profile of the oscillation part of total velocity of pulsatile blood flow was displayed no more a parabolic form rather than nearly a two-peak shape at phases $\pi/12$ and $7\pi/12$. The Womersley number affects the total velocity and the oscillation component velocity profiles of pulsatile blood flow in blood vessels, especially when the blood vessel diameter is large. Besides, the frequency of pulsatile blood flow does not seem to affect the contours of thermal dose in the solid tumor tissue.

Lunchon Seminor 1

Clinical Practice and Studies on Oncothermia Therapy

September 5 (Fri.) 12:00 — 13:00
Room 1

Chairs

Andras Szasz
St. Istvan University, Hungary
Yasunori Akutsu
Chiba University, Japan

Lunchon Seminor 2

The Latest Therapy for Peritoneal Metastasis

September 6 (Sat.) 12:15 — 13:15
Room 1

Chair

Kanji Katayama
University of Fukui, Japan

LS1-1 Lunchon Seminor 1

Oncothermia in Clinical Practice

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Background: Oncothermia clinical applications have been started in the 1990s in Germany. It is a German medical method based on a Hungarian invention which reached the approval in the European Union in 1998, and is still rapidly spreading all over the world. Oncothermia is nowadays present in 30+ countries, and 100,000+ treatments are provided per year. Together with the 'classical' EHY2000 locoregional device, the intraluminal EHY1000 and the multilocal EHY3000 series are popular on the market. The marketed products are completed with devices for in-vitro and in-vivo laboratory research, as well as with numerous accessories helping the oncothermia applications in practice.

Oncotherm as company has 3 branches: in Germany, in Hungary and in the USA.

The R&D work and the production is based on a wide range outsourcing network, including 300+ contracted partners. The production of the flagship device (EHY2000) has presently been started in Toyama, Japan (Tateyama Machines Co .).

Method: Oncothermia is theoretically a well-based [1], [2], treatment modality, fortified by 7 patents. Numerous publications (400) and running clinical trials (25) show its forceful present in the oncological field. The number of research projects in various universities of the international oncothermia community is 23. The number of the finished clinical studies (mainly retrospective, Phase I and Phase II) is over 60, originated from 5 countries and involving more than 3,700 patients.

Discussion: Our aim is to show the clinical case-reports, the systemic studies and the solution of the medical challenges by oncothermia. Based on the actual research results, oncothermia goes further on the way of the non-artificial nanoheating technology (membrane rafts are selected, [3]) and using the very promising laboratory and preliminary clinical results Oncotherm points the tumor-vaccination by inducing immune effects with the method, [4].

Conclusion: Oncothermia is a feasible and reliable method in oncology, hoping it will step into the position of the fourth column of the oncological gold standards.

References

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[3] Szasz A. (2013) Electromagnetic effects in nanoscale range in book Cellular response to physical stress and therapeutic application, ed. Shimizu T, Kondo T, chapter 4, pp. 55-81, Nova Science Publisher

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LS2 Lunchon Seminor 2

The latest therapy for peritoneal metastasis

Yutaka Yonemura

NPO Organization to Support Peritoneal Surface Malignancy Treatment, Oosaka, Japan

Department of Regional Cancer Therapies, Peritoneal Metastasis Center, Kishiwada Tokusyukai Houspital, Kusatsu General Hospital, Shiga, Japan

In the past, peritoneal metastases (PM) were considered as a final stage of cancer, and patients were offered the best supportive care. Recently, a new therapeutic alternative approach based on the combination of surgery with chemotherapy was developed. In this curative intent, the macroscopic disease was treated with cytoreductive surgery (CRS) combined with periopertaive chemotherapy, including neoadjuvant chemotherapy, hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC), early postoperative intraperitoneal chemotherapy (EPIC) and extensive intraoperative peritoneal lavage (EIPL).

However, this comprehensive treatment might increase the risk of postoperative mortality and morbidity. After learning by well trained surgeons at the specialized centers, this treatment is justified a safe method with acceptable postoperative morbidity and mortality rates and a hopeful strategy to achieve a significant better survival as compared with the ordinary treatments. In addition, the treatment is performing in a curative intent for gastric, colorectal, appendiceal, ovarian cancer with PM, and diffuse malignant peritoneal mesothelioma.

This lecture includes a systematic overview of PM from various cancers and all the essential aspects as followings; 1. mechanism of the formation of PM, 2. quantitative estimation of PM, 3. evaluation of residual tumor after CRS, 4. multimodal treatment of PM, 5. value of laparoscopy, 6. prognostic factor, and 7.postoperative mortality and morbidity.

Poster / Short-Oral Presentation

September 6 (Sat.) 09:00 — 12:14
Room 2

GSE1 — GSE43
GSJ1 — GSJ6 (Japanese)

September 6 (Sat.) 13:30 — 15:26
Room 2

GSJ7 — GSJ35 (Japanese)

GSE1 Poster / Short -Oral Presentation

Mechanism of Hyperthermia in Magnetic Nanoparticles

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K. O'Grady, T. Ford

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Magnetic hyperthermia is currently used as a treatment for patients with Glioblastoma multiforme and is currently in phase I feasibility studies for prostrate and pancreatic carcinomas. This is achieved by injecting the tissue with magnetic nanoparticles of iron oxide and then subjecting the particles to an alternating magnetic field, which in turn causes the particles to generate heat. [1]. Until recently no definitive study of the mechanisms of heat generation in magnetic nanoparticles was available.

We report on a theoretical framework for magnetic hyperthermia where the amount of heat generated by nanoparticles can be understood when both the physical and hydrodynamic size distributions are known accurately.

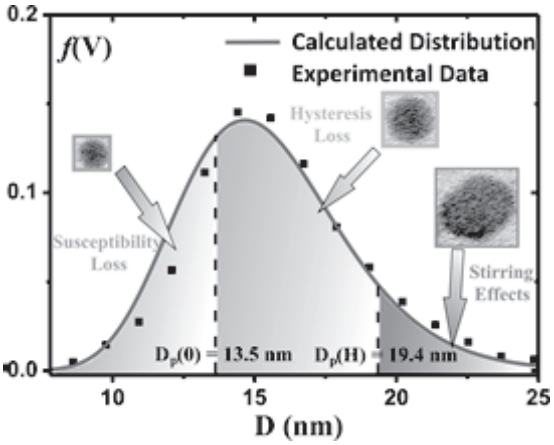

Figure 1 - The critical diameters ($D_p(0)$ = 13.5nm and $D_p(H)$ = 19.4nm) fitted to the particle size distribution for the 15.4nm CGP particles.

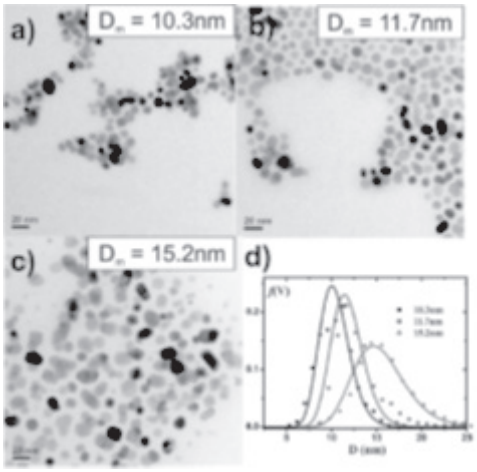

Figure 2 - TEM images for samples prepared by the Controlled Growth Process (a-c) and particle size distributions (d) for the samples used in this study.

We show that heating arising due to susceptibility losses can be neglected with hysteresis heating being the dominant mechanism. We show that it is crucial to measure the specific absorption rate of the samples only when embedded in a solid matrix to avoid heating by stirring (Figure 1). The particles that were used for this study were manufactured using the Controlled Growth Process (CGP) by Liquids Research which produces highly crystalline, monodisperse nanoparticles, TEM images and particle size distributions are shown in Figure 2.

References

1. Thiesen et al; *Int. J. Hyperthermia,* 2008, 24, 467

GSE2 Poster / Short -Oral Presentation

Development of combination therapy with cisplatin and hyperthermia generated with ferucarbotran (Resovist) in an alternating magnetic field for oral cancer

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Background: Radical surgery for patients with advanced oral cancer causes dysfunctions as well as decreases quality of life. To overcome this issue, we developed a new combination therapy of cisplatin and inductive hyperthermia using ferucarbotran (Resovist®). Ferucarbotran, which is made of superparamagnetic iron oxide, generates heat when exposed to an alternating magnetic fields (AMF). Herein, we explored whether ferucarbotran could be used as a heat source for hyperthermia upon exposure to AMF in the presence of cisplatin. Our aim is to evaluate the simultaneous therapeutic efficacy of chemotherapy and inductive hyperthermia for oral cancer.

Materials and Methods: OSC-19 and HSC-3, human oral cancer cell lines, were used in this study. Cell proliferation was assessed by methyl thiazolyl tetrazorium (MTT) assay. The intracellular level of reactive oxygen species (ROS) was measured using fluorescent dye 2', 7'-dichlorodihydrofluorescein diacetate. Apoptotic cells were stained with Annexin V, allophycocyanin conjugate and 7-amino-actinomycin D, and measured by fluorescence activated cell sorting (FACS), to evaluate early and late apoptosis. Thermal images and temperature were obtained by thermography and thermometer. AMFs were generated by a transistor-driven vertical coil at a frequency of 308 KHz and electric current (EC) 250 A.

Results: Cisplatin inhibited proliferation of OSC-19 and HSC-3 cells in a dose-dependent manner. Simply heating the medium to 42.5 degrees C enhanced the effect of cisplatin. Similarly, ROS production was increased in the presence of cisplatin, and was further increased upon heating. Heating to 42.5 degrees C was also achieved in cell culture medium to which ferucarbotran had been added and then exposing the medium to alternating magnetic fields. Ferucarbotran-induced heating, enhanced both early and late cellular apoptosis. Cell cycle analysis demonstrated that cisplatin decreased G0/G1, and increased G2/M accumulation. However, no further changes in cell cycle were induced when ferucarbotran-induced heating was observed.

Conclusion: Our findings suggest that combination therapy of cisplatin and ferucarbotran in an AMF may be used to develop a new combination therapy for oral cancer.

GSE3 Poster / Short -Oral Presentation

A Combination therapy with hyperthermia and IL-13 cytotoxin for human oral cancer cells

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Background: Hyperthermia is often utilized together with chemotherapy and radiation as the increase in blood flow in tumor tissue results in increasing treatment efficacy. Previous studies showed that interleukin-13 receptor α2 chain (IL-13Rα2), a unique tumor-associated antigen, is a promising target for cancer immunotherapy. IL13-PE, a targeted cytotox in composed of IL-13 and mutated Pseudomonas exotoxin, induces specific killing of IL-13Rα2 positive tumor cells. Our objective is whether hyperthermia treatment of oral squamous cell carcinoma (OSCC) can modulate the expression of IL-13Rα2 and increase their sensitivity to IL13-PE, especially in IL13-PE-resistant cells.

Methods: OSCC cell lines, HSC-3 and SCC-25 cells were heated with 43°C for 1 hour. Then, the expression levels of IL-13Rα2 and HSP70/HSP90 were analyzed by RT-PCR. Cytotoxic activity of IL13-PE was evaluated by protein synthesis inhibition assay. We also determined whether IL13-PE after hyperthermia causes apoptosis in OSCC cells by TUNEL assay in vitro.

Results: The proliferation of heat-stressed OSCC cells showed > 50% growth inhibition compared to control cells. IL-13Rα2 was up-regulated after heating of OSCC cells. Western blot analysis of heat-stressed HSC-3 cells revealed that HSP70/HSP90 expression increased in time-dependent manner. Protein synthesis inhibition assay with IL13-PE showed that heat-stressed OSCC cells decreased the number of IC50 compared to that of without heated OSCC cells. The percentages of apoptotic cells increased in HSC-3 and SCC-25 treated with IL13-PE after hyperthermia compared with controls.

Conclusion: These data suggest that hyperthermia of human OSCC sensitize to IL13-PE most likely by up-regulating the expression of cell-surface IL-13Rα2. Now we are studying to observe the efficacy of IL13-PE after hyperthermia in a mouse model.

GSE4 Poster / Short -Oral Presentation

Carcinostatic activities of L-ascorbic acid and its derivatives combined with a capacitive-resistive electric transfer (CRet) hyperthermic apparatus.

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Background: Although L-ascorbic acid (Asc) is an antioxidant that scavenges reactive oxygen species (ROS), in higher concentrations it also works as a pro-oxidant. Asc has been reported to be a potent antitumor agent, but very high doses were needed for acquiring its carcinostatic effects. To potentiate the activity, Asc-derivatives have been employed as previously reported by our team (Oncol Lett. 2012; 3(5):1042-1046). The purpose of the present study is to determine the anti-proliferative activity of diverse Asc derivatives in Ehrlich ascites tumor (EAT) cells by combined use of hyperthermia as compared to Asc.

Methods: 1) Asc/derivatives were administered to EAT cells for 1 hr, and hyperthermia with CRet System (Indiba Japan Co., Tokyo) was applied at 42ºC for initial 15 min. Then Asc or its derivatives was rinsed out. After further 24 hr incubation at 37ºC, cell proliferation was determined with WST-8 method.
2) We observed on the proliferation and apoptosis of EAT cells resulting from a combination of Asc and hyperthermia, using time-lapse imaging and caspase-3/7 Green assay.
3) Using catalase and the SOD-like compound Tempol, we investigated the relationship of ROS to the growth-inhibitory effects by Asc combined with hyperthermia.

Result: 1) The combination of Asc and hyperthermia decreased cell survival rate to 10.5-37.9%, while cytostatic effect was not observed until 0.1-2 mM when solely Asc was used. The combination of 6-O-palmitoyl- L- ascorbic acid (Asc6Palm) and hyperthermia decreased cell survival rates to 5.5 and 29.3% at 0.1 and 0.15 mM, respectively, while Asc6Palm dropped cell survival rates by 2.3% and 28% in 0.1 and 0.15 mM, respectively.
2) Asc-combined hyperthermia activated caspase-3/7 after 12 hr in comparison with controls. Cell growth of EAT cells was also seen to be stopped.
3) The cytostatic effects were reduced by 26.0%, 36.7%, and 39.6% depending onconcentrations of catalase at 100, 300, and 500 μg/mL, respectively, although not reduced by the SOD-like compound Tempol.

Conclusion: Asc combined with hyperthermia was shown to exert carcinostatic effects at concentrations lower than those of Asc alone. The catalase-induced carcinostasis-repression suggested that H_2O_2 appreciably contributes for Asc-combined hyperthermia. Both carcinostasis and caspase-3/7 activation by Asc-combined hyperthermis suggested that cell-cycle stagnation and apoptosis also contribute. Thus, Asc/hyperthermia combination is expected to produce carcinostatic benefits at lower concentrations than with the conventional higher-dose Asc therapy.

GSE5 Poster/Short -Oral Presentation1

Molecular mechanisms of hyperthermia-induced apoptosis enhanced by romidepsin (FK228)

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Romidepsin (FK228) is a potent histone deactylase inhibitor (HDAC) and has been known for its potent anti-cancer activity. This study was aimed to investigate whether FK228 enhances apoptosis induced by hyperthermia. For this purpose, cells were treated with FK228, and then exposed to HT 44°C for 20 min. Nuclear morphological changes, DNA fragmentation assay, Annexin V-FITC/PI and cell cycle analysis was used to determine the effects of combination treatment. Studying the apoptosis pathway involved in the enhancement we found that loss of mitochondrial membrane potential, activation of caspase-3 and caspase-8 was enhanced after the combined treatment. Taken together, our findings indicate that FK228 can enhance the hyperthermia induced apoptosis as evidenced by nuclear morphological changes, increased DNA fragmentation and Annexin V-FITC/PI staining.

GSE6 Poster / Short -Oral Presentation

Short-time Focused Ultrasound Hyperthermia Enhances Liposomal Doxorubicin Delivery and Anti-tumor Efficacy for Brain Metastasis of Breast Cancer

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The blood brain/tumor barrier (BBB/BTB) inhibits the uptake and accumulation of chemotherapeutic drugs. Hyperthermia is able to enhance the delivery of chemotherapeutic agent into tumors. In this study, we investigated the effects of short-time focused ultrasound (FUS) hyperthermia on the delivery and therapeutic efficacy of pegylated liposomal doxorubicin (PLD) for brain metastasis of breast cancer. Murine breast cancer 4T1-luc2 cells expressing firefly luciferase injected into female BALB/c mice striatum was used as a brain metastasis model. The mice were intravenously injected with PLD (5 mg/kg) and with/without 10 min transcranial FUS hyperthermia on Day-6 after tumor implantation. The amounts of doxorubicin accumulated in normal brain tissues and tumor tissues with/without FUS hyperthermia were measured using fluorometry. The responses of tumor growth for the control, hyperthermia, PLD, and PLD+hyperthermia groups were measured by IVIS system every other day from day 3 to day 11. Cell apoptosis and tumor characteristics were assessed using immunohistochemistry. The experimental results showed that short-time FUS hyperthermia was able to significantly enhance the PLD delivery into brain tumors. The tumor growth was effectively inhibited by a single treatment of PLD+Hyperthermia, as compared with both PLD alone and short-time FUS hyperthermia alone. The immunohistochemical examination further demonstrated the therapeutic efficacy of PLD plus short-time FUS hyperthermia for brain metastasis of breast cancer. The application of short-time FUS hyperthermia after nanodrug injection may be an effective approach to enhance nanodrug delivery and improve the treatment for brain metastases of tumors.

GSE7 Poster / Short -Oral Presentation

Heating properties of coaxial needle applicator made of SMA for brain tumor hyperthermia treatment with 3-D anatomical human head model

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As the human brain is protected by the skull, it is not easy to heat deep brain tumors non-invasively with electromagnetic energy. Several heating methods have been proposed to treat brain tumors. We have already developed a radio frequency (RF) interstitial hyperthermia system with a needle applicator and treated malignant brain tumors. This method results in a direct and local heating area around the needle. However, the RF electric current flows between the needle applicator and the discoid electrode. To overcome this problem, we proposed a coaxial needle applicator to avoid the undesirable RF electric current in the previous study. The coaxial needle applicator has no discoid electrode, because it contains two electrodes inside the needle.

In this study, to expand the heating area of the coaxial needle applicator, we developed a new coaxial needle applicator made of a shape memory alloy (SMA) which expands automatically when a tumor temperature rises. We estimated the temperature distributions inside an agar phantom using the finite element method (FEM) and heated the agar phantom with the developed coaxial needle applicator. Comparing computer simulation results and experimental heating results of agar phantoms, we discussed the basic heating properties of the coaxial needle applicator. Furthermore, we estimated temperature distributions inside the brain tumor using a 3-D anatomical human head model.

Here, first, the developed coaxial needle applicator made of a SMA was presented. Second, the results of the heating agar phantom obtained by computer simulations and the experimental heating results of the agar phantom with the developed coaxial needle applicator were presented. Third, the results of computer simulations using the 3-D anatomical human head model were presented. Finally, from these results, it was concluded that the developed coaxial needle applicator is useful for hyperthermia treatments.

GSE8 Poster / Short -Oral Presentation

Resonant cavity applicator with ultrasound monitoring system

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In this study, we discuss the effectiveness of an ultrasound monitoring system for a resonant cavity applicator to treat deep-seated brain tumors. We have confirmed the possibility of controlling heating area and location inside human head without contact. However, this applicator does not have the monitoring system to know the location and the size of the target. To overcome this problem, we proposed the monitoring system using a commercial diagnostic ultrasound imaging system and discussed the effectiveness of the developed resonant cavity applicator with the ultrasound monitoring system.

First, we reconstructed a three-dimensional human head model from two-dimensional medical images to know the location and the size of the target. The proposed reconstruction method consists of four steps. The first step is to collect two-dimensional medical images by using the diagnostic ultrasound imaging system. The second step is to trace the outline of the phantom on the ultrasound images. The third step is to collect and combine the outlines of the phantom. The last step is to create a solid model from the data in the third step. Next, we measured the location and the size of the target using the diagnostic ultrasound imaging system. Finally, we calculated temperature distributions inside the reconstructed human head model. In the computer simulations, we presented temperature distributions by changing the position of the human head model inside the resonant cavity applicator.

From these results, it was found that the developed resonant cavity applicator with the ultrasound monitoring system is useful for effective hyperthermia treatments.

GSE9 Poster / Short -Oral Presentation

Heating properties of resonant cavity applicator for treating osteoarthritis

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This paper describes the experimental results of new heating methods for treating osteoarthritis (OA) inside a knee using a resonant cavity applicator. OA is a common musculoskeletal disorder that causes pain, stiffness, swelling, and loss of function in a joint. A joint, where two bones meet, is surrounded by a capsule that protects and supports it. As the disease progresses, the inflamed synovium invades and damages the cartilage and bone of the joint. In clinics, there are several treatments for OA, for example, operation, thermal therapy, and chemotherapy. Physical methods, such as thermal therapy, with hot packs, paraffin baths, ultra-short waves, infrared lamps and microwave diathermy system are widely used for musculoskeletal disorders in the clinic. However, the skin penetration depth of these methods is less than approximately 20 mm. It is not easy to heat the affected part of the human knee. For an effective treatment of osteoarthritis, the deep seated joint cavity region in the human knee must be heated between approximately 36 and 38 °C.

In the previous study, a resonant cavity applicator for thermal therapy of OA was proposed. Experimental results of temperature distributions when using the resonant cavity applicator and using microwave diathermy systems were discussed.

In this study, a more useful resonant cavity applicator was developed for OA with a shield to reduce leaked electromagnetic fields around the applicator. From the results of computer simulation and experimental heating, it was found that the proposed heating method is useful for treating OA inside a knee.s

GSE10 Poster / Short -Oral Presentation

Does the success of hyperthermia depend on the heating-method?

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Background: Oncothermia has a quarter-century history [1]. It was started by typical invasive solution (ECT, electro-cancer-therapy) and tried also invasive interstitial technology; even systemic heating was also in the production range. However, the non-invasive loco-regional (EHY2000 series) and the multilocal (EHY3000 series) products, together with the intraluminar application (EHY1000 series) became popular among professionals. Why has Oncotherm tried so many forms of synergy of electric and thermal effects? Because it had historically the same frustration as hyperthermia had in general with the start of A. d'Arsonval through W. Coley or HI. Robins to H. LeVeen. My objective is to discuss the challenges and show the possible solutions of present status of oncological hyperthermia.

Method: Hyperthermia is traditionally an overheating of the tissue. Its definition has a huge variety in the medical literature. The varieties of the definitions are uniform in the 'higher as usual temperature', but is very much different in their localization ranging from the cellular level to the whole body (WBH). There are various concepts to heat-up the tumor with different approaches to follow the effects. The model systems and the clinical applications differ completely. The model systems are mostly treated by monotherapies while the medical practice uses complementary hyperthermia. The models try to investigate mainly molecular mechanisms of hyperthermia, while the clinical applications are connected to physiological reactions like drug-delivery or oxygenation.

Discussion: The difference between the medicine and poison is only the dose. In hyperthermia this is a real challenge. The dose has to be in strict correlation with the desired results, and has to be limited by safety issues; in local heating the surface blistering, while in WBH the 42C. However, the definition of the 'results' is complicated. In monotherapy the result could be the necrosis, (CEM-unit, in-vitro calibration). However, dose has to consider the physiologic factors and immune-stimulations. In modern hyperthermia applications the immune-effects have central role. This prefers 'mild temperature', because the upper limit of immune-activity is 39-40C. The immune effects are connected to electromagnetic effects, and their conjunction with complementary applications [2].

Conclusion: Effects of various heating methods are certainly different even at the same steady-state temperature. References[1] Szasz A, et al. (2010) Oncothermia: Principles and Practices, Springer, Heidelberg[2] Szasz A. (2013) Challenges and solutions in oncological hyperthermia, Thermal Med, 29(1):1-23

GSE11 Poster / Short -Oral Presentation

Thermal lesion deflection of blood vessel on the thermal lesion formation during radio-frequency ablation for liver tumors

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The major obstacles of Radiofrequency ablation (RFA) heat treatments are non-uniform heating in the thermal lesion and heat sinks caused by large blood vessels during treatments which could lead to high tumor recurrence in patients. The objective of this study is to help comprehending RFA heat treatment through thermal lesion formation using computer simulation, and thus to provide helpful assistance in planning RFA. RFA heat treatment is a popular minimally-invasive treatment method for both primary and metastatic liver tumors, and the heat treatment is studied by numerical calculation. A finite difference model is used to solve all partial differential equations (PDEs) for a simple three dimensional (3-D) cubic geometry model. Maximum tissue temperature is used as a critical index for reaching thermal lesion during RFA. Cylindrical RF cool-tip electrode is internally cooled at constant water temperature. RFA thermal lesion is studied at various impacts by single and counter-current blood vessel(s) traversing the thermal lesion. Several factors are considered, such as location, diameter and orientation of the blood vessel(s) to the electrode. Results show the thermal lesion size decreases as the lesion blood perfusion rate increases. And, single large blood vessel which is orthogonal to RF electrode will cause less under-cooled volume in the thermal lesion than one which is parallel to RF electrode. Furthermore, convective energy may easily damage parallel vessel and its surrounding normal tissues during RFA. Small blood vessels (or larger vessels with slow blood flow rate) during RFA could form Tail-like thermal lesion formation, which could damage vessel downstream spots.Studies suggested that, incomplete RF tumor ablation still exists within 1 cm distance between large blood vessel and RF electrode in a liver. This could have significant impact on local tumor recurrence rates. Secondly, if thermally significant vessel existed inevitably within the lesion, avoiding the RF cool-tip electrode placement next to the parallel large blood vessel would have a better heat treatment during RF heating. Additionally, reduced blood flow rate could help reducing significant cooling by large blood vessel.

GSE12 Poster / Short -Oral Presentation

A fast adaptive power scheme using Sentinel Convergence Value, based on temperature and convergence value for optimal hyperthermia treatment

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To elevate tissue temperature to therapeutic level (i.e. in the range of 41-45°C) fast with optimal power deposition during hyperthermia treatment planning (HTP) is a key treatment processing step. This can facilitate proper management of thermal dose distribution in the treated volume. Traditionally we have treated the tumor volume, without considering possible existing thermally significant vessels, using a simple 1st-order temperature-based adaptive power scheme to determine optimal power deposition distributions. The objectives of this study were to reveal the difficulty of that approach and propose a new fast scheme that could improve upon and substitute for the traditional temperature-based adaptive power scheme. In this study, we presented a new three-coefficient-and-two-SCV 5th-order temperature-based adaptive power scheme to resolve the induced large blood vessel problem in 3-D temperature distribution and introduced a new parameter, SCV (Sentinel Convergence Value), to handle interior scheme shift. Results showed the traditional power scheme was sufficient to apply during the optimization process, when the process to obtain optimal absorbed power deposition involves thermal diffusion (i.e. conduction) process only. However the addition of thermal convection by large blood vessel existing in the tumor volume indicated the cooling effect that was the cause for impediment of optimization. Secondly, the new improved scheme showed its robustness in reducing number of iterations. This paper addresses a procedure to speed up the optimization process using SCV as a scheme-shift, although the tumor volume consisted of only one thermally significant blood vessel. A new, improved three-coefficient-and-two-SCV 5th-order temperature-based adaptive power scheme has shown its robustness to fast-approach optimal temperature distribution or power density distribution with high precision in the tumor volume when considering the existence of thermally significant blood vessel. Optimally, we are able to effectively calculate the absorbed power density distribution of 3-D biological tissues with a complicating vasculature in the volume.

GSE13 Poster / Short -Oral Presentation

Pulsed RF Heating Using MRI

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Objective: MRI has a great potentiality not for diagnostic but also for heating. In this paper, RF heating using pulsed RF from MRI is applied for heating. Experimental verification has been performed to know the heating ability of MRI.

Methodology: Heating experiment has been performed using MRI with magnetic field of 0.3 Tesla. The heating target is prepared for artificial dielectric material and resonant type miniature circuit. The temperature elevation is measured by using MRI and optical fiber thermometer as well.

Result: The measured temperature elevation shows the possibility to apply MR scanner not for the diagnostic equipment to measure temperature but also for the treatment equipment to heat up the temperature inside body to realize such as hyperthermia to heat up the cell temperature.

Conclusions: The result shows the possibility to apply MRI not only as for the temperature measuring equipment but also as for the heating equipment in the application of pulsed RF power.

GSE14 Poster / Short -Oral Presentation

Microwave Focusing Using Metamaterials

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To focus and dissipate microwave energy efficiently, artificial dielectric material with magnetic material has been developed. Metamaterials are a new class of ordered composites using artificial dielectric and magnetic material that exhibit exceptional electromagnetic (EM) properties. In particular, artificial dielectric materials with both negative permittivity and permeability have attracted widespread interest in recent years. In this paper, microwave energy absorption in artificial dielectric material as well as metamaterial is studied. The specific phenomenon of metamaterial can be applied to special heating effects for hyperthremic heating.

GSE15 Poster / Short -Oral Presentation

Temperature Distributions with Blood Perfusion inside Artery and Vein during Hyperthermia Treatment

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In the previous study, a non-invasive heating method using a resonant cavity applicator for deep-seated brain tumors was proposed. We already confirmed the effectiveness of the developed heating system through heating agar phantom experiments and computer simulations with a 3-D human model. In computer simulations with the 3-D human model, it is not easy to express all blood vessels in a FEM model for calculating temperature distribution inside a human body. Therefore, mean blood flow rates through human tissues were used in FEM calculations. As a result, the accuracy of the calculated temperature distribution around a large blood vessel was not so high. In the present study, temperature distributions around the blood vessels during hyperthermia treatments through heating agar phantom experiments and computer simulations are discussed. In order to heat tumors around the blood vessel, discussions on the cooling effect of blood circulation of the arteries, veins and capillaries are needed. The purpose of this study is to demonstrate the cooling effect of blood perfusion inside the human body heated by the developed resonant cavity applicator. An agar phantom model with Teflon tubes assumed to be artery and vein for calculating the temperature distributions by the FEM is presented. Also, temperature distributions calculated by using the bio-heat transfer equation and the heat-flow equation with blood flow in the vessels are presented. The agar phantom is placed between the two inner electrodes and is heated by electromagnetic fields stimulated inside the cavity without contact between the agar phantom and the applicator. Comparisons of the temperature distributions between experiments and computer simulations are discussed. From these results, it was found that the cooling effects of blood perfusion appear within the heated area approximately 2 cm away from blood vessels.

GSE16 Poster / Short -Oral Presentation

MRI-Compatible Testing of Dual-Curvature High-Intensity Focused Ultrasound Phased Array Transducer

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A 256-channel dual-curvature focused ultrasound phased array transducer has been tested in this study. The array was constructed in-house with a 1-3 PZT4-epoxy composite structure with a aperture of 10 cm by 16 cm and two radii of curvature, i.e. 16 cm and 24 cm. Electro-acoustic conversion efficiency of the array was measured to be 65% approximately by a radiation force balance. In vitro experiments of phantom and pork demonstrated the array could move the focus from 14 cm to 20 cm in the depth direction and steer the focus from -3 cm to 3 cm in the azimuthal direction by tuning the phase of each element where the center of the array was the reference point. Ultrasonic ablations of pork by the array were performed in the MRI bore. The MRI system is 1.5T Siemens scanner. MRI displayed the formation and movement of an ultrasonic hot spot in the pork and its corresponding temperature in real time. MRI also illustrated the lesions induced by hot spots off line. The experimental results verified the compatibility of the array with MRI system.

GSE17 Poster / Short -Oral Presentation

Oncothermia treatment induced immunogenic cancer cell death - New possibilities for therapeutic cancer vaccine

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Introduction: Oncothermia method (OTM) is a long time applied tumor treatment modality in the human clinical practice. Experimental results showed that OTM can effectively and selectively destroy the tumor tissue, but recent investigations revealed some unusual immunological aspect of OTM. The immunogenic characteristics of immunogenic cell death (ICD) are mainly mediated by damage-associated molecular patterns (DAMPs) We summarize our results regarding the OTM induced ICD in Study I. Based on these observations we hypothetised a method for in vivo, in situ, personalized tumor vaccination. To prove this theory we designed an other study (Study II.) using immunocompetent animal model.

Materials and Methods: Study I. Animal model: HT29 cell line xenografted to both femoral regions of BalbC/nu/nu mice were treated on one side with a single shot OTM treatment for 30 minutes of ~1 cm diameter tumors. Sampling was made after 0, 1, 4, 8, 14, 24, 48, 72, 120, 168, 216 h in 3 mice each group by keeping 5 animals as sham treated controls. Histomorphological analysis (HMA) and immunhistochemistry (IHCH) and TUNEL assay were performed to analyze samples. Study II. C26 mouse colorectal adeno-carcinoma cell line allograft was applied to both femoral region of BalbC mice. One of the lesions (right leg) were treated with a single shot mEHT treatment for 30 minutes, the other (left leg) was kept for individual control of every animal. The groups formed for parallel study were: (1) Sham control; (2) injected with 7.5 ml/kg Marsdenia tenacissima, intraperitoneal; (3) mEHT treated; (4), combined mEHT and Marsdenia tenacissima injection 30 min before mEHT. Various histomorphologic and immunhistochemical analysis, TUNEL assay were tested in treated and control tissue samples.

Results: Study I. Oncothermia treatment can induce programmed cell death (apoptosis) in the tumors. Tunel assay proved the apoptotic cell death. OTM treatment induced cell death is higly immunogenic, showing many aspects of the key molecular pattern dynamic changes what is characteristic of ICD. OTM treatment can induce strong and very unusual local immune reaction at the site of the treatment. Study II. OTM treatment, induced an apoptotic tumor death. The Marsdenia tenacissima injection was not effective alone, however the combined therapy was effective far from the OTM localization.

Conclusions: These experimental findings can be the strong scientific theoretical basis to develop a special oncothermia treatment-based immunotherapeutical approach to fight against not just solitaire tumors, but malignant metastatic disease.

GSE18 Poster / Short -Oral Presentation

In what kind of advanced or recurrent cancer do immunotherapy and/or hyperthermia show effect ?

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[patients and methods] We treated 2,011 patients with advanced or recurrent cancer using hyperthermia or immunotherapy between July 2005 and November 2013. Hyperthermia (HT) was applied in 1,896 patients, activated lymphocytes therapy (CAT) in 1,157 patients, and dendritic cell therapy (DC) in 1,190 patients. We treated 260 colorectal cancer patients, 254 gastric cancer patients, 242 lung cancer patients, 231 pancreatic cancer patients, 198 breast cancer patients and others.

[results] The response to therapy was evaluated in 1,939 patients. In these patients, standard therapy showed no results or it was refused. Clinical benefit case (CR, PR and SD more than 6 months) was observed in 293 (15.1%) cases, including 51 CR. The response to immunotherapy increased from 9.9% to 18.9% when it was combined with hyperthermia, and the response was the highest in patients who received the combination of CAT+DC+hyperthermia (20.6%). According to the kind of cancer, clinical benefit rates of ovarian cancer was the highest at 25.0%, and prostatic cancer at 22.6%, and head and neck cancer at 20.0%, and lung cancer at 18.6%. According to the recurrent sites, hyperthermia only was effective to skin metastases and regional lymphocytea metastases. And immunotherapy only was effective to liver and lung metastases. Combined therapy of hyperthermia and immunotherapy was most effective to metastases in multiple solid organs.

GSE19 Poster / Short -Oral Presentation

The Systemic Efficacy of Combined Immunotherapy with Oncothermia and Intratumoral Injection of Dendritic Cells

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Purpose: Oncothermia is a significant and definite technical development in the hyperthermia field, using capacitive (impedance) coupling of 13.56MHz amplitude-modulated radiofrequency energy on the tumor site. As a result, turning local apoptosis effect into a systemic anti-tumor immune response is possible. Oncothermia method is capable of turning tumor microenvironment into an immunological more favorable environment. In this study, our aim was to enhance the therapeutic effect of dendritic cells (DCs) immunotherapy after Oncothermia treatment.

Materials & Methods: CT26 murine colorectal cancer model was used in this study. Mice were injected subcutaneously with CT26 cells into the right leg and left flank, respectively. DCs were matured by CT26 specific tumor antigen, AH1. When both tumors were palpable mice were randomly assigned to 4 groups receiving no treatment, DCs alone, Oncothermia in combination with or without DCs. Growth inhibition of the tumor and the systemic anti-tumor immune response were measured. Oncothermia treatment was carried out by an Oncotherm-Labehy device, with an in vivo mouse applicator system, capacitively coupled the 13.56MHz amplitude-modulated RF current to the tumors. During the oncothermia treatment the treated tumor core temperature reached 42°C measured by an intratumoral temperature measurement probe.

Results: Intratumoral injection of DCs after Oncothermia treatment resulted in significant inhibition of CT26 tumor growth in compare to DCs alone or Oncothermia treatment alone. Moreover, an abscopal effect, defined as the inhibition of tumor growth at a distance from the treated site occurred in mice treated with the combination of Oncothermia treatment and intratumoral injected DC. In immune response assay, Oncothermia treatment combined with intratumoral DC injection induced tumor-specific T cell activity (IFN-gamma ELISPOTS) and cytotoxicity T lymphocyte activity (CTL assay).

Conclusion: In this study, we demonstrated that intratumoral injection of DCs after Oncothermia treatment is an attractive and effective immunotherapy protocol.

GSE20 Poster / Short -Oral Presentation

Challenges and perspectives of hyperthermia in oncology

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Background: Hyperthermia could not find its established place among the 'gold standards' of the oncotherapies until now. We have to understand better the basic effects induced thermally and/or non-thermally.

Challenges: Dosing of hyperthermia is completely different from other therapies. In case of hyperthermia the dose connected to tumor-temperature which is indefinite, spread by blood and surrounding tissues. There are numerous electromagnetic hyperthermia methods distinguished by the kind of the fields, frequencies, heated volume, and conjunction with other methods, etc. The technical challenge of the deep-heating and the surface overheating is serious, and by the surface heat-sink blocks applying energy as dose parameter. Current therapies target the cell/DNA replication, the angiogenesis, the invasion process metastazing, so the recognized processes in the actual tumor-development. The new trend targets the evolution of the disease, targets the control of the processes instead of blocking one or two of its components. Like it is formulated by B. West (US Army Research) [1]: 'Disease is not loss of regularity, but the loss of complexity'.

Solution: Hyperthermia must go on the immune-direction, too. A couple of years ago Oncotherm patented a pioneering knowledge about the tumor-vaccination which completes the molecular biology knowledge and the integrative medicine approach based on immuno-stimulation effects.

There is a new method emerging: oncothermia. The careful, patented control of physiology of the skin at the treated volume makes it possible to pump the highest available energy through the epidermis without toxicity. This makes it possible to use the precisely matched and measured energy as control parameter. The new technology focuses the energy selectively to nano-range of the membrane of malignant cells [2]. The main medical advantages of the method together with the effective selection and distortion of the malignant cells are the blocking of their dissemination as well as promoting the bystander (abscopal) effect acting on far distant metastases by immune stimulation induced by oncothermia local treatment. Numerous clinically proven results are published.

Conclusion: Oncothermia applies synergy of the bioelectromagnetism with the fractal physiology. It is a vivid way solving the old-problems in hyperthermic oncology: it is a controlled, reproducible and reliable treatment. Oncothermia treatment induces massive cell death leading to immunogenic cell-death which is the basis of patented tumor-vaccination.References:[1] West B.J. (2007) Where medicine went wrong: Rediscovering the path to complexity, World Scientific[2] Szasz O, Szasz A. (2014) Oncothermia - Nano-heating paradigm, J. Cancer Sci. Ther. 6:117-121

GSE21 Poster / Short -Oral Presentation

Effect of local hypothermia combined with highly active anti-retroviral therapy on the immunologic function of patients with AIDS

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Since $CD4^+$ T cells play pivotal roles in maintaining the cellular immunity and humoral immunity, the decrease of their population and compromise of their function is the main cause of human immunodeficiency. Hyperthermia has been combined with radiotherapy and chemotherapy to treat cancer by not only augmenting combined therapies, but also boosting the immunity in patients. We reason that hyperthermia may also be used to treat acquired immunodeficiency syndrome (AIDS) patients by improving immunity. The main goal of this study is to evaluate the effect of local hyperthermia combined with highly active anti-retroviral therapy (HAART) on the immunologic function of patients with AIDS. We selected 16 AIDS patients, and treated them with either HAART alone (8 patients) or combined with local hyperthermia on thymus (8 patients). In the HAART group, patients underwent anti-retroviral therapy for three months. Patients in combination group were treated by microwave hyperthermia at 40.5-41.5 degree Celsius for 40 minutes after the HAART, twice per week for three months. Venous blood was obtained before the first treatment and after the last treatment. Lymphocyte transformation index was examined by 3H-TdR method, and $CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$T cells were assayed by flow cytometry. We found that the lymphocyte transformation index after combination treatment was significantly increased. The numbers of $CD3^+$, $CD4^+$ T cells and $CD4^+/CD8^+$ after treatment in both groups were higher than those before treatment, and the combination group after treatment has higher $CD3^+$, $CD4^+$ T cell numbers and $CD4^+/CD8^+$ than HAART alone group after treatment. On the other hand, the $CD8^+$ T cells number after treatment was lower than that before treatment, but there was no statistically significant difference. Our study provided evidence that local hyperthermia combined with HAART can improve AIDS patients T lymphocyte immunologic function, which may help the treatment of AIDS.

GSE22 Poster / Short -Oral Presentation

Enhancement of heat sensitivity by depression of homologous recombination repair

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Background: We have reported that heat as well as ionizing radiation induces DNA double-strand breaks (DSBs). Mammalian cells are well known to possess main two pathways for DSBs, namely homologous recombination (HR) and non-homologous end joining (NHEJ). We investigated the possibility that the inhibition of HR repair or NHEJ repair enhances the heat sensitivity in cancer cells.

Methods: To analyze heat sensitivity at 44°C by colony-forming assay in mammalian cultured system, we used non-cancer cells of Chinese hamster (CH) lung fibroblast cell lines and human tongue squamous cell carcinoma SAS cells with different capacities in DNA repair.

Results: There was no difference in the heat sensitivities of *Ku80* defective cells and the parental cells in CH cells. However, *BRCA2*-mutated CH cells were sensitive to heat as compared with the parental wild-type cells. In SAS cells, *BRCA2*-siRNA transfected cells were more sensitive to heat than the negative control-siRNA transfected cells. By Hoechst33342-staining analysis, apoptotic bodies were increased more efficiently in the *BRCA2*-siRNA transfected cells than the negative control-siRNA transfected cells at 48 h after heat treatment at 44°C for 20 min. In CH cells, a G2/M phase arrest was observed in the parental cells, but not in *BRCA2*-mutated cells at 12 h after heat treatment. We measured DSB-recognizing γH2AX positive foci by flow cytometry. DSBs were decreased to 85.2% at 18 h in the parental cells as compared with them at 0.5 h after heat treatment. In contrast, the amounts of DSBs were not decreased at all in the *BRCA2*-mutated CH cells. In immunocytochemical staining for Rad51 following heat treatment, the foci were detected at maximum about at 4 h in the parental cells.

Conclusion: These results suggest that heat induces DSBs and they are repaired by HR but not NHEJ.

GSE23 Poster / Short -Oral Presentation

Hyperthermia enhances the therapeutic efficacy of cetuximab in human oral squamous cell carcinoma

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Background: The epidermal growth factor receptor (EGFR) signaling pathway is commonly activated in head and neck squamous cell carcinoma (HNSCC) and represents a validated target for therapy. Cetuximab, an antibody directed against the EGFR, is an effective clinical therapy for patients with HNSCC. Despite great clinical promise, however, only 13% of patients respond to cetuximab when used as a single agent. Hyperthermia is often utilized together with chemotherapy and radiation as the increase in blood flow in tumor tissue results in increasing treatment efficacy. Our objective is whether hyperthermia treatment of oral squamous cell carcinoma (OSCC) can modulate the expression and activation of EGFR and increase their sensitivity to cetuximab, especially in cetuximab-resistant cells.

Methods: OSCC cell lines, OSC-19 and HSC-3 cells were heated with 43°C for 1 hour. The proliferation of heated OSCC cells was observed by MTT assay. Then, the expression levels of total EGFR and phosphorylation of EGFR were analyzed by western blot. Cytotoxic activity of cetuximab was evaluated by protein synthesis inhibition assay.

Results: The proliferation of heat-stressed OSCC cells showed growth inhibition compared to control cells. The expression level of total EGFR was gradually increased and phosphorylation of EGFR was up-regulated after heating of OSC-19 cells. Protein synthesis inhibition assay with cetuximab showed that heat-stressed OSCC cells decreased the number of IC50 compared to that of without heated OSCC cells.

Conclusion: These data suggest that hyperthermia of human OSCC sensitize to cetuximab most likely by up-regulating the expression and activating of EGFR. Now we are studying to understand the biological mechanisms which are directly involved in OSCC cells to hyperthermia. Such understanding is more useful to enhance the efficacy of therapeutic regimens of cetuximab involving hyperthermia.

GSE24 Poster / Short -Oral Presentation

Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy: a case report.

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Generally, peritoneal dissemination of gastrointestinal cancer has a poor prognosis, and most patients with advanced stages have undergone palliative procedures or had no surgical resection. To resolve the problem, the package combining complete cytoreductive surgery (CRS) plus hyperthermic intraoperative peritoneal chemotherapy (HIPEC) could be done safely, leading to improvement of prognosis in Western countries and few institutions in Japan. We describe our first case of a 46-year-old man who underwent CRS plus HIPEC for peritoneal dissemination from rectal cancer. The patient underwent neoadjuvant chemoradiotherapy followed by abdominoperineal resection for locally advanced rectal cancer. Although he received CapeOX as an adjuvant chemotherapy, 6 months after the first operation, pelvic dissemination was detected by CT. Standard chemotherapy including FOLFIRI with or without bevacizumab, cetuximab, and panitumumab. However, all of the systemic chemotherapy had no effects, and follow-up CT revealed progressive disease. Therefore, CRS plus HIPEC were indicated. After cytoreductive surgery for pelvic pelvic dissemination, the peritoneal cavity was lavaged with more than 10,000 ml of saline. Then, HIPEC was performed with cisplatin, mitomycin C and etoposide as chemotherapeutic agents. Operative time was 472min (HIPEC – 50min), and blood loss was 1272g. He underwent intensive care management for 3 days after CRS plus HIPEC. On POD2, he had grade1 renal dysfunction and grade1 liver dysfunction, but had been improved. By doing carefully, we have successfully introduced CRS and HIPEC. In the future, we go through the accumulation of cases, and hope that it would be indispensable tools in our oncological strategy.

GSE25 Poster / Short -Oral Presentation

Definitive radiotherapy plus regional hyperthermia for high-risk and very high-risk prostate carcinoma: Thermal parameters correlated with biochemical relapse-free survival

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Purpose: Previous phase I/II clinical trials have confirmed that radiotherapy (RT) in combination with regional hyperthermia (HT) is promising and feasible without severe toxicity in patients with prostate cancer. We added deep regional HT to RT in order to enhance the effects of RT in patients with high-risk or very high-risk prostate cancer, and hypothesized the positive relationships between the clinical outcomes and thermal parameters. The purpose of this study was to assess the efficacy of definitive RT plus regional HT and investigate the potential contribution of HT to clinical outcomes in patients with prostate carcinoma.

Methods and Materials: According to our institution's treatment protocol, regional HT was combined with definitive RT to improve the clinical outcomes in selected patients with high-risk or very high-risk prostate cancer. Eighty-two patients treated with RT plus HT and 64 patients treated with RT alone were retrospectively analyzed. For HT, the median number of heating sessions was five. All patients also received androgen deprivation therapy prior to RT. Efficacy and prognostic factors, including thermal parameters, for biochemical disease-free survival (bDFS) were analyzed.

Results: The median follow-up duration was 61 months. The 5-year bDFS rate in 82 patients treated with RT plus HT was 78%, while that in 64 patients treated with RT alone was 72%; however, the differences were not significant. Among 75 patients treated with RT plus HT with intra-rectal temperature measurements, a T stage of T1-2, membership in the high-risk group and higher thermal parameters (%T>=41.5 degrees, Tave, Tmin and Tmax) were significant prognostic factors for bDFS in the univariate analyses. According to the multivariate analyses, a higher thermal parameter of %T>=41.5 degrees and T stage of T1-2 were significant prognostic factors. The 5-year bDFS rates for the 31 patients with a higher %T>=41.5 degrees and 64 patients treated with RT alone were significantly different (p=0.003), whereas those for the 44 patients with a lower %T>=41.5 degrees and 64 patients treated with RT alone were not.

Conclusions: The addition of regional HT with higher thermal parameters to definitive RT may improve the bDFS in patients with high-risk or very high-risk prostate cancer. The importance of selection of treatable patients with higher thermal parameters is also indicated.

GSE26 Poster / Short -Oral Presentation

Peritoneal perfusion of rAd-p53 combined with thermo-chemotherapy for peritoneal carcinomatosis model of advanced cancer (a report of forty-one cases)

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Objective: To evaluate the safety and efficacy of peritoneal perfusion of rAd-p53 combined with thermo-chemotherapy for peritoneal carcinomatosis model of advanced cancer.

Patient and Methods: Between November 2002 and July 2011, a total of 41 patients with peritoneal carcinomatosis of advanced cancer were enrolled in the study. All the patients were received intraperitoneal perfusion of rAd-p53 (Gendicine) at a dose of 1 × 1012 virus particles, diluted in 1500 ml normal saline, through intraperitoneal catheter, once a week for 8 weeks. 48 hours later, cisplatin (DDP) 40~50 mg and 5-FU500~1000 mg, diluted in 1500 ml normal saline, was intraperitoneally infused before hyperthermia at 41~42°C using a 41MHz radiofrequency machine for abdominal cavity heating for 1 hour

Results: Of 41 patients, CR 3 case, PR 20 cases, SD 14 cases, PD 4 cases. Response (including CR, PR) rate was 56.1%, Clinical benefit (including CR, PR, SD) rate was 75.6%. 5 cases received operation later, and the tumor were completely removed. One year overall survival rate (OS) was 72.5%, two year OS was 42.5%, three yeas OS was 16.2%.

Conclusion: Peritoneal carcinomatosis model of advanced cancer treated by rAd-p53 via peritoneal perfusion combined with thermo- chemotherapy showed encouraging benefit on survival with excellent tolerance. Most patients' disease were under control. What's more, a few got a chance of radical surgery after treatment.

GSE27 Poster / Short -Oral Presentation

Effect of Hyperthermic Intraperitoneal Perfusion Chemotherapy in Combination with Intravenous Chemotherapy as Postoperative Adjuvant Therapy for Advanced Gastric Cancer

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Background/Aims: The aim of our study is to evaluate the preliminary efficacy and side effects of paclitaxel, 5-fluorouracil and leucovorin intravenous chemotherapy in combination with cisplatin hyperthermic intraperitoneal perfusion chemotherapy (HIPEC) as postoperative adjuvant therapy for patients of locally advanced gastric cancer (GC) who was at high risk for recurrence after curative resection in our center.

Methodology: 41 GC patients who underwent radical gastrectomy with D2 lymphadenectomy were enrolled in the study. All patients received paclitaxel 135mg/m^2 on day 1, 5-FU 500mg/m^2 on days 1-5, LV 200mg/m^2 on days 1-5 intravenous chemotherapy and cisplatin 75mg/m^2 on day 5 HIPEC one month after surgery. It was repeated at 3 weeks interval and administered at least two cycles.

Results: A total of 181 cycles of chemotherapy were administered (median, 4 cycles). The median disease free survival time (DFS) of patients was 40.8 months. The median overall survival time (OS) was 48.0 months. The one-year, two-year and three year recurrence rate was 14.6%, 26.8% and 46.3% respectively. The main relapse patterns were remnant GC and metastases of retroperitoneal lymph nodes. The mobidity of grade 3 and 4 toxicities of myelosuppression, nausea/vomiting were less than ten percent. The side effects of grade 1 and 2 of hematologic toxicity, nausea and vomiting, abnormal function of liver, kidney or cardiac, fatigue and neurotoxicity were well tolerated.

Conclusions: Cisplatin HIPEC combined with paclitaxel, 5FU and LV intravenous chemotherapy regimen could improve the survival rate and decrease the postoperative recurrence of locally advanced GC. The side effects were slight with good tolerability.

Key words: gastric cancer, heat, regional hyperthermia, antineoplastic agents, cisplatin, hyperthermic intraperitoneal perfusion chemotherapy

GSE28 Poster / Short -Oral Presentation

Seven cases of pancreatic cancer treated with chemo proton beam therapy and hyperthermia

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Introduction: Pancreatic cancer is a representative refractory cancer. Although surgery is the only curative treatment method, the patients who are eligible to the surgery is less than expected. Many pancreatic cancer patients are obliged to receive chemotherapy or chemo radiotherapy. However, treatment outcome of chemo radiotherapy is not satisfactory, thus various treatment protocol has been conducted with chemo radiotherapy. Hyperthermia is one of them. The hyperthermia has a feature to kill the cancer cells which are radio-resistant. We have used hyperthermia to the pancreatic cancer patients since 2011. We reviewed the treatment outcome of inoperable loco-regional pancreatic cancer patients who were treated using hyperthermia concurrently with chemo proton beam therapy in our institute.

Materials and Methods: A total of 7 cases of pancreatic cancer patients treated in the Proton Medical Research Center, University of Tsukuba since 2011 to 2013 were investigated (men 2, women 5, age: 59-66). Inoperable loco-regional pancreatic cancer patients were retrospectively reviewed and patients who had distant metastasis were excluded. Clinical stage was Stage IIB: 1, III: 6. Total proton beam irradiation dose was 50-67.5 (median 50) GyE. All patients received chemotherapy using gemcitabine. Moreover, all patients received hyperthermia once a week. We investigated survival and local control of those patients.

Results: A total of 4 patients are alive and remaining 3 patients are dead at June, 2014. The longest survival period was 15.8 months after onset of pancreatic cancer at present. No patient observed local recurrence so far. Hepatic metastasis was observed in 1 patient. Moreover, one patient whose tumor markers increase without evidence of recurrence or metastasis in conventional imaging was existed.

Conclusions: Although definite conclusion is not stated for the small number of patients, local lesions were well controlled, and survival period was comparable with that of the latest chemo radiotherapy. We plan to continue hyperthermia concurrently with chemo proton beam therapy to the inoperable loco-regional pancreatic cancer patients and investigate the treatment outcome with more number of patients.

GSE29 Poster / Short -Oral Presentation

A case of long-term survival after intrathoracic perfusion hyperthermo-chemotherapy for pleural dissemination of non-small cell lung cancer

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A 79-year-old female patient was admitted to our hospital when she was 69-year-old. She was diagnosed as primary lung adenocarcinoma of left lower lobe, by bronchial lavage cytology. And, because of malignant pleural effusion, she was diagnosed as cT4N0M0 stage IIIA (NCI 5th edition). We performed left lower lobectomy, lymph node dissection and an intrathoracic perfusion hyperthermo-chemotherapy (IPHC) with 120mg of cisplatin and 4000ml of hot saline. Recognizing the progress after the operation, She received several courses of chemotherapy (gefitinib, carboplatin with pacritaxel, carboplatin with gemsitabine, cisplatin with docetaxel, second course of gefitinib and pemetrexed). The state of her illness was kept a stable disease for 7 years. But now her disease is progressed, she is received palliative therapy in our hospital. It is recognized that, even for with positive pleural lavage cytology, prognosis of lung cancer is poor. She had pleural disseminations in her left pleural cavity. Now, she has multiple pulmonary metastases, multiple brain metastases and multiple bone metastases, but never found a recurrence of left pleural cavity during her history. This is because we could make a good local control of pleural cavity by IPHC.

GSE30 Poster / Short -Oral Presentation

The Outcomes of Oncothermia with Chemotherapy for Far Advanced Lung Cancer

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Nowadays, most oncologists face the challenge of ideal therapies without side-effects for cancer treatment. Conventional Hyperthermia can not achieve curative higher temperature in deep-seated tumors. Oncothermia can raise temperature and changing pH environment around the tumor. Combination of oncothermia with chemotherapy may enhance chemo-sensitivity, induce higher drug concentration around and inside the tumor, resulting tumor destruction. We report the outcomes of treatment by oncothermia with chemotherapy for 3 far advanced lung cancer in CHA Bundang Medical Center and Gangnam Severace Hospital.

GSE31 Poster / Short -Oral Presentation

Clinical evaluation of thermochemoradiotherapy using retrograde superselective intra-arterial infusion for advanced oral squamous cell carcinoma with cervical lymph node metastases

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Background:

For patients with locally advanced oral squamous cell carcinoma, surgery is the standard treatment and is thought to be the most effective curative therapy. Extended surgery causes loss of oral function, including swallowing and speech, and reduces patient's quality of life. To preserve organ function, retrograde superselective intra-arterial chemotherapy and daily concurrent radiotherapy is applied for patients with advanced oral cancer. However, patients of oral cancer with bulky or multiple cervical lymph node metastases have a poor prognosis. Our strategy for patients with cervical lymph node metastases is to use the thermochemoradiotherapy using superselective intra-arterial infusion via the superficial temporal and occipital arteries. This study was to evaluate the therapeutic results and histopathological effects of thermochemoradiotherapy.

Patients and Methods:

Seventeen patients with cervical lymph node metastases of oral squamous cell carcinoma underwent thermochemoradiotherapy using retrograde superselective intra-arterial infusion with docetaxel and cisplatin. Treatment consisted of hyperthermia (3-8 sessions), superselective intra-arterial infusions (docetaxel, total 40-60 mg/m^2, cisplatin, total 100-150 mg/m^2) and daily concurrent radiotherapy (total 60Gy) for 6 weeks. After intra-arterial chemoradiotherapy, primary site CR was achieved in all cases. Radical neck dissection was performed 5-8 weeks after the end of treatment.

Results:

In 11 of those 17 patients, hyperthermia-targeted metastatic lymph nodes were diagnosed as pathological complete response (64.7%). In the remaining 6 patients, pathological diagnoses were partial response (35.2%). During follow-up, 13 patients were alive without disease, 3 patients died due to pulmonary metastasis and 1 patients died due to noncancer-related cause. Overall survival and locoregional control rates (range, 6-75 months) were 76.4% and 93.3%, respectively.

Conclusion:

Thermochemoradiotherapy using retrograde superselective intra-arterial infusion provided good survival and locoregional control rates in advanced oral cancer.

GSE32 Poster / Short -Oral Presentation

Thermochemoradiotherapy using superselective intra-arterial infusion for N3 cervical lymph node metastases of tongue squamous cell cancer

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Oral cancer patients with cervical lymph node metastases are particularly difficult to treat, especially when cervical lymph node metastases exceed 6 cm (N3), and have a poor prognosis. A case of tongue carcinoma with N3 cervical lymph node metastases treated with thermochemoradiotherapy using superselective infusion is reported. An 80-year-old woman was diagnosed with squamous cell carcinoma of the tongue (T4aN3M0). The patient rejected radical surgery, definitive thermochemoradiotherapy using superselective intra-arterial infusion was planned. The target arteries for the primary focus and cervical lymph node metastases were the lingual, facial, superior thyroid, and transverse cervical arteries, both the superficial temporal artery and transfemoral artery with Seldinger method were approached for superselective intra-arterial infusion. The patient was treated with a combination of radiotherapy (2 Gy/day, total 60 Gy), superselective intra-arterial chemotherapy (docetaxel, total 124 mg; cisplatin, total 135 mg), and four sessions of hyperthermia for cervical lymph node metastases. Hyperthermia was administered for 50 min within 30 min after each session of chemoradiotherapy using a radiofrequency capacitive heating device. Grade 3 neutropenia, oral mucositis, and dermatitis associated with treatment were observed following therapy. Both primary tumor and N3 neck disease responded well and 18-fluorodeoxyglucose uptake on positron emission tomography-computed tomography in both sites disappeared after treatment. The patient has shown no clinical or radiological evidence of local recurrence or distant metastasis 7 years after treatment. This method of chemoradiotherapy using superselective infusion combined with hyperthermia seems a promising modality for patients with N3 cervical lymph node metastases of oral cancer.

GSE33 Poster / Short -Oral Presentation

Successful Treatment of N3 Cervical Lymph Node Recurrence from Oropharyngeal Cancer with Thermochemoradiotherapy: A case report

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It is generally hard to treat N3 cervical lymph node metastases from the head and neck cancers without neck dissection. Because we experienced a case of N3 lymph node recurrence from squamous cell carcinoma of the oropharynx, who achieved complete remission with thermochemoradiotherapy, we present the clinical course of this case.

A 65-year-old woman was diagnosed as having squamous cell carcinoma of the soft palate (cT2N0M0) and treated with surgery without neck dissection. Eight years after the surgery, a lymph node appeared in the left neck. Fine needle aspiration biopsy was performed, and cytology specimen confirmed the squamous cell carcinoma diagnosis. Because there was no evidence of primary tumor in the head and neck after physical and radiological examinations including computed tomography, magnetic resonance imaging (MRI), and ^{18}F-fluorodeoxyglucose positron emission tomography, she was diagnosed as having cervical lymph node recurrence from squamous cell carcinoma of the soft palate (rTxN3M0). The maximum diameter of the recurrent lymph node was 61 mm with central necrosis. She was considered not a candidate for neck dissection because the lymph node involved the carotid artery. Thus, she was treated with a combination of chemoradiotherapy and hyperthermia. Radiotherapy was delivered to the left neck with 6-MV X-rays using linear accerelator. A dose of 2.0 Gy per fraction, 5 times per week, for a total dose of 70.0 Gy was prescribed. Hyperthemia was given once or twice a week using a Thermotron RF-8, and applied for approximately 40 minutes to achieve a temperature of over 42 degree Celsius in the tumor. A total of 9 times of hyperthermia was performed during radiotherapy. Two courses of concurrent chemotherapy with cisplatin, 5-fluorouracil, and leukocovorin were also performed. Although Grade 3 acute dermatitis and mucositis were observed, radiotherapy was completed without interruption. The lymph nodes in the left neck were gradually decreasing in size during the treatment. MRI was done 9 months after the treatment and showed no residual lymph nodes in the left neck. After 11 months, she was alive with no evidence of disease.

A combination of chemoradiotherapy and hyperthermia is considered to be an effective treatment option in cases of huge tumors with necrosis, which are generally resistant to radiotherapy.

GSE34 Poster/Short -Oral Presentation

Preoperative thermochemoradiotherapy using retrograde superselective intra-arterial infusion for locally advanced oral cancer with cervical lymph node metastases.

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Background:

This study was to evaluate the therapeutic results and histopathological effects of treatment with preoperative thermochemoradiotherapy using superselective intra-arterial infusion via superficial temporal and occipital arteries for cervical lymph node metastases of advanced oral cancer.

Patients and Methods:

Eight patients with cervical lymph node metastases of oral squamous cell carcinoma underwent thermochemoradiotherapy using superselective intra-arterial infusion with docetaxel and cisplatin as preoperative therapy. Treatment consisted of hyperthermia (3-8 sessions), superselective intra-arterial infusions (docetaxel, total 40-50 mg/m^2, cisplatin, total 100-125 mg/m^2) and daily concurrent radiotherapy (total 40-50 Gy) for 4-5 weeks. All patients underwent radical surgeries both primary lesion and neck disease in 5-8 weeks after the end of thermochemoradiotherapy.

Results:

In 5 of those 8 patients, hyperthermia-targeted metastatic lymph nodes were diagnosed as pathological CR (62.5%). In the remaining 3 patients, pathological diagnoses were partial response (PR) (37.5%). During follow-up, 4 patients were alive without disease, 1 patient was alive with regional relapse and 3 patients died due to pulmonary metastasis. Overall survival and locoregional control rates (range, 7-75 months) were 62.5% and 87.5%, respectively.

Conclusion:

Preoperative thermochemoradiotherapy using intra-arterial infusion provided good survival and locoregional control rates in advanced oral cancer.

GSE35 Poster / Short -Oral Presentation

Locally advanced unresected uterine leiomyosarcoma with triple;modality treatment combining radiotherapy, chemotherapy and hyperthermia

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Advanced uterine leiomyosarcoma (LMS), though rare, is an extremely aggressive disease. In a patient with advanced and unresected uterine LMS, although no consensus exists on the efficacy of treatment, multidisciplinary therapy is the best option. A 41 year old woman was performed laparotomy due to huge her uterine tumor. Laparotomy revealed a huge tumor that had extended pelvic wall, outside the pelvis and invaded colon. Large tumors were residuals in the pelvis after suboptimal debulking surgery. After surgery, she was treated adjuvant radiotherapy, to be followed by chemotherapy with regional whole pelvis hyperthermia (HT). A CT scan showed stable disease (SD) before and after combination treatment. While the patient was being treated for grade 3/4 burns and subcutaneous fatty necrosis, she developed multiorgan failure. And she died. In the present case report, we outline the potential for the treatment of combination with chemotherapy, HT, and radiotherapy. An effective protocol needs to be explored for the administration of chemotherapy, HT, and radiotherapy in patients with advanced unresected LMS.

GSE36 Poster / Short -Oral Presentation

Conversion of chemo-sensitivity by adding electro-hyperthermiain recurrent endometrial cancer: A Case Report

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Modulated electro-hyperthermia is an emerging complementary treatment option for refractory solid tumor. Early experience suggests that it may have advantages over conventional hyperthermia with exceeding efficacy, and less complication. Herein, we describe a case of chemo-resistant, recurrent endometrial cancer patient; a successful conversion of chemo-sensitivity by the combination of electro-hyperthermia. On the way of chemotherapy for relapsed endometrial cancer, elevation of CA-125 marker frequently means chemo-resistance of the tumor. In this case, we observed sudden decrease of tumor marker during refractory chemotherapy by adding electro-hyperthermia. The gross lesion was finally disappeared completely on CT scan and PET imaging, and the serum CA-125 marker was also normalized and maintained. Adding electro-hyperthermia could be a good treatment option even for the chemo-resistant endometrial cancer by converting chemo-sensitivity.

GSE37 Poster / Short -Oral Presentation

Clinical effectiveness of recombinant adenovirus-p53 combined with hyperthermia in advanced soft tissue sarcoma (a report of 30 cases)

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[Abstract] Objective To evaluate the efficacy and safety of recombinant adenovirus— p53 (rAdp53) combined with hyperthermia in advanced soft tissue sarcoma.

Methods: From Nov.2001 to July 2011, 30 patients with advanced soft tissue sarcoma enrolled into this clinical study on Adp53 (Gendicine) combined with hyperthermia plus or not plus radiotherapy. 29 of 30 cases were intratumorally injected Gendicine solution, 1 case was introperitoneally infused with Gendicine solution, 1x1012 vp (virus particle) once a week with a total 8 times usually, All cases were combined with hyperthermia, once or twice a week for total 9 times usually. Hyperthermia were carried out at 48 hours after Gendicine treated, 29 cases were concurrently followed by irradiation with the conventional fractionation 2Gy/f, five fractions a week to a total dose 16~70Gy /8~35f/2~8w, average 56.3±5.3Gy.

Results: Among 30 cases, the treatment achieved CR in one case (3.3%), pCR (completely resected after treatment and no alive cell in pathologic sample) in two cases (6.6%), PR in nine cases (30.0%), SD in eighteen cases (60.0%).1-year survival rate is 56.6% (17/30), 3-year survival rate is 10.0% (3/30), 5-year survival rate is 6.7% (2/30), SD>6 monthes in 6 cases. The actual clinical effectual rate (CR+PR+SD>6monthes) is 83.3.0% (25/30). No dose-limiting toxicity and adverse events were noted, except transient fever after Gendicine administration.

Conclusions: The treatment with hyperthermia combined with Adp53 plus or not plus radiotherapy in advanced soft tissue sarcoma was safe and effective.

GSE38 Poster / Short -Oral Presentation

Effects of a shower bathing or whole body bathing on HSP70 induction of the bathing after that

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(Purpose and back ground) We have aimed at the establishment of a healthier bathing method (HSP bathing method) using HSP70, NK-cell activity, and physical index, etc, as the indexes up to now. These indexes are significant increase, and they are useful for the prevention of infection, the tiredness recovery, and the stress defense in daily life though HSP70 and NK-cell activities by the HSP bathing method improve of the index in the physical index is a little. However, the case to make the whole body bathing a shower has increased from the change in the lifestyle. In this report, whole body bathing and shower to which a lot of people were daily doing examined the influence on the HSP bathing done next.

(Methods) The 11 subjects were randomly allocated to group A (5days shower bathing) and B (5days whole body bathing at 40 degrees C. for 10min), and then A and B were bathing at 40 degrees C. for 15min (HSP-test bathing). One month later, group A and B took a bath according to mode B and A, respectively. Oral temperature was measured before, every 5min during, and up to 30min after bathing. Since the subjects were extremely wet with sweat during the rest period after bathing, great attention was given to prevent dehydration. HSP70, NK cells activity and physical index and were measured before and 1 and 2 days after HSP-test bathing.Approval No. 24-3 from Ethics Committee of Shubun University Faculty of Health and Nutrition

(Results) Oral temperature of B (5days bathing) under HSP-test bathing was higher than A (5days shower). HSP-test bathing after B increased significantly the induction of HSP 70, NK cell activity and physical index. From the results of the questionnaire, it became clear that tiredness and muscular pain were reduced and the confusion of feelings was controlled by continuance of whole body bathing.

(Conclusion) It may be concluded that the whole body bathing in daily life will improve mentally and physically than shower from the results of HSP70, NK-cell activity, physical index and the questionnaire.

GSE39 Poster / Short -Oral Presentation

Mixed Response to TS-1 and Oncothermia in a Esophageal Cancer Patient with Lung Metastases: Case Report

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Introduction; Management of patients suffering from esophageal cancer with lung metastasis remains challenging in routine clinical practice. Oncothermia has recently been applied as novel therapeutic option for metastatic or recurrent esophageal cancer patients. We report a case of esophageal cancer patient with showing a restricted response in the Oncothermia application field during TS-1 systemic chemotherapy.

Case report; A 57-year-old male esophageal cancer patient had received esophagectomy. Pathologic specimens showed stage IIIA (T3N1M0) squamous cell carcinoma in the upper esophgus. After operation he received 3 times adjuvant FP (5-FU and cisplatin) chemotherapy. Three months later after completing chemotherapy two lung metastases were noted. Since then three times palliative docetaxel chemotherapy was applied but not showing any response. He received three times concurrent chemo (DEF)-Oncothermia treatment in the painful left lung lesion invading a rib. Tumor response was not observed after completing treatment. Since then he took 2 cycles TS-1 chemotherapy with Oncothermia treatment. After completing 2 cycles concurrent chemo-Oncothermia treatment, a mixed response was noted. On the one hand left metastatic lung lesion applied Oncothermia showed decreasing tumor size, on the other hand right lesion not applied Oncothermia revealed the increasing tumor size despite of systemic chemotherapy.

Discussion; In some esophageal cancer patients concurrent chemo-Oncothermia treatment may become a new option for palliation of these patients.

GSE40 Poster / Short -Oral Presentation

Analysis of Respiratory-induced Deformation and Translation of Liver using Branching Structure of Portal Vein Observed by MR Imaging for HIFU

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[Background] High intensity focused ultrasound (HIFU) treatment of the liver requires a "lock-on" technique for placing the focal spot at the target tissue region during respiratory-induced motion. In order to maintain sufficient tracking accuracy, both translation and deformation of the tissue need to be detected. In this study, we analyzed the deformation and transformation of the liver under slow breathing based on the morphological changes of the branching structures of the portal vein obtained by MR imaging.

[Method] Multi-slice MR images were acquired in a healthy volunteer liver with Fast Imaging Employing Steady state Acquisition (FIESTA) at 3T. Imaging conditions were as follows: TR/TE, 4.85/1.98 ms; slice thickness, 5mm; inter-slice spacing, 0 mm; field of view, 35 x 35 cm^2; spatial matrix, 512 x 512; flip angle, 90 degrees. Six slices covering a sagittal slab of 3-cm thickness were continuously acquired during slow breathing. The images in a slab were then linearly interpolated to have isotropic voxel data. The slabs at different time points were re-ordered according to the diaphragm position extract from each image. Nine regions of interest (ROI) including branching vessels in the volume were tracked using three-dimensional pattern-matching method. In the tracking method search area were set in order to height of diaphragm. Distance between reference the center of ROI and other eight ROIs' center were calculated for each image sets. Expansion and contraction of each ROI pair were calculated.

[Result] The expansion and contraction was 5 mm in anterior-posterior (AP) direction, 60 mm in superior-inferior (SI), and 20 mm in left-right (LR, out-plane). The expansion in the anterior region was 5 to 6 mm larger than the posterior region, suggesting that the organ motion is more restricted in the posterior region by the surrounding tissues.

[Conclusion] The results demonstrated that the three-dimensional motion tracking of the liver is feasible by observing the vessel branches with rapid MR imaging and the pattern matching techniques.

GSE41 Poster / Short -Oral Presentation

Feasibility of Noninvasive Magnetic Resonance Thermometry of The Knee Joint under Thermal Therapy

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POURPSE: The aim of this study was to examine feasibility of noninvasive magnetic resonance (MR) temperature imaging of knee joint under thermally induced pain-relief therapy for osteoarthritis.

METHODS: A porcine knee joint sample ex vivo was place in lateral position and heated in a thermostatic bath. Temperature of the bath was set from 34 to 40 °C. Actual temperature of the sample was monitored by a 4-channel fiber optic thermometer at the suprapatellar bursa (Ch1), meniscus (Ch2), muscle (Ch3) and surrounding water (Ch4). Proton MR imaging with a fast field echo technique was performed in the saggittal slices with the following conditions; repetition time (TR), 11.3 ms; echo time (TE), 8 ms; flip angle (FA), 15 degree; slice thickness, 5 mm; field of view (FOV), 30 cm; and acquisition matrix, 212 x 161. After compensating the static magnetic field drift approximated by a first order plane estimated from the phase change in the complex MR signals in the bone marrow regions or in four olive oil tubes around the sample. Phase change induced by the water proton resonance frequency shift in the aqueous tissues such as articular cartilage and meniscus was converted to temperature elevation using a coefficient of -0.01 ppm/°C.

RESULTS: Temperature of the suprapatellar bursa elevated from 33.1 to 38.8 °C. That of the meniscus elevated from 33.7 to 39.2 °C. Signal to noise ratio in the magnitude image was 34 at the articular cartilage or 20 at the meniscus. The resultant temperature images in these tissues agreed fairly with the actual temperature elevation.

DISCUSSION: The signal to noise ratios in the cartilage and meniscus were sufficient for appreciating the thermal shift of the water proton resonance frequency. In the present experiment setup, feasibility of noninvasive MR thermometry was demonstrated. There are, however, several points to be examined to translate this technique into clinical practice. First, the magnetic field compensation was not sufficient in some slices, where the field inhomogeniety seemed to be complex due to the tissue structure in the articluar region. Second, water-fat separation is necessary to eliminate the effect of fat signal in obtaining the phase change of water proton for temperature quantification, or the effect of water signal in estimating the phase change of fat proton for field drift compensation. Third, model function of the drift has to be optimized. Heating methods and motion compensation techniques have to be investigated as well.

GSE42 Poster / Short -Oral Presentation

Enhancement of hyperthermia-induced apoptosis by isofraxidin in human lymphoma U937 cells

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Previously, we have already reported that isofraxidin protected human leukemia cells from radiation-induced apoptosis via ROS/mitochondria pathway. Based on that, we exposed U937 cells to hyperthermia (44C, 20 min) with/without isofraxidin pre-treatment. Interestingly, we found that isofraxidin could enhance hyperthermia-induced apoptosis in U937 cells. To demonstrate the molecular mechanism of this enhancement by isofraxidin, we measured ROS generation, mitochondrial membrane potential (MMP), content of ATP, expressions of apoptosis-related proteins such as caspases, HSP70, JNK, P38, and intracellular calcium levers. The results showed that the combined treatment could enhance MMP loss, reduce superoxide generation and intracellular ATP, increase the expressions of caspase-3, caspase-8, phospho-JNK and intracellular calcium levels. Moreover, we confirmed the role of caspases and JNK by using zVAD-FMK (the pan caspases inhibitor) and SP10025 (the JNK inhibitor) in U937 cells. Taken together, the data elucidate that isofraxidin enhances hyperthermia-induced apoptosis via caspase/mitochondria pathway in U937 cells.

GSE43 Poster/Short -Oral Presentation

P53 gene therapy combined with whole body hyperthermia and local hyperthermia

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The p53 gene is one of the most frequently mutated genes in cancer cells. Recombinant adenovirus-p53 (rAd53) has been approved by the State Food and Drug Administration of China (SFDA; Beijing, China). We report some experiences the gene therapy combined with hyperthermia.

Method: rAd53 (Gendicine, Shenzhen SiBiono GeneTech) is injected to metastatic tumors of 7 advanced patients with real time monitoring by CT. 24~72 hours after from the injection, We treat Whole body hyperthermia by RHS7500 or local hyperthermia by RF-8.

Result: All patient show the decreasing effect of tumor marker and some patients show reduce of tumor size. Our result supports the use of p53 gene transfer with hyperthermia as a potential treatment for advanced cancer.

GSJ1 Poster / Short -Oral Presentation (Japanese)

Anti-tumor and anti-invasive effects of diverse delta- and gamma-lactones and the combined hyperthermia

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Background: On the screening studies of new antitumor substances in perfume and musk components, we have found diverse potent lactones which exhibited carcinostatic activity and promotive effect by hyperthermia. In the present study, anti-tumor and anti-invasive effects of δ- and γ-lactones in perfume components were examined by combination with hyperthermia.

Methods: Ehrlich ascites tumor cells supplemented with a lactone were incubated for 20- or 48-hr sequent to heating at 37ºC or 42ºC for 30 min. The carcinostatic effect of lactones and hyperthermia was measured by the WST-8 assey, with diminishing mitochondrial dehydrogenase activity reflecting cell survival rate. Furthermore, the ability of anti-tumor lactones to inhibit invasion of tumor cells into blood vessels prior to tumor metastasis was examined to human fibrosarcoma (HT1080) cells

Results: Of the δ-lactones, 2-decen-5-olide at the low dose of 50 μM exhibited marked carcinostatic activity and of the γ-lactones, (S)-4-dodecanolide was remarkable. These carcinostatic activity is dependence on binding site of double bonds in a lactone ring and molecular side-chain length.Invasion of human fibrosarcoma HT-1080 cells through the reconstituted basement membrane was inhibited by some δ- and γ-lactones, even at dose as low as 5-10% of those necessary for carcinistic activity.

Conclusion: These antitumor effects were promoted by combination with hyperthermia at 42ºC. Thus, 2-decen-5-olide (δ-lactone) and (S)-4-dodecanolide (γ-lactones) is appear to be potent as an antitumor agent.

GSJ2 Poster / Short -Oral Presentation (Japanese)

Trial of treatment-standardization; similar quality of treatment of hyperthermia by "Thermotron RF-8".

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Purpose: To provide hyperthermia treatment in cancer patients based on new conception; treatment-standardization (similar quality of treatment of hyperthermia (Neo-thermia)), we investigated the relationship between Neo-thermia and treatment condition in cancer patients.

Materials and Methods: Total number of 106 cancer patients (65-year-old average age (31-89 years, male: female = 68:38) underwent hyperthermic treatment alone or concomitant with chemotherapy or, radiotherapy. Total of 507 eradiation by Thermotron RF-8 in December 2011 to April 2014. Cumulative output Watt/50 min., body weight pre and post irradiation, and complications (symptoms not to increase the power output; pain, tingling sensation, etc.) during irradiation were evaluated in patients. Thermotron RF-8 treatment was undergone once a week and 2-5 (common)-11 times depending upon patients' status. Total of 347 and 160, Neo-thermia and not Neo-thermia, respectively were evaluated.

Results: Average irradiation output Watts of patients with and without Neo-thermia were 750.9 Watt/50 min and 691.4 watt/50 min, respectively. Decrease Body weight averages with and without Neo-thermia were 213.5 g and 188.7 g, respectively. Complications during irradiation were shown 31.7% in patients with Neo-thermia, and 47.5% in those without Neo-thermia. Complications during irradiation decreased after Neo-thermia (no complication occurred /5 times, 1/5, 2/5, 3/5, 4/5 and 5/5 in patients with Neo-thermia were 20.6%, 41.3%, 14.3%, 11.1%, 6.3%, and 6.3%, respectively, and those without Neo-thermia,17.9%, 25.0%, 14.3%, 14.3%, 25.0% and 3.6%, respectively.

Conclusion: Treatment-standardization by Thermotron RF-8 could be safety underwent. In this way the contribution of hyperthermic therapy must be evaluated. We now try to fumble higher power output treatment without complication of RF eradiation.

GSJ3 Poster / Short -Oral Presentation (Japanese)

Correlation between complications induced by [Thermotron RF-8] and physical status.

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Purpose: Complications (symptoms not to increase the power output; pain, tingling sensation, etc.) are commonly encountered during RF thermic therapy and should be discontinued treatment or should be decreased power output. Correlations between complications induced by [Thermotron RF-8] and physical status were valuated.

Materials and Methods: Total number of 106 cancer patients (65-year-old average age (31-89 years, male: female = 68:38) underwent hyperthermic treatment alone or concomitant with chemotherapy or, radiotherapy. Total of 507 eradiation by Thermotron RF-8 in December 2011 to April 2014. Two-hundred seventy six patients received Neo-thermia; treatment-standardization (similar quality of treatment of hyperthermia) and 126 no Neo-thermia. Among Neo-thermal patients 80 underwent RF irradiation with [AKIMist [E] TN; dry fog humidifier (H.Ikeuchi & Co., Ltd, Japan)] during hyperthermic treatment. Blood biochemical tests were performed once a week.

Results: In patients with Neo-thermia, significant correlation between initial output Watt when complications were occurred, thickness of the fat of the abdominal wall, subcutaneous fat area, all fat area, BMI, abdominal girth, body weight, offal internal organs fat area and complication first time (min.) ($p<0.01$), and in those without Neo-thermia, complication first time, subcutaneous fat area, all fat area, thickness of the fat of the abdominal wall and offal internal organs fat area ($p<0.01$). Patients with complications showed the decrease of Ly and the increase of the Neutrophil.

Conclusion: The complications induced by [Thermotron RF-8] can be predicted. Patients with complications may not receive a benefit of this treatment. We must try to fumble higher power output treatment without complications of RF eradiation.

GSJ4 Poster / Short -Oral Presentation (Japanese)

Trial of prevention for complications induced during "Thermotron RF-8" treatment.

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Purpose: Complications (symptoms not to increase the power output; pain, tingling sensation, etc.) are commonly encountered during RF thermic therapy and should be discontinued treatment or should be decreased power output. To prevent the complications during "Thermotron RF-8" treatment, we used "AKIMist "E" TN; dry fog humidifier (H.Ikeuchi & Co., Ltd, Japan)" during hyperthermic treatment.

Materials and Methods: Total number of 106 cancer patients (65-year-old average age (31-89 years, male: female = 68:38) underwent hyperthermic treatment alone or concomitant with chemotherapy or, radiotherapy. Total of 507 eradiation by Thermotron RF-8 in December 2011 to April 2014. Cumulative output Watt/50 min., body weight pre and post irradiation, and complications (symptoms not to increase the power output; pain, tingling sensation, etc.) during irradiation were evaluated in patients. Thermotron RF-8 treatment was undergone once a week and 2-5 (common)-11 times depending upon patients' status. Total number of 97 and 310, humidification and not humidification, respectively were evaluated. "AKIMist "E" TN" is a non-wetting dry frog humidifier, having no large particles, without getting anything wet.

Results: Average irradiation output Watts of patients with and without "AKIMist "E"TN" were 831.2 Watt/50 min and 996.9 watt/50 min, respectively. Decrease Body weight averages with and without "AKIMist "E" TN" were 682.6 g and 62.3 g, respectively. Complications during irradiation were shown 50.5% in patients with "AKIMist "E" TN", and 33.4% in those without "AKIMist "E "TN".No complication occurred /5 times, 1/5, 2/5, 3/5, 4/5 and 5/5 in patients with "AKIMist "E" TN" were 14.3%, 14.3%, 21.4%, 28.6%, 7.1%, and 14.3%, respectively, and those without "AKIMist "E" TN" ,20.8%, 40.3%, 13.0%, 9.1%, 13.0%, and 3.9%, respectively.

Conclusion: By using "AKIMist "E" TN" we could put out higher power output, but complications itself did not prevent. We continue to use this method and try to decrease complications with higher output treatment, then to evaluate whether this higher output bring good clinical results or not.

GSJ5 Poster / Short -Oral Presentation (Japanese)

Evaluation on heating characteristics of multiple coaxial-slot antenna as a feeding probe of metallic stent for bile duct carcinoma

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[Introduction] In recent years, many researchers have been conducted on the medical applications of the electromagnetic wave. In particular, microwave hyperthermia using the thermal action of the electromagnetic wave for human body has been attracted attention. Today, placement of self-expandable metallic stents is the standard treatment for patients suffering from bile duct obstruction. Therefore, we have been studying a microwave intracavitary hyperthermia for bile duct carcinoma after the stent placement. In this treatment, we are supposing to insert a flexible and thin diameter coaxial-slot antenna using an endoscope into a metallic bilialy stent. After that, the antenna heat tumor around the stent. When this treatment is established, the bile duct carcinoma can be treated non-invasively. However, our previous study shows that it is difficult to obtain effective heating region along the metallic stent, because of the electromagnetic wave shield. Therefore, in this study, a new type of coaxial-slot antenna which has multiple slots near the tip, is proposed for effective heating along the stent. Moreover, we evaluate the heating characteristics around the stent with proposed antenna by numerical analysis and heating experiment.

[Method] We employed the FDTD (Finite-Difference Time-Domain) method for the electromagnetic field analysis. The analytical model consists of the multiple coaxial-slot antenna, a stent, and muscle. We calculated the SAR (Specific Absorption Rate) distribution around the metallic stent using this analytical model, and the SAR is used as an evaluation index of heating effect of microwave. In the heating experiment, we inserted a metallic stent and the antenna in the muscle-equivalent phantom. In order to evaluate the validity of the analytical result, we measured the temperature distribution around the metallic stent by an infrared camera.

[Result] As a result, we confirmed that the multiple coaxial-slot antenna is able to heat around metallic stent extensively. Here, we found the higher SAR region along the metallic stent up to 60mm.

[Discussion] In this study, we proposed multiple coaxial-slot antenna for bile duct carcinoma. As a result of investigations, under the stent placement, it is possible to perform effective microwave hyperthermia for bile duct carcinoma.

GSJ6 Poster / Short -Oral Presentation (Japanese)

Effects of laser radiation on Hela cells using diode laser (ADL-20)

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Purpose: There is a limit in the intracavitary irradiation of the cervical cancer at the current radiation therapy, and the following new therapeutic instrument is needed. In hyperthermia, the heating devices using RF are used in general, and they have problem of size (large) of device and cost (expensive). In laserthermia, if the best wavelength is used and to determine optimal condition of radiation, a small and low-cost device is possible. Laser radiation device (ADL-20: Asuka medical) has developed to treat intrcavity tumors like cervical cancer, by intravaginal laser radiation heating. Because this laser radiation device in 810 nm do not absorbed in water and absorbed in hemoglobin, it can reach laser to some depth and heat the tissues. Therefore, in order to determine whether this device is effective for tumors, we examined the cell viability of tumor cells in vitro using colony assay method.

Method: Hela carnival cells (JCRB) were cultured with minimum essential medium (MEM) adding FBS, non essential amino acid and penicillin streptomycin in CO_2 incubator under the condition of 5 % CO_2 at 37 degree. Hela cells ($3.0x10^4$ cells) were cultured in 24 well plate at 2-4 days under 37 degree, 5% CO_2. Laser was radiated on a well of plate at each 37, 40, 42 43 44 and 45 degree temperature for 2hours. Laser output was 20W in all study. The radiated cells were cultured for 1-2 weeks and analyzed by the colony assay method. Besides the non-irradiation cells nearby radiated well were used as control, and treated similar to radiated cells.

Result: Colony viability of Hela cells was increased slightly at 37, 40 degree and not changed at 42 degree by laser radiation. At 43, 44 and 45 degrees, survival rate of Hela cells were decreased according to the radiation temperature.

Conclusion: By above 43 degree temperature using laser radiation, viability of Hela decreased significantly according to the temperature. It was suggested that laser radiation by ADL-20 was effective on survival of tumor cells. Furthermore, it is proved that the laser radiation by this device can heat up to animal tissue (pork meat) in deep. These results on tumor cells and tissue were suggested the possibility that the laser hyperthermia using this device was useful as a therapeutic instrument for intravaginal laser radiation heating. In addition, more details are being examined.

GSJ7 Poster / Short -Oral Presentation (Japanese)

Capacitive coupling-type hyperthermia treatment method combined with wireless energy transmission system; Measurement of temperature with transmission power of 1 W

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Introduction: We propose a hyperthermia treatment for deep and local cancer based on capacitive heating of two electrodes implanted in the target organ. However, deep and local hyperthermia needs 1-5 W of electric power to heat the target organ. Therefore, we also propose an energy transmission transformer that places a transmitting coil around the body and a flexible ribbon-type receiving coil in the body. The receiving coil is connected directly to the two electrodes, and the frequency of the input power to electrodes is not converted from the frequency of receiving power. To investigate the validity of the proposed deep and local hyperthermia and energy transmission system, we measured the temperature rise in an agar gel phantom and the transmission efficiency of the energy transmission system.

Method: The implantable electrodes (ellipse-shaped) had dimensions of 32 mm X 16 mm. These two electrodes were inserted in the center of the cylinder-shaped agar gel phantom, which was adjusted to have the conductivity of human muscle, and had a frequency of 1 MHz. The separation distance between the two electrodes varied from 30 mm to 60 mm, and a graphite mixed gel phantom (1 cm^3, graphite: 0.56 g/cm^3) was implanted in this space. In the experiment, the input power to the electrodes was fixed at 1.1 W. The rise in temperature at the center of the two electrodes (point A), edge of the electrodes (point B), and non-target part (i.e., 50 mm away from the electrodes) (point C) was measured. For the wireless energy transmission, the diameter of the transmitting coil was 290 mm, and the receiving coil was 110 mm. These coils were flexible and hollow. The output frequency was fixed at 1 MHz. The energy transmission efficiency of the prototype energy transmission transformer was measured and analyzed using an electromagnetic simulator.

Results: The increases in temperature at points A, B, and C were 5.5, 4.0, and 0.6 degrees Celsius, respectively, when the two electrodes were 30 mm apart. When the distance between the two electrodes was increased to 60 mm, the temperature rise at point A was reduced to 2.1 degrees Celsius. The results showed that an AC-AC energy transmission efficiency of 90% could be obtained.

Conclusion: The results indicate that our proposed hyperthermia method is capable of heating deep and local cancer targets despite the lower amount of heating energy.

GSJ8 Poster / Short -Oral Presentation (Japanese)

Hyperthermia-induced tumor-specific T-cell immunity and its role in the therapeutic efficacy of hyperthermia.

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Purpose: Hyperthermia is an effective modality of cancer therapy. Meanwhile, recent studies have demonstrated the pivotal contribution of T-cell-mediated anti-tumor immunity to the anti-tumor effect of various cancer therapies including radiotherapy and chemotherapy. Together, this study aimed to elucidate the contribution of T-cell-mediated anti-tumor immunity in the anti-tumor effect of hyperthermia.

Methods and Materials: C57BL/6 mice received injection of its syngeneic lymphoma cell line E.G7-OVA (2.0 x 10^6 cells) in the right femurs. Local hyperthermia was performed by right femur immersion in a water bath at 42°C for one hour on day 7, followed by administration of anti-CD8 antibody, anti-CTLA-4 antibody or PBS (day 8, 11 and 14). Tumor size was measured three times a week in three dimensions. The effect of hyperthermia on tumor growth was assessed by tumor growth delay (TGD) calculated by subtracting the day tumor volume reached 1000 mm^3 in the untreated mice from that in the mice received given treatment. Survival of the mice was assessed using median survival time (MST). On day 21, the mice were sacrificed, and the splenocytes were incubated ex vivo with irradiated-E.G7-OVA cells, followed by enzyme-linked immunospot (ELISPOT) assay specific for IFN-γ. Seven mice were used in each experimental condition.

Results: Hyperthermia significantly prolonged TGD (2.0 ± 35.3 days, p = 0.01) and MST (22.5 ± 30.6 days in the hyperthermia-treated mice and 19.0 ± 2.5 days in the untreated mice, p = 0.047). Strikingly, the TGD and MST in the hyperthermia-treated mice were mitigated by addition of anti-CD8 antibody, to the levels comparable to those in the hyperthermia-untreated mice (TGD, -1.0 & plusmn 0.5 days; MST, 20.0 & plusmn 2.8 days), Consistently, the TGD and MST in the hyperthermia-treated mice were prolonged but not significantly by addition of anti-CTLA-4 antibody (TGD, 5.0 & plusmn 32.3 days, p = 0.65; MST, 27.0 & plusmn 2.6 days, p = 0.92) The ELISPOT assay showed that hyperthermia significantly increased a number of IFN-γ-producing cells; the number of spots in the hyperthermia-treated mice and the hyperthermia-untreated mice was 276.3 ± 14.5 and 59.0 ± 4.4, respectively ($p < 0.001$), confirming the activation of E.G7-OVA-specific T cell immunity by hyperthermia.

Conclusions: Our results indicate that tumor-specific immune responses play an important role in the therapeutic efficacy of hyperthermia.

GSJ9 Poster / Short -Oral Presentation (Japanese)

Treatment of advanced castration resistant prostate cancer with multiple metastases by regional hyperthermia under thermosensitization with Parthenolide: A case report.

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<Back ground> Parthenolide (PTL) has a significant thermo-enhancement effect. The purpose of this presentation is to report our clinical experience of using PLT in regional hyperthermia (R-HT) using Thermotron-RF8 combined with low dose chemotherapy in an advanced castration resistant prostate cancer (CRPC).

<Patient and Methods> Patient is a 70 years old male with recurrent prostate cancer who was treated by radical prostatectomy (RP) in October, 2007 and followed by surgical castration in January, 2009 at a medical school hospital. The recurrence of the disease was detected 11 months after RP and treated with irreadiation and chemotherapy with dosetaxel (DCX). On his first visit to our hospital, serum PSA level elevated to 154.26 ng/ml. His tissue diagnosis was Gleason score 4+3=7. Administration of PTH (Natsusirogiku PTL. 03, 2 tab/day) started before R-HT (AV.1400W 2/W). The treatment was also combined with DCX (70 mg) and predonisolon (10 mg/day) for 5 days of hospitalization. The treatment was repeated every 4 weeks for 24 times up to present.

<Results> After 7 course of treatment, serum PSA dropped as lowers as 4 ng/ml and CT revealed CR of metastatic lesions at lymph-nodes. The patient has continued to be in good physical condition with serum PSA around 1 ng/ml since then.

<Conclusion> Though further treatment and longer follow-up is needed, the use of PTL combined with R-HT and chemotherapy will be a potential modality for treatment of advanced CRPC.

GSJ10 Poster / Short -Oral Presentation (Japanese)

Retrospective Analysis of Hyperthermia Therapy in 47 case of Unresectable Pancreatic Cancer

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<Objectives>

Gemcitabine-based chemotherapy or chemoradiotherapy is often used to treat unresectable, advanced pancreatic cancer. However, treatment outcomes remain unsatisfactory, and toxic effects such as vomiting and anorexia are frequent. We evaluated the therapeutic effectiveness and adverse events of hyperthermia therapy in patients with unresectable, advanced pancreatic cancer treated at our hospital.

<Subjects and Methods>

The study group comprised 47 patients who were given a diagnosis of unresectable, advanced pancreatic cancer (20 with stage IVa disease and 27 with stage IVb disease) from April 2007 through April 2014 and received hyperthermia therapy for at least 3 months. Hyperthermia therapy was performed with the use of Thermotron-RF8 once or twice per week. 33 patients concurrently received chemotherapy with gemcitabine.

<Results>

There were each of leucopenia and anemia as adverse events of grade 3. However, serious events was not observed in other patients. After 3 months of hyperthermia therapy, the response rate (CR+PR) was 2%, but the disease control rate (CR+PR+SD) was 85.1%. Survival from the time of disease onset ranged from 4 to 40 months, with a median survival time (MST) of 17.2 months. Progression-free survival ranged from 3 to 24 months, with a mean duration of 5.8 months.

<Conclusions>

Hyperthermia therapy has a low response rate in patients with unresectable, advanced pancreatic cancer, but may help to maintain stable disease for a prolonged period. Hyperthermia is considered a clinically significant, minimally invasive treatment with a low incidence of serious adverse effects.

GSJ11 Poster / Short -Oral Presentation (Japanese)

The effect and benefit of hyperthermia therapy combined with chemotherapy and/or hormonal therapy for breast cancer patients with liver metastasis.

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Background: Liver metastasis is one of the life-threatening factors for the breast cancer patients. Although there are a number of anticancer drugs for the treatment of breast cancer, the effect of them have limitations. We evaluate the efficacy and tolerability of mild hyperthermia therapy combined with chemotherapy and/or hormonal therapy for patients who have liver metastasis of breast cancer.

Objectives: We evaluated 12 patients who had diagnosed liver metastasis of breast cancer. They ware underwent weekly hyperthermia therapy combined chemotherapy and/or hormonal therapy more than 3 months duration in our institute.

Result: The duration of the therapy ranges 3 to 48 months and no severe adverse effects have occurred. Survival time after liver metastasis ranges 12-61 months (median 24 months). Six patients achieved 3 months or more progression free survival time. Three years survival rate after liver metastasis is 40.4%.

Conclusion: Hyperthermia therapy combined with chemotherapy and/or hormonal therapy could achieve long stable disease for liver metastasis of breast cancer. Furthermore, hyperthermia therapy is tolerable and might maintain the QOL of the patients.

GSJ12 Poster / Short -Oral Presentation (Japanese)

Treatment with hyperthermic intraperitoneal chemotherapy for pseudomyxoma peritonei arising from appendix, Report of 3 cases

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Pseudomyxoma peritonei is a rare and slowly progressive tumor arising from the appendix or bowel, which spreads throughout the peritoneal cavity and produces a large amount of mucus. We report three cases of pseudomyxoma peritonei, in which the hyperthermic intraperitoneal chemotherapy (HIPEC) following debulking the tumor were effective. Three patients (all female) were diagnosed as pseudomyxoma peritonei arising from appendix by CT scan or/and MRI. All of them underwent appendectomy and debulking surgery, followed by HIPEC with a protocol based on administration of cisplatinum 50mg/body, mitomycin C 10mg/body, and 5-FU 1000mg/body in 5 L of saline, at a temperature of 42 to 43 degree Celsius for 60 minutes. After the treatment, there was no mortality or significant complications associated with HIPEC. Two cases needed second HIPEC for local recurrence 4 months /2 years after first HIPEC. Now 1year/4years/3months have passed since their first HIPEC, no recurrent lesion is found in all cases. HIPEC following debulking surgery of pseudomyxoma peritonei arising from appendix was safe and effective for these three cases.

GSJ13 Poster / Short -Oral Presentation (Japanese)

Colon cancer with peritoneal dissemination and lung metastasis,survived for 22months received multidisciplinary treatment:A case report

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68-year-old female felt appetite loss and weight loss before 3 months, and consulted our hospital with abdominal distention before a week. The diagnosis was colonic ileus caused of ascending colon cancer, peritoneal dissemination and a lung metastasis. We performed emergency operation next day, not improve to use a long tube. Ascending colon cancer was unresectable for abdominal wall invasion and multiple peritoneal dissemination. Ileus had caused multiple small intestine stenosis by dissemination of mesentery, and stenosis of sigmoid colon by peritoneal dissemination. We performed operation (partial resection of small intestine (about 2m),bypass of ileum and transverse colon, sigmoidectomy and descending colostomy). Because of K-ras mutation and remained primary tumor and multiple peritoneal dissemination, it was difficult to use anti-EGFR antibody, bevacizumab and CPT-11. Therefore, we performed chemotherapy with 5 course of mFOLFOX6 regimen,after the 1st operation. After the chemotherapy,peritoneal dissemination were disappeared,and primary tumor and a lung metastasis were reduced, and new lesions were not appeared. Therefore,we performed right hemi-colectomy (D3), colostomy closure, and Hyperthermic IntraPeritoneal Chemotherapy (HIPEC). Final diagnosis was ascending colon cancer, T4bN1M1 (P3, lung). She had received chemotherapy with 10 courses of mFOLFOX6 regimen after the 2nd operation. But a lung metastasis was remained.We performed stereotactic body radiotherapy (50Gy/4fr) to the lung lesion. After the radiotherapy,she had been received chemotherapy with Uzel/UFT regimen. She is disease-free surviving, 22 months after the 1st operation. We reported a case of ascending colon cancer with peritoneal dissemination and a lung metastasis,surviving with disease-free after 22 months received multidisciplinary treatment(operation, chemotherapy, HIPEC, and radiotherapy). Recently, chemotherapy and molecular-targeted drugs for colorectal cancer were development, but peritoneal dissemination was difficult to long-term survival. But, like this case, chemotherapy were rarely good reactive for peritoneal dissemination, we considered to present cases possible for long-term survival by active treatment.We considered to HIPEC is effective for peritoneal dissemination from colorectal cancer, and widen clinical choice for treatment to peritoneal dissemination.

GSJ14 Poster / Short -Oral Presentation (Japanese)

Two cases of rectal cancer with urinary bladder invasion treated with chemo-hyperthermia and radiotherapy surviving with complete response (CR)

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Case 1: A 40 years-old generation male with an advanced rectal cancer that invaded to urinary bladder visited our hospital in April 2013. Radiotherapy, chemotherapy (5-FU/LV), and hyperthermia was performed. Then, 8 cycles of chemo-hyperthermia using mFOLFOX6 PR was added to this patient. Pelvic tumor showed complete response (CR). CR condition is still being maintained up to now.

Case 2: A 70 years-old generation male with an advanced rectal cancer that invaded to urinary bladder visited our hospital in June 2011. Chemo-hyperthermia was performed for the doubt of pulmonary metastasis. The first regimen for chemotherapy was mFOLFOX6 and the second one was Cmab- mFOLFOX6. Near CR of the pelvic tumor and disappearance of pulmonary metastasis was obtained by chemo-hyperthermia. Additional radiotherapy, chemotherapy (Cmab-5-FU/LV), and hyperthermia was performed from January to March 2012. The pelvic tumor came to CR, and it remains CR up to now.

GSJ15 Poster / Short -Oral Presentation (Japanese)

Chemo-hyperthermia with hyperbaric oxygen therapy for stage IVb pancreatic cancer

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Backgrounds: To evaluate the efficacy of systemic chemotherapy using gemcitabine plus regional hyperthermia and hyperbaric oxygen treatment for stage IVb pancreatic cancer.

Methods: Fourteen pancreatic cancer patients clinically diagnosed as stage IVb (mean age, 60.9; males, n = 7) were included in this study. Of 14 cases, 6, 4 and 4 cases presented with retroperitoneal lymph node metastasis (LN), other organ metastasis (OM) and peritonitis carcinomatosa (PC), respectively. Weekly gemcitabine was chosen as a first line chemotherapy, and S-1 was selected as a second line. Just after chemotherapy, a combination of hyperthermia and hyperbaric oxygen therapy was performed. Radiotherapy was performed for 7 cases with locally abdominal tumor.

Results: Median overall survival was 13.1 months and 1 year survival rate was 47%. The median overall survival for the LN group (19.0 months) was much longer than that for the OM group (8.1 months) or the PC group (5.7 months).

Conclusions: As for the stage IVb pancreatic cancer treatment, the systemic chemotherapy using gemcitabine plus regional hyperthermia, hyperbaric oxygen treatment, and radiotherapy could contribute patients to prolong survival, especially in the case of retroperitoneal lymph node metastases.

GSJ16 Poster / Short -Oral Presentation (Japanese)

Preliminary result of hyperthermochemoradiotherapy using IMRT and capecitabine for advanced low-rectal cancer

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[Purpose] It is reported that the preoperative chemoradiotherapy for locally advanced low-rectal cancer contributes to the improvement of a local control rate and the anal preservation rate. In this hospital, concurrent hyperthermia for chemoradio-sensitization is added to preoperative chemoradiotherapy. Phase I, II Clinical trial of preoperative concurrent hyperthermochemoradiotherapy (HCRT) was started from December, 2011. We report a preliminary result of treatment response and acute adverse events of this study.

[Subject, method] Eligible patients had previously untreated T3 or T4 locally advanced Rb-rectal cancer without metastasis. Fifteen patients were enrolled in this study. The median follow-up time was 11.3 months (3.0-24.1 months). The median age was 58 years old (38-70 years old). Twelve were male, 3 were female. Clinical T3 was 12, and cT4 was 3, respectively. Lymph node metastasis, diagnosed by minimal diameter >10mm, was observed in seven patients. Intensity modulated radiation therapy (IMRT) using Tomo Therapy was performed, by the total dose of 50Gy/25fr., five times per week. Chemotherapy consisted of Capecitabine, 1,700 mg/m^2/day, and it was administrated concurrently during radiation therapy. The hyperthermia using Thermotron-RF8 was given once a week, total of 5 times. Surgery was undergone in 8-10 weeks after HCRT. We evaluated the initial treatment response based on imaging of post HCRT and postoperative histopathological findings and evaluated the acute adverse event using National Cancer Institute-Common Toxicity Criteria (Ver 4.0).

[Results] Planned preoperative HCRT was performed in all 15 patients. Of 15 patients, surgery was performed in 9 patients. Four patients refused the surgery, and one assessed to be inoperable. In 9 cases underwent surgery, Grade 3 pathological effect was observed in 3 patients (33%). Anal preservation was possible in 8 of 9 cases (89%). The acute adverse events Grade 3 or more was not observed.

[Conclusion] A good pathological effect and an anal preservation rate were shown in preoperative HCRT for advanced inferior part rectal cancer. Severe acute adverse event was not observed, preoperative HCRT was considered to be tolerable encouraging with response rates.

GSJ17 Poster / Short -Oral Presentation (Japanese)

Combination therapy combining low dose chemotherapy and regional hyperthermia for the treatment of castration-resistant prostate carcinoma

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Castration-resistant and progressive prostate carcinomas are difficult to treat and therefore have a poor prognosis. A new therapeutic modality is proposed herein which consists of combination therapy combining low dose chemotherapy and regional hyperthermia delivered with an 8 MHz-RF. Twenty patients were enrolled from April, 2004 to December, 2013 and were treated in the Nagoya Prostate Center. These patients were all classified as having stage D2 progressive castration resistant prostate carcinomas, and their Gleason scores ranged from 7 to 9. Cisplatin(5 mg/body weight) or Docetaxel(5 mg/body weight was administered intravenously at weekly intervals one hour before regional hyperthermia, and was applied for maximum of 10 cycles. Of the twenty patients evaluated, fifteen cases were confirmed to have achieved a greater than 50% decrease in prostate specific antigen(PSA) levels(75.0%). The regimen was well tolerated, minor general fatigue was recognized in 3 cases.

GSJ18 Poster / Short -Oral Presentation (Japanese)

Two cases of small cell lung cancer (SCLC) treated with multidisciplinary treatment surviving with good disease control

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Case 1: A 63-year-old woman with a history of 4 cycle's chemotherapy treatments for stage IV (T4N3M1a) SCLC visited our hospital in January 2011. Radiotherapy, chemotherapy (CPT-CDDP), hyperthermia and hyperbaric oxygen therapy was performed for thoracic tumor. Though PR was obtained, recurrence of mediastinal tumor with right atrium invasion was found in October 2012. Thereafter, 3 times of multidisciplinary therapy were performed and she survives with tumor-bearing up to now.

Case 2: A 70-year-old man was admitted to our hospital for treatment of stage IIIB (T4N2M0) SCLC in January 2011. Radiotherapy, chemotherapy (CPT-CDDP), hyperthermia and hyperbaric oxygen therapy was performed. PR was obtained and maintenance chemo-hyperthermia was performed for 15 months. Liver metastasis was found in October 2012. Multidisciplinary therapy was performed and he survives with tumor-bearing up to now.

GSJ19 Poster / Short -Oral Presentation (Japanese)

Long-term outcomes of hyperthermic treatment combined with chemotherapy for patients with residual or recurrent esophageal cancer after definitive chemoradiotherapy

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Backgrounds: Definitive chemoradiotherapy (dCRT) is frequently applied for esophageal cancer. The increased use of dCRT has resulted in increases in either residual or recurrent disease after dCRT. However, there is no established salvage therapy for esophageal cancer after the failure of dCRT. The efficacy of chemoradiation is generally affected by the blood flow and oxygenation in the tumor. Hyperthermic therapy can improve these conditions by heating the lesion and is a less invasive treatment than chemotherapy, radiotherapy or surgery. We have carried out hyperthermochemotherapy (HCT) for residual or recurrent cases after dCRT for esophageal cancer. The purpose of this study was to elucidate the usefulness of salvage HCT for unresectable or recurrent esophageal cancer.

Method: HCT was performed for 11 patients with residual or recurrent esophageal cancer. The patients had all received dCRT for esophageal squamous cell carcinoma between 2005 and 2009 at our institute. Seven patients had recurrent primary tumors after dCRT for unresectable esophageal cancer, while hyperthermia was performed for recurrent lymph node disease after dCRT in the other four patients who underwent curative esophagectomy. We used an 8-MHz radiofrequency heating system (Thermotron RF-8, Yamamoto Vinita Co, Ltd, Osaka, Japan) for the hyperthermic therapy with 400 - 1200 W for 50 min once or twice per week. The combined chemotherapy comprised cisplatin/5-fluorouracil (5-FU) or an oral fluoropyrimidine (S-1).

Results: Salvage HCT was performed for 11 patients. The treatment was conducted for 2-26 cycles. HCT was tolerated by all patients. The best responses to HCT were as follows: a complete response (CR) was achieved in three patients and stable disease (SD) was noted in five patients. The symptoms, such as dysphasia, were improved in the other three patients. There were no severe (NCI-CTC Grade 3 or 4) adverse events caused by hyperthermia. One patient, who obtained a CR, is still alive, while the other 10 patients have died. The surviving patient has maintained a good quality of life as an outpatient for 88 months after the start of HCT. The median survival time after HCT was 12 months (3-88 months).

Conclusion: HCT is therefore considered to be a feasible and potent salvage therapy for patients with residual or recurrent esophageal cancer after dCRT, unless salvage surgery is indicated.

GSJ20 Poster / Short -Oral Presentation (Japanese)

Sequential boost HCRT using IMRT after conventional 3DCRT for cervical esophageal squamous cell carcinoma: Pilot experience in 6 patients.

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PURPOSE: To investigate the efficacy and safety of sequential boost hyperthermo-chemo-radiotherapy (HCRT) using Intensity Modulated Radiation Therapy (IMRT) after conventional 3D conformal radiation therapy (3DCRT) for cervical esophageal squamous cell carcinoma (ESCC).

PATIENTS AND METHODS: Six Patients with cervical ESCC received conventional 3D conformal radiation therapy (3DCRT) with 40Gy and concurrent chemotherapy using DCF (docetaxel (50 mg/m^2) and cisplatin (60 mg/m^2) on day 1 and a continuous intravenous infusion of 5-fluorouracil (600 mg/m^2/day) on days 1 to 5), or FP (cisplatin (70 mg/m^2) on day 1 and a continuous intravenous infusion of 5-fluorouracil (700 mg/m^2/day) on days 1 to 5). Sequentially, they received boost HCRT using IMRT and concurrent FP. Hyperthermia was performed using an 8-MHz radiofrequency (RF)-capacitive regional hyperthermia device (Thermotron RF-8) once a week for 50 minutes in two weeks. The clinical complete response (cCR) rate for primary tumors, cCR rate for lymph node metastasis and toxicity were investigated.

RESULTS: Characteristics of the 6 Patients were; median age, 65 years; TNM classification, T4bN2M1LYM in one patient, T4bN1M0 in one patient, T3N2M1LYM in one patient, T3N1M0 in two patients, T2N1M0 in one patient. For primary tumors, of 6 patients, 5 had a local cCR for primary, 1 had a stable disease. The cCR rate for primary tumors was 83%. For lymph node metastasis, 1 had cCR, 3 had a partial response, 1 had a stable disease and 1 had a progressive disease. The cCR rate for lymph node metastasis was 16.7%. Grade 3 toxicity were leukopenia (66.7%), neutropenia (50.0%), hypokalemia (16.7%).

CONCLUSIONS: Sequential boost HCRT using IMRT after conventional 3DCRT is well tolerated and has the potential to improve the rates of locoregional control in patients with cervical ESCC.

GSJ21 Poster / Short -Oral Presentation (Japanese)

Re-irradiation with hyperthermia in patients with recurrent tumor

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Background Re-irradiation may induce serious complications because of over dosage to previously irrdiated areas. We have applied regional hyperthermia with re-irradiation to more effective and less toxic.

Methods 25 cases and 27 sites in which local recurrence was observed after radiotherapy and re-irradiation was performed concurrently with hyperthermia therapy. Primary disease included breast 8, lung 6, rectum 4, liver/ bile duct/ esophagus/ ovary/ skin 1. The period from previous radiation was 3 to 68 months (median 13 months) and the doses were 39 to 79Gy (median 50Gy).

Results For primary responce, 21 of the 27tumors responded to the treatment (CR:1, CRh:2, PR:11, pain relief:7 NC:2 NCh:1, PD:1, no pain relief:1). The median recurrence time was 10 months in effective patients and median survival was 13 months in all cases. No patient has experienced significant treastment-induced acute/late side effect.

Conclusion Re-irradiation with hyperthermia in patients with recurrent tumor yielded no serious side effect and good local control.

GSJ22 Poster / Short -Oral Presentation (Japanese)

Two cases of myxofibrosarcoma treated with Radiohyperthermochemotherapy (RHC)

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The current standard care for local treatment of extremity soft tissue sarcoma (STS) favors limb preservation over amputation. Most patients with extremity STS undergo wide or radical resection combined with pre/postoperative radiotherapy. Myxofibrosarcoma (MFS) is a historically heterogeneous group of tumors that exhibit a propensity for local recurrence. The subject are two patients, two males, 61 and 69 years old. The follow-up period is 29 and 17 months. The affected sites are forearm and lower leg, both located superficially. One patient had been had wide resection only in our hospital and recurred at 12months after surgery. Another patient had primary tumor. After treatment of RHC according to our protocol, wide resection and reconstruction surgery was done. Surgical margin was both microscopically positive. One patient received additional postoperative radiotherapy, and another patient received postoperative chemotherapy. At present, neither recurrence nor metastasis occurs. In several literatures, 15 to 60% of local recurrences rates are reported. Some experts have suggested that the perceived high propensity of MFS to recur locally is caused by a characteristic infiltrative growth pattern with extension along vascular and fascial planes, besides it can penetrate fascia. For these nature, positive surgical margin rates are high in MFS and those may cause high recurrence rate. Nicole et al. reported that the use of radiotherapy, in tandem with aggressive surgical resection, demonstrated low rate of recurrence. In this study, despite microscopically positive margin, no local recurrence has occured. The RHC is expected to prevent local recurrence of MFS.

GSJ23 Poster / Short -Oral Presentation (Japanese)

Chemoradiotherapy combined with hyperthermia and hyperbaric oxygen therapy for three cases of malignant fibrous histiocytoma (MFH)

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Backgrounds: The purpose of this study was to evaluate the efficacy of chemoradiotherapy combined with hyperthermia and hyperbaric oxygen therapy for MFH.

Methods: The patients were 3 cases, all were males, mean age were 68.6.1 case was treatment for primary lesion with axillary lymph node (LN) lesion, remaining 2 cases were recurrence with retroperitoneal lesion and metastasis with mediastinal LN. Radiotherapy, chemotherapy, hyperthermia and hyperbaric oxygen therapy was performed for these lesions. For the new recurrence lesion, combination of these therapies was performed appropriately.

Results: In the retroperitoneal recurrence case, we were able to continue treatment from a recurrence for five years four months. The local control of a treated part was good, and it seems that this led to prognostic extension.

Conclusion: Chemoradiotherapy combined with hyperthermia and hyperbaric oxygen therapy for MFH could contribute to a better clinical outcome and it was suggested that these treatment was very useful.

GSJ24 Poster / Short -Oral Presentation (Japanese)

A fundamental study for the mechanism of cell death by special effects of microwave

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Introduction

Microwave can generate heat efficiently and has been used cancer therapies, such as microwave coagulation therapy and hyperthermia. On the other hand, special effects of microwave called 'non-thermal effects' which are different from heat generation have been discussed recently. We suggest that cancer cell death derived from microwave irradiation is related to non-thermal effects. To investigate this hypothesis, we developed 2.45 GHz semiconductor microwave generator and application which can regulate microwave output and temperature of medium minutely. Using this device, we examined the proliferation of human promyelocytic leukemia HL-60 cells under the irradiation of microwave. In addition, we investigated the mechanism of this cell death in detail.

Materials and Methods

HL-60 cells were seeded in 35 mm dish at a density of $5x10^5$ cells/mL and were irradiated under microwave for 1 hr. Dishes were incubated in microwave applicator at 12ºC and irradiated microwave on condition that cells in dishes were fixed at 37ºC. Negative and positive control groups were incubated without microwave irradiation at 37ºC and heat-stressed at 42.5ºC, respectively. It was found that almost all of cells lived in the negative control group, whereas apoptotic cell death is occurred in the positive control group. After irradiation with microwave, cells were incubated for 24 h in 5% CO_2 incubator at 37ºC. And then cellular proliferation and mechanism of cell death were investigated.

Results and Discussions

Cellular proliferation and viability of HL-60 cells decreased by microwave irradiation at 37ºC and the proliferation rate at this condition has almost the same value at 42.5ºC. As the mechanism of cell death analysis, cell cycle analysis and annexin V and propidium iodide (PI) staining assay were performed, and few Sub G_0G_1 cells existed in the microwave irradiation group and there were more late apoptotic/necrotic cells compared to the positive control group. In addition, assay for caspase 3/7 activity and expression of heat shock protein 70 (HSP70) were conducted, and cells were observed under confocal laser scanning microscopy by hoechst33342 and PI staining. The caspase 3/7 activity and expression of HSP70 in the microwave irradiation group were significantly lower than the positive control group and nuclear fragmentation was not observed in the microwave irradiation group but observed in the positive control group. It is suggested that the mechanism of cell death by microwave irradiation at 37ºC was different from these of heat-stressed cell death and would be related to non-thermal effects.

GSJ25 Poster / Short -Oral Presentation (Japanese)

Change of QOL and stage of cancer progression for patients getting long-term hyperthermia treatment

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<Purpose>

We have been using THERMOTRON-RF8 in our hospital for 12 years. At the end of March 2014, total 1502 patients were treated with hyperthermia. The patients treated with long-term treatment have also been increasing. The hyperthermia treatment has yielded good outcomes in therapeutic effects and QOL of the patients. In this study, we have collected the QOL questionnaires from the patients and analyzed the effect of the hyperthermia treatment by comparing change of QOL and stage of cancer progression

<Method>

15 patients continued hyperthermia treatment more than 5 years in our hospital. We excluded those who are in stage I, II and whose questionnaires are less than 5 times, and the rest 12 patients were studied. We compared change of their stage of cancer progression by CT images and QOL deduced from their questionnaires conducted every 3 to 6 months in a period.

*QOL questionnaire is 900 point scale with nine items and five-level.

We set QOL evaluation standards as within 100 points difference between first and last answer of questionnaire is conservation, more than that is increase and less than that is decrease.

<Study patients>

Treatment period: 60 months to 118 months<avg. 84.7months>

Ratio of male to female: Male 3 patients,Female 9 patients

Age: 35 to 83<avg. 65.2>

<Result>

1, 7 patients: CT - No change in tumor size / Questionnaire comparison -Wthin100 points difference QOL has been keeping.

2, 1 patient: CT - No change in tumor size / Questionnaire comparison -425 points increase QOL has been increased.

3, 1 patient:CT - Left lung tumor disappeared, right lung tumor getting worse / Questionnaire comparison - Within 100 points difference QOL has been keeping.

4, 1 patient: CT - Multiple metastasis at cervical lymph node / Questionnaire comparison -325 points decrease QOL has been decreased.

5, 1 patient: CT- Achoresis of cervical lymph node tumor / Questionnaire comparison -125 points increase QOL has been increased.

6, 1 patient: CT- Getting worse of peritoneal dissemination / Questionnaire comparison -200 points increase QOL has been increased.

<Consideration>

The hyperthermia treatment has few side effects so that it seems efficient method of treatment to keep high QOL level of the patients for long-term.

Further, we need to seek for a way how the change of QOL would be associated with evaluation of treatment.

GSJ26 Poster / Short -Oral Presentation (Japanese)

Usefulness of pat and jelly in hyperthermia

Mai Ito[1], Hideyuki Morosawa[1], Yoshiki Miya[1], Yumiko Sato[1], Yoshihiko Furuta[1],
Katsuyuki Aketa, Yoshiyuki Yanai, Rika Fukui, Takahiro Yasoshima, Motoharu Kondo

[1]Shinsapporo Keiaikai Hospital Department of Clinical engineering, Japan

<Purpose>

During treatment to rise output, many people heat and pain to the skin often. We report to perform treatment by changing the method of jelly and pat, a case of considering again the usefulness of as improvement of heat and pain.

<Method>

Do treatment to the upper abdomen in the supine position. Electrode using the 30cm in both back and abdominal. Circulation water temperature setting 5 degrees abdomen, back to 15 degrees.Pat Yamamoto Binita Corporation, jelly using Sonojelly of Toshiba Corporation.

I want to record the output where the output at the start of each 50w up to every two minutes at 600w, heat came out. Pat and jelly are compared using the four methods of M1 not jelly and pat, M2 only jelly, M3 jelly and three pats of 30cm, M4 jelly and one pat of 30cm.

<Subject>

Five men our hospital staff

1. 25years old, height 182cm, weight 70kg, BMI21.1
2. 25years old, height 166cm, weight 58kg, BMI21.0
3. 26years old, height 173cm, weight 75kg, BMI25.0
4. 34years old, height 168cm, weight 72kg, BMI25.5
5. 32years old, height 181cm, weight 55kg, BMI16.7

<Result>

1. M1 650w, M2 1050w, M3 1100w, M4 1000w
2. M1 600w, M2 650w, M3 900w, M4 850w
3. M1 700w, M2 700w, M3 750w, M4 750w
4. M1 700w, M2 700w, M3 800w, M4 750w
5. M1 1500w, M2 1500w, M3 1500w, M4 1500w

Output is the lowest way not jelly and pat, without putting subject other than 5, I was able method using a pat of 30cm and jelly increase the output most. After the heat has appeared, but did not reduce the heat A decrease in output. Only 5 did not appear to heat in any way.

<Consideration>

Did not improve heat in the adjustment of the output. Jelly is considered to be useful because the output was lower in the method without jelly and pat. It is believed to be the most useful for the method using a pat of 30cm were raised output the most.

GSJ27 Poster / Short -Oral Presentation (Japanese)

Hyperthermia as an effective alternative treatment for advanced cancers refractory to conventional therapies

Hiroshi Terunuma[1], Atsushi Toki[1], Atsushi Terunuma[1], Akiko Yoshimura[1],Tatsuaki Ishiguro[1], Noriyuki Nishino, Yoshinao Takano, Kan Abe, Yasushi Teranishi, Kazuo Watanabe[1]

[1] *Tokyo Clinic, Tokyo, Japan*

Hyperthermia is well known to enhance the effects of radiotherapy in cancer treatment. Recently, hyperthermia has been tried in combination with chemotherapy or immunothearpy because hyperthermia increases the uptake of anti-cancer drugs by tumors and also activates immune reaction against cancer cells. Most advanced cancers eventually become refractory to conventional therapeutic modalities and patients are suggested to take palliative care, also known as 'best supportive care (BSC)', as the only choice. However, patients and their family often eagerly seek alternative therapies to BSC. In such situation, hyperthermia can serve as an option to treat the disease. When combined with low-dose chemotherapy, immunotherapy, or both, hyperthermia can improve the clinical outcome of patients with advanced cancers.In this presentation, we demonstrate successful cases of hyperthermia, when combined with low-dose chemotherapy, immunotherapy or both, in treating cancers that were refractory to conventional therapies. The results suggest that hyperthermia is useful in treating advanced cancers with a limited choice of effective treatment.

GSJ28 Poster / Short -Oral Presentation (Japanese)

Numerical evaluation on heating characteristics of microwave forceps with cutting blade

Yuta Endo, Yoshito Tezuka, Kenta Suzuki, Kazuyuki Saito, Koichi Ito

Chiba University, Japan

<Introduction> In recent years, bipolar electric scalpel forceps has widely been used in the surgery for hemostasis, blood vessel sealing and so on. It employs the radio frequency (RF: from several hundred kHz to several MHz) current. Biological tissue grasped between pair of active electrode is coagulated by joule heating. Here, since the device generates excessively high temperature, the biological tissue is carbonized and adheres to active electrode of the device. Adhesion of carbonized tissue increase rebleeding risk. By the way, heating effect of biological tissue by the microwave energy is not so excessively compared to that of the RF current. Therefore, coagulation devices using microwave energy can safely heat biological tissue without carbonization. We have been studying a novel microwave coagulation device capable of cutting thin biological tissue such as blood vessel. This device has the grasping mechanism like bipolar electric scalpel forceps. This device is consisted of an upper part equipped with heating antenna and a lower part equipped with a cutting blade. Thin biological tissue is grasped between those parts and heated by the heating antenna. Then, coagulated tissue can be cut with the cutting blade.

<Method> In this study, heating characteristics of the proposed device are evaluated by the thermal analysis using the SAR (specific absorption rate) calculated in electromagnetic field analysis, as a heat source. We employed the finite-difference time-domain (FDTD) method for numerical calculation.

<Result> As a result, grasped region of biological tissue model was heated over 60 oC within 10 seconds. In this study, we are assuming that the coagulation temperature of biological tissue is 60 oC.

<Discussion> Results of this study show that the proposed device has sufficient heating capability. As a further study, cutting mechanism of the device will be investigated.

GSJ29 Poster / Short -Oral Presentation (Japanese)

Evaluation on heating performances of microwave forceps for biological tissue coagulation

Kazuyuki Saito, Kenta Suzuki, Yuta Endo, Koichi Ito

Center for Frontier Medical Engineering, Chiba University, Japan

Introduction

Recently, various types of medical applications using microwave energy have widely been investigated and reported. In this study, microwave tissue coagulation device, which is employed microwave thermal effect, is developed. Until now, the authors have investigated some different type of devices. In this time, forceps type device is introduced and heating performances of it is evaluated.

Material and method

In the forceps type device, the biological tissue is grasped between upper part equipped with heating antenna and lower part. The grasped tissue is heated by the heating antenna with helical structure. The heating characteristics of the antenna is evaluated with numerical calculation by finite-difference time-domain (FDTD) method and finite-difference computation of bioheat transfer equation. Moreover, an animal experiment is also performed for confirmation of its validity.

Results

According to results of the numerical calculations, enough temperature rises (more than 60 oC) around the forceps device for tissue coagulation could be observed. Moreover, during the animal experiment of swine, blood flow of mesentery could be stopped by the microwave radiation.

Conclusion

In this study, forceps type tissue coagulation device by the microwave energy have been introduced. As a result of numerical calculation, effective temperature rise was observed. Moreover, ability to stop bleeding could be confirmed in the living tissue.

GSJ30 Poster / Short -Oral Presentation (Japanese)

Hyperthermia and team medical treatment

Keishi TAKEDA[1], Hisako KOBAYASHI[1], Kazuma SHIBUYA[1], Yuuya SHIGEMATSU[1], Yoshiki KON[1], Hiromichi SAKAGAMI[1], Hideyuki MOROSAWA, Yoshiyuki YANAI, Takahiro YASOSHIMA, Motoharu KONDOU

[1]*Shinsapporo Keiaiaka Hospital Radiology department, Japan*

Team Approach to Health Care is practiced by cooperation and complement with a variety of medical staffs. The following are expected as concrete effect caused by Team Approach to Health Care;1,Improvement of medical quality <e.g. Early detection of disease, stimulating recovery, and presentation of exacerbation> 2,mitigation of the burden for medical workers by improving medical efficiency 3,improvement of safety of medical by standardization and systematization.

In our hospital, we have started team approach to health care since 2007, and built the system extending and overlapping the service in other fields to mitigate the burden for doctors and nurses. Radiology technicians have also started new works such as assisting of image reading or explaining about radiographic examination.

We introduced in 2002.Thermotron RF-8; developed in cooperation with Yamamoto Vinyter Co.in 2002. 3 machines are currently in service and work 400~500 times in a month.

Clinical engineers were in charge if the treatment at first but we decided that Radiology technicians operated one out of three machines since September, 2010 because clinical engineers participated not only on hyperthermia but also in operating, medical device management and dialysis.

We didn't have radiation therapy devices and radiology technicians didn't involve in treatment directly but that became possible due to hyperthermia. Therefore, it became possible for radiology technicians to get information of treatment <e.g. only hyperthermia, hyperthermia + chemotherapy, hyperthermia + radiation therapy, and hyperthermia + immunotherapy> and they get to interpret radiograms while considering treatment outcome. This caused stabilization of medical service and establishing the new system supporting works in hospital ward by clinical engineers. This also caused reducing burdens on work of nurses indirectly and promoting team approach health care.

Radiology technicians will be required to recognize the treatment area by reading inspection images and enhance the effectiveness of curative effect, and get qualification certified by Japanese Society for Thermal Medicine as workers participating in hyperthermia in the future.

GSJ31 Poster / Short -Oral Presentation (Japanese)

Improvement of heating methods of hyperthermia under daily clinical practice by team medical care

Rumiko Yamada[1], Wakana Tanaka[1], Fumi Sasaki[1], Yukari Seita[1], Nozomi Kouta, Sachiko Suzuki, Saki Sato, Atsushi Toki[1], Hiroshi Terunuma[1]

[1] *Tokyo Clinic, Japan*

Hyperthermia is a useful therapeutic method against cancer. In our daily clinical practice we are using Thermotron RF8 for hyperthermia treatment. Thermotron RF8 is an 8-MHz radiofrequency (RF) heating device. In our clinic hyperthermia was administered regionally with this device supported by the hyperthermia team including nurses, medical engineers, laboratory technicians as instructed in doctors. To perform effective heating, it is important to reach high-power RF output for enough time. To achieve high power RF output for enough time, the team members shared the information on patients and discussed how to do hyperthermia for each patient. To motivate patients toward hyperthermia, the team members also explained the meaning of hyperthermia for cancer treatment to patients. Through these efforts of the team, the RF output and the heating time for treatment improved. In conclusion, the team medical care is useful efforts to maximize the capacity of the device.

GSJ32 Poster / Short -Oral Presentation (Japanese)

Investigation of thermal efficiency in measures of hot spot with hyperthermia

Kaname Oka[1], Risa Bito[1], Kana Kawasaki[1], Yoshiaki Fujii[1], Tatsuzo Matsuyama[1], Tetsuya Okayama, Satoshi Kokura

**Takeda clinic, Japan*

<Background and purpose> Patients who receive hyperthermia treatment sometimes feel the excess heat sensation and the pain at electrode area (this phenomenon is called as "hot spot" phenomenon). Once patients feel hot spot, the operator of hyperthermia can't turn up the sufficient electromagnetic wave power. The alleviation of hot spot is very important for more effective hyperthermia treatment.So we need to take measures for easing hot spot. The procedures to ease hot spot in our clinic are 1) installation of a water pat, 2) massage using cold gel, 3) switching from normal mode to the mode of the intermittent oscillation. While these procedures often lead to ease pain of patients, we need to pay attention to occur the attenuation of the electromagnetic wave transmission and the decrease in thermal efficiency.So in this study, we evaluated thermal efficiency with our procedures for hot spot.<Materials and methods> We used the agar phantom as a simulated human body for measure of temperature. We set generating power as 1200 or 1500W. Total 4 thermometers were set in the phantom at surface and inside (2 at surface and 2 at inside) in imitation of patient's skin and inside body respectively. We measured temperature with thermometers during the electromagnetic radiation with or without our procedures. In addition, we measured inside temperature of phantom with thermography after the electromagnetic radiation. Thermal efficiency was calculated as follows: (alteration of temperature after radiation with procedure) divided by (alteration of temperature without procedure) multiplied by 100 (%)<Results> The result of thermal efficiency with a water pat was 95%, and with the mode of the intermittent oscillation was 80%. While thermal efficiency of several massage (5 seconds, 3 times) with cold gel was 96.5%, frequent massage (30 seconds, 3 times) reduced thermal efficiency to about 90%. <Conclusion> The procedure with a water pat makes it possible to augment the electromagnetic wave power in many cases because this procedure can alleviate patients' discomfort well. Thermal efficiency of intermittent oscillation was 80% and this result consist with the theoretical value, 4 seconds break after 20 seconds oscillation. So we need to turn up 20% power when we use intermittent oscillation compared with previous normal mode to get sufficient thermal efficacy. In addition we also should be careful about the attenuation of thermal efficiency with frequent massage.

GSJ33 Poster / Short -Oral Presentation (Japanese)

Noninvasive Temperature Measurement during Acupuncture Treatment Using MRI

Suguru Nakamura[1], Masamichi Nakamura, Eiichi Maeda, Yoshio Nikawa[1]

[1]*Kokushikan University, Tokyo, Japan*

[Purpose] Various heating treatments are performed in the medical field throughout the world. To monitor the temperature distribution in the treatment area, it is strongly recommended to develop a noninvasive temperature measuring technique. Due to the fact that the temperature change can generate minute difference in the physical parameter in tissues, It becomes very difficult to measure the temperature change noninvasively for the deep target. Recent development of electromagnetic wave technique enables noninvasive temperature measurement inside the material using Magnetic Resonance Imaging (MRI). In this paper, the temperature distribution is measured using MRI by measuring the phase of longitudinal relaxation time of proton. [Methodology] Measurement of temperature distribution with imaging of temperature elevation in human leg during acupuncture treatment on the skin patch at ST 36 in shank has been performed using equipment of MRI. The MRI equipment used a static magnetic field value of 0.3 Tesla. In this experiment, silver acupuncture needle is applied not to disturb external magnetic field. [Result] Result of temperature elevation distribution can be obtained by phase change of T1 of MRI signal in human leg. The result of temperature distribution of deep tissue using MRI and the result of surface temperature distribution using thermometer were compared and reported. [Conclusions] Using MRI, temperature distribution inside human shank at ST36 has been measured. The measured temperature using MRI under acupuncture treatment was obtained. This paper concluded that the noninvasive temperature distribution measurement is an innovative methodology for research in the not only traditional oriental medicine but also western medicine and hyperthermia field.

GSJ34 Poster / Short -Oral Presentation (Japanese)

BAG3 acts protectively against Hyperthermia-induced apoptosis through modulation of nuclear factor kappa B activity in human retinoblastoma Y79 cells

Tatsuya Yunoki[1], Yoshiaki Tabuchi, Takashi Kondo[1]

[1]*Department of Radiological Sciences, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Toyama, Japan*

<Background and purpose> Patients who receive hyperthermia treatment sometimes feel the excess heat sensation and the pain at electrode area (this phenomenon is called as "hot spot" phenomenon). Once patients feel hot spot, the operator of hyperthermia can't turn up the sufficient electromagnetic wave power. The alleviation of hot spot is very important for more effective hyperthermia treatment.So we need to take measures for easing hot spot. The procedures to ease hot spot in our clinic are 1) installation of a water pat, 2) massage using cold gel, 3) switching from normal mode to the mode of the intermittent oscillation. While these procedures often lead to ease pain of patients, we need to pay attention to occur the attenuation of the electromagnetic wave transmission and the decrease in thermal efficiency.So in this study, we evaluated thermal efficiency with our procedures for hot spot.<Materials and methods> We used the agar phantom as a simulated human body for measure of temperature. We set generating power as 1200 or 1500W. Total 4 thermometers were set in the phantom at surface and inside (2 at surface and 2 at inside) in imitation of patient's skin and inside body respectively. We measured temperature with thermometers during the electromagnetic radiation with or without our procedures. In addition, we measured inside temperature of phantom with thermography after the electromagnetic radiation. Thermal efficiency was calculated as follows: (alteration of temperature after radiation with procedure) divided by (alteration of temperature without procedure) multiplied by 100 (%)<Results> The result of thermal efficiency with a water pat was 95%, and with the mode of the intermittent oscillation was 80%. While thermal efficiency of several massage (5 seconds, 3 times) with cold gel was 96.5%, frequent massage (30 seconds, 3 times) reduced thermal efficiency to about 90%. <Conclusion> The procedure with a water pat makes it possible to augment the electromagnetic wave power in many cases because this procedure can alleviate patients' discomfort well. Thermal efficiency of intermittent oscillation was 80% and this result consist with the theoretical value, 4 seconds break after 20 seconds oscillation. So we need to turn up 20% power when we use intermittent oscillation compared with previous normal mode to get sufficient thermal efficacy. In addition we also should be careful about the attenuation of thermal efficiency with frequent massage.

GSJ35 Poster / Short -Oral Presentation (Japanese)

Effects of whole-body heat treatment on T cell-mediated immune response in cancer patients

Yusuke Ito, Yasunobu Kobayashi, Ayumi Yatagawa, Yuka Matsuura, Keishi Tanigawa

Bio-Thera Clinic, Japan

Increase in body temperature has been thought to play an important role for regulation of immune responses, and accumulating evidence in thermal medicine indicates that hyperthermia could be useful combination therapy to enhance the efficacy of cancer immunotherapy. However, the intrinsic effects of elevated body temperature on the immune system, particularly in humans are poorly understood. The aim of this study is to examine the effects of increase in core body temperature on the induction of T cell-mediated immune responses in cancer patients who received dendritic cells (DCs)-based vaccination therapy.

Patients with various solid tumor were vaccinated once a week with antigen-pulsed DCs vaccine prepared from autologous monocyte-derived DCs. These DCs were pre-treated with tumor antigenic peptide as well as KLH as a vaccine adjuvant, and were injected intradermally near an inguinal nodal region. Some patients simultaneously received whole-body hyperthermia in combination with DC-vaccination. For whole-body hyperthermia, patients were exposed to infrared A using heckle HT-3000 until the rectal temperature reached at 38.5 deg C. They were then wrapped in synthetic leather tent for 60 min in order to maintain the core body temperature above 38.5 deg C.

To assess the induction of immune responses in patients who received antigen-pulsed DC-vaccination, we examined the onset of skin reaction at vaccination site. The onset of this DTH-like skin reaction indicates antigen specific T cell response was established, and we thus examined how much vaccine treatment was required in each patients whose skin reaction sizes after 48 hours of DC-vaccination became larger than 1.5 cm in diameter two times in a row. The average number of vaccination in patients who received DC-vaccination only was 3.94. By contrast, in patients who received both DC-vaccination and whole-body hyperthermia, induction of skin reaction appeared to be slightly accelerated, and the average number of vaccine treatment was 3.53.

We conclude that whole-body heat treatment in fever-range appeared to make a positive impact on the induction of T cell-mediated immune response, and could be a possible combination therapy to enhance the efficacy of DC-based vaccination therapy.

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2013年11月作成

HIPEC トレーニングコース

日　時：**平成 26 年 9 月 6 日 (土) 大会 2 日目　12:00 ～ 17:30**

会　場：**AOSSA**

〒 910-0858 福井県福井市手寄 1 丁目 4-1
http://www.aossa.jp/
第 1 会場：福井県県民ホール（AOSSA 8 階）　Tel:0776-87-0003, FAX:0776-87-0303
第 2 会場：福井市地域交流プラザ (AOSSA 6 階)　Tel:0776-20-1535, FAX:0776-20-1536

概　要：

1. ランチョンセミナー　（第 1 会場 /12:15 ～ 13:15）

“The latest therapy for peritoneal metastasis”

講師 : NPO 法人腹膜播種支援機構理事長　米村　豊

2. シンポジウム 1　（第 1 会場 /13:30 ～ 15:30）

“Hyperthermic Effects of HIPEC on Peritoneal Surface Malignancies”

3. HIPEC トレーニングコース　（第2会場 /15:45 ～ 17:45）

1: Thermal Dose と輸液管理

福井大学医学部附属病院がん診療推進センター　片山 寛次

2: 腹腔鏡の役割

草津総合病院　外科　平野 正満

3: LHIPEC の方法

草津総合病院　外科　一瀬 真澄

4: 術後合併症十対策

草津総合病院　外科　水本 明良

5: 温熱療法の適応

NPO 法人 腹膜播種治療支援機構 理事長　米村 豊

6: 腹膜播種に対する包括的治療を立ち上げる際の要点

岸和田市民病院　外科　鍛 利幸

7: HIPEC と CRS に有用な手術機器

岸和田徳洲会手術室 ME　寺下 義一

＜経歴＞

片山 寛次 （かたやま　かんじ）

●プロフィール

昭和 28 年	8 月 15 日	福井市生まれ
		（本籍地は駅前のユアーズホテル）
昭和 47 年	3 月	福井県立藤島高等学校　卒業
昭和 54 年	3 月	関西医科大学医学部医学科　卒業
昭和 54 年	6 月	金沢大学第二外科・研修医
昭和 62 年	9 月	金沢大学・大学院 卒業
昭和 63 年	4 月	福井医科大学第一外科・助手
平成 4 年	6 月	ミネソタ大学 Visiting associate
平成 7 年	4 月	福井医科大学第一外科・講師
平成 12 年	12 月	福井医科大学手術部・助教授
平成 15 年	4 月	福井医科大学第一外科・助教授
平成 18 年	11 月	福井大学医学部がん診療推進センター長・診療教授
平成 23 年	12 月	福井大学医学部がん診療推進センター長・教授
平成 25 年	4 月	福井大学医学部腫瘍病態治療学教室教授・兼任

日本消化器外科学会評議員、指導医.

日本外科学会、指導医.

日本静脈経腸栄養学会、代議員、北陸支部会長.

日本緩和医療学会、代議員.

日本ハイパーサーミア学会、理事.

September 6th　16:00-17:30　Room 1

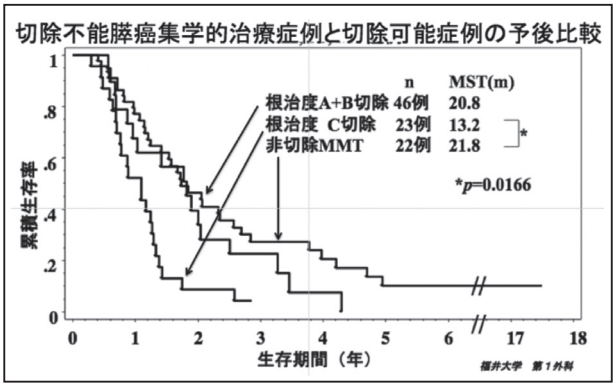
市民公開講座

福井県におけるがん温熱療法の実際

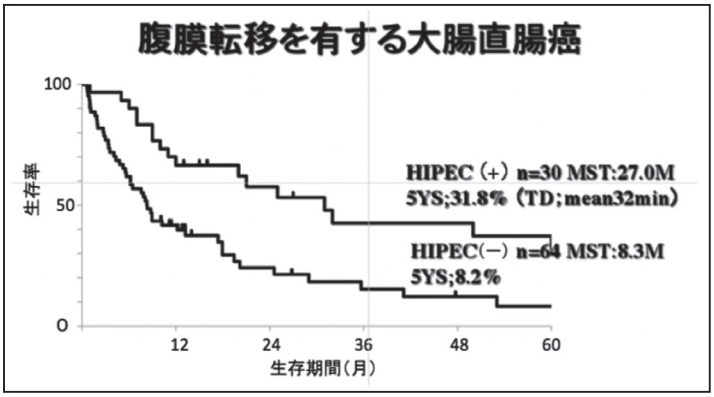
片山　寛次
福井大学医学部附属病院がん診療推進センター

福井県では、福井大学医学部附属病院で２種類の温熱療法が行われています。電磁波を使った肝臓や膵臓、胸部などの局所温熱療法と、もう一つは腹膜転移や胸膜転移に対する温熱灌流化学療法です。

電磁波温熱療法は，Thermotoron-RF-8 という治療器を使っています。身体の一部に限局して、しかも大きな血管などに浸潤していて外科的に取れない症例が適応です。肝臓がん、転移性の腫瘍、膵臓がん、直腸がん、再発乳がん、肺がん等ですが、多発していたり、他にも切除できない転移がある場合、つまり癌が直径 15cm 程の範囲に収まっていることが必要です。熱を加えることによって効果が増強される抗がん剤や、放射線治療を併用する事で効果が上がります。膵臓癌は、見つかったときすでに手術不能である場合が 70% もあり、切除できてもその生存期間は平均して２年に達しない、特に悪性のがんです。福井大学では、進行しすぎて取ることができない膵臓癌に対して、積極的に開腹手術と術中術後の放射線治療、化学療法を併用して効果を挙げています。



大腸がんなどが腸の外側にまで及んで、お腹の中にこぼれ落ちて腹腔内全体で発育する、腹膜転移では、手術で取り去ることはできず、従来の化学療法でも効果が上がりませんでした。一般的には、腹膜転移があった場合は外科的治療は行いません。福井大学では、大腸，直腸癌の腹膜転移や、虫垂原発の腹膜偽粘液腫などに対して積極的に開腹手術を行い、切除できない腹膜全体に広がったがんは腹腔内温熱化学療法 (HIPEC) で治療しています。この治療方は、日本で始まったのですが、今ではヨーロッパの多くの国や米国で行われているにも関わらず、日本では限られた施設でのみ行われています。今回、福井大学での治療方や成績についてお話しします。



＜経歴＞

大西　武雄　（おおにし　たけお）

●略歴

昭和 43 年　大阪大学理学部卒業。

昭和 48 年　大阪大学理学部大学院博士課程修了。

昭和 49 年　奈良県立医科大学助手 / 講師 / 助教授を経て、昭和 63 年教授。

平成 18 年　医学部長 / 副学長を経て、平成 22 年に退任 / 特任教授。

現在一般社団法人日本ハイパーサーミア学会理事長

September 6th　16:00-17:30　Room 1

市民公開講座

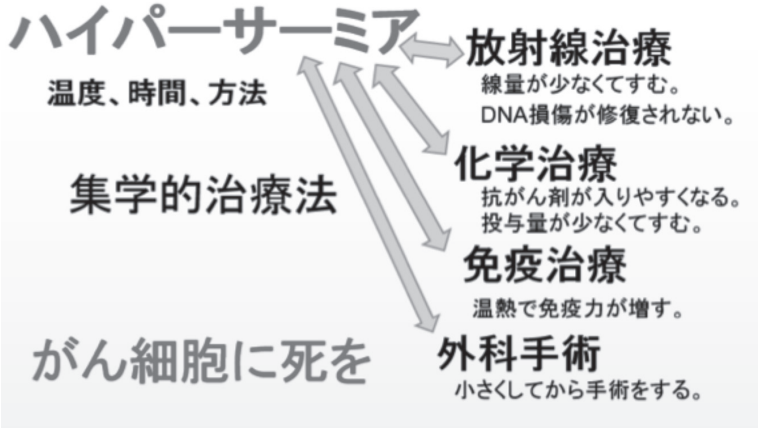
ハイパーサーミアがん治療法のしくみ

大西　武雄

奈良県立医科大学

日ごろから生活習慣に注意をして、がんにならないことが何よりです。年間 40 万近くもの人が、がんでなくなりつつあると言われています。どうしてこんなに多くの方々が、がんで亡くなるのでしょうか。がんは大きくなるまで症状がでない、わずかな症状に気づいても病院に行かない、がん検診を受ける人が少ない、自覚症状がでた時は進行がんであることが多い、などがその理由とされています。しかし、がんになってしまった方にとって、最も効率的ながんの治療法を求めるのは当然のことです。これまでは、外科的手術、放射線治療、抗がん剤治療が三大治療とされてきました。現在ではさらに内視鏡手術・重粒子線治療などさまざまな新しい治療法が開発されてきております。それらを組み合わせることによって (集学的治療)、さらに効果的な治療成果が得られています。日本ハイパーサーミア学会では温熱を利用することによって、さらなるがん治療効果の向上を目指してきました。すでに国内・外の多くの施設で治療がなされ、数多くの治療成果が報告されてきました。すでに保険適応にもなっております。

がん組織は血管の状態が正常組織に比べ温熱に弱くなっています。がん組織に熱を加えると、がん細胞がより死にやすくなります。また、がん組織に放射線を照射して、ハイパーサーミア治療で温熱を加えると放射線単独よりも、さらにがん細胞にダメージを大きくすることができ、効率的にがん細胞の細胞死が狙えます。抗がん剤を投与する治療では、がん組織の部位にハイパーサーミア治療で温熱を加えると、抗がん剤が効率的にがん細胞に取り込まれます。したがって、がん組織に同じダメージを狙うには抗がん剤投与量を少なくして、体に負担を少なくすることもできます。さらには、ハイパーサーミア治療で温熱を加えることによって、患者自身が持つがん細胞に対する免疫機能を増進することができます。当然、免疫治療法とハイパーサーミア温熱治療法との組み合わせも行われています。このハイパーサーミア温熱治療法は痛みをともなわない治療法であり、多くのがん患者さまにぜひとも推奨したい治療法であります。今回の公開講座ではハイパーサーミア治療で温熱を加えることによって、それらのがん治療効果があらわれるしくみを紹介いたします。



＜経歴＞

寺嶋　廣美　（てらしま　ひろみ）

生年月日　昭和 20 年 1 月 28 日生、本籍；福岡県

昭和 45 年　3 月	山口大学医学部　卒業
昭和 45 年　4 月	九州大学医学部放射線科学教室　入局
昭和 51 年　4 月	国立病院九州がんセンター放射線治療部
昭和 55 年　4 月	産業医科大学放射線科・講師
平成 11 年　3 月	九州大学医療技術短期大学部・教授
平成 14 年 10 月	九州大学医学部保健学科・教授
平成 19 年　4 月	九州大学大学院医学研究院保健学部門
	医用量子線科学分野教授
平成 20 年　3 月	九州大学退職（5 月、九州大学名誉教授）
平成 20 年　4 月	医療法人原三信病院放射線科顧問
現在に至る。	

September 6th 16:00-17:30 Room 1

市民公開講座

残されたがんの治療―安心･安全なハイパーサーミアの応用

寺嶋 廣美

原三信病院放射線科

はじめに；

生涯のうち２人に一人は「がん」になり、３人に一人は「がん」で死亡するという時代となりました。しかし医療の進歩で、「がん」になっても 60% の人は５年以上生きられるようになり、がんを持っても仕事を続けて行ける人が多くなりました。そのため、生活の質（QOL）を保ち続けることも重要となりました。昔から癌が熱に弱いということはわかっていましたが、この 30 年の間に生物学的基礎研究と、加温機器の発達で臨床的応用が進んで来ました。がんの温熱療法は 40℃から 45℃の熱を利用した治療法で「ハイパーサーミア」と呼びます。電磁波を用いたハイパーサーミアのみが健康保険の適用治療で、民間療法や代替療法とは明らかに違います。

ハイパーサーミアの長所：

温熱単独でもある程度のがんの治療効果は得られますが、放射線治療や化学療法と併用することによってさらに優れた効果が認められます。これまでは無効とあきらめていたがんにも、ハイパーサーミアを組み合わせることで大きな効果が得られることが知られています。また、ハイパーサーミアは放射線や化学療法と違って、臓器や組織型に関係なく効果が得られることも長所の一つです。身体には優しい治療で、１年や２年と長期間でも続けることができます。がんの縮小効果と共に、食欲が増したり睡眠や便通が良くなるなど、生活の質が好転する人たちを多く見受けます。副作用はほとんどなく、安心・安全な治療法です。

がん難民とならないために：

近年は、治療法の進歩によって「がんは死の病」という概念はやや薄れ、慢性疾患なみの数年間の長期にわたる治療も必要となってまいりました。初回治療でがんが消失や縮小して以後の時間をいかに無事に有意義に過ごすか、再発･転移をきたした場合の治療も重要となっています。手術、放射線治療、化学療法では、これ以上の治療法はないと宣告された、いわゆる「がん難民」と言われる人々も増加してまいりました。ハイパーサーミアはこのような方々にも適用される治療法の一つです。

今後の課題と展望：

がんの温熱療法（ハイパーサーミア）は、まだ医師の間でさえもよく知られていません。しかし、恩恵に浴する人たちの間では人づてに拡まったり、インターネット上で探し求めて治療を受けに来られる人たちが多くなっています。

また、診療報酬が低いため需要に応じられるほどは治療施設が普及しておりません。日本ハイパーサーミア学会では、さらなる研究と普及に努めて参ります。

市民公開講座

＜経歴＞

阿部　光幸　（あべ　みつゆき）

学歴

１９５９年　3月３１日　京都大学医学部　卒業

職歴

１９７７年１１月　1日　京都大学医学部教授
１９９４年　4月　1日　国立京都病院院長
１９９８年　4月　1日　兵庫県立成人病センター総長
２００１年　4月　1日　兵庫県立粒子線医療センター名誉院長
２００６年　4月　1日　同医療センター名誉顧問

受賞

シーボルト賞（１９８３年、ドイツ）、科学技術庁長官賞（１９８８年）、高松宮妃癌研究基金学術賞（１９９２年）、
レントゲン賞（１９９５年、ドイツ）、
京都府文化賞特別功労賞（２０１２年）

資格

米国放射線科医会名誉会員、英国王立放射線科医会名誉会員、ヨーロッパ放射線治療学会名誉会員、
日本癌治療学会名誉会員、日本放射線腫瘍学会名誉会員、日本ハイパーサーミア学会名誉会員

学会長

１９８９―１９９０年　国際術中照射シンポジウム会長
１９９０－１９９１年　日本医学放射線学会会長
１９９０－１９９３年　国際放射線腫瘍学会会長

市民公開講座

「温熱療法（ハイーパーサーミア）は、がん治療の鍵」

－ 司会 －

阿部　光幸

京都大学　名誉教授

1.　残されたがんの治療――安心・安全なハイパーサーミアの応用

寺嶋　廣美

原三信病院放射線科

2.　ハイパーサーミアがん治療法のしくみ

大西　武雄

奈良県立医科大学

3.　福井県におけるがん温熱療法の実際

片山　寛次

福井大学医学部附属病院

サーモトロンユーザーズミーティング

戸畑共立病院のハイパーサーミアについて

大田 真
社会医療法人共愛会 戸畑共立病院 臨床工学科

【概要】
当院は H15 年にサーモトロン RF-8 を導入し、化学療法との併用療法を開始。その後 H20 年に新設された病院にがん治療センターを設け、ハイパーサーミア、放射線治療、化学療法、高気圧酸素治療といった、がん治療に特化した治療設備を導入し H22 年に福岡県指定がん診療拠点病院に認定された。
ハイパーサーミアの H25 年度の年間症例数は 277 例、年間治療件数 2,527 件（2 台）、内訳は化学療法併用：176 例（63.5％）、化学療法＋放射線治療併用：67 例（24.2％）、放射線治療併用：18 例（6.5％）、ハイパーサーミア単独：16 例（5.8％）となっている。

【治療について】
時間は 50 分、体位は腹臥位で実施し、高齢の方、PS レベル 3 以上、当日の体調が優れない症例においては背臥位での治療を実施。加温出力は各症例で熱感が出現しない状態での最大加温出力としている。
装置では冷却効率の増加、RF 波の減衰軽減、ホットスポット軽減を目的として、電極内には 4％、循環水に 0.5％の NaCl を混入させ、2 ヶ月に 1 度の交換を実施。電極パッドは 0.3㎜、オーバレイボーラスは全例において使用している。

【人材育成】
臨床工学技士 4 名（男 1：女 3）が従事し、女性患者は全例で女性技師が対応している。教育は全 36 項目のマニュアルを用いて 3 ヵ月と 6 ヵ月で評価し、治療中は認定教育者、認定技師が新人技師と共に治療にあたっている。
トラブル対応においては上記マニュアルとは別にトラブルに特化した物を活用する事で経験年数にかかわらず、迅速かつ的確な対応をとる事が可能となっている。また、症例報告を含めた学会発表を積極的に行う事で、自己啓発とモチベーションの向上維持に努めている。

【熱傷対策】
浅在部を中心に電極サイズの小さなものでは、患部との密着性が弱い事や僅かなポジションのずれにより熱傷が引き起こされる為、10cm 以下の電極で治療を行う際は必ず表面温度が 43.0℃を超えないようモニタリングし、電極は患部にできるだけ垂直に密着させる。
深在部では、腹部は皮下脂肪の肥厚や人工肛門の有無、胸部では CV ポート留置部により熱傷のリスクが増加する為、既知事項であるテープの貼付が最も重要であり、幅の広い 5cm の物を使用し、内側から外側へ脂肪を引っ張った状態で固定する。凹凸のある人工肛門では内容物、ガスを完全に抜いた状態で、ガーゼの四方にテープを貼付し上から覆い保護する事で発生リスクが軽減される。
また、豊胸をされた症例で腹部加温時において、治療後に胸部熱傷が生じた経験から、今後はステント同様に豊胸を施した症例においても十分な検証が必要とされる。

【まとめ】
今回、当院のハイパーサーミアについて紹介した。
いくつかの取組みや工夫例は一つ一つを見れば小さな事ではあるが、その積み重ねが今後のハイパーサーミアの発展に繋がる事を期待し、今後は本学会を通じて積極的な施設間での情報共有、治療の標準化を進めていきたい。

サーモトロンユーザーズミーティング

新札幌恵愛会病院におけるハイパーサーミアの現状

諸澤 英之

社会医療法人 新札幌恵愛会病院 臨床工学科

[はじめに]

当院が THERMOTRON － RF8 を平成 14 年 9 月に導入後、経年毎に需要も増え、それに応えるべく 3 台まで拡大し治療を行っている。また平成 20 年に認定施設となり、北海道でのハイパーサーミア治療の中核的役割をはたしていると考える。

[当院の治療コンセプト]

①癌患者は基本的に全て受け入れる（ハイパーサーミア禁忌症例を除く）
②患者の希望、病態に合わせた治療を行う
・癌の縮小を目的とする場合…高出力、高温を目指す
・癌との共存・緩和治療の一法を目的とする場合…マイルドハイパーサーミアで、無理のない加温領域で施行

[治療実績]

平成 14 年度　455 回（平成 14 年 9 月一台目導入）
平成 15 年度 1317 回
平成 16 年度 1374 回
平成 17 年度 1944 回（平成 17 年 10 月二台目導入）
平成 18 年度 2984 回
平成 19 年度 3221 回
平成 20 年度 4172 回
平成 21 年度 4413 回（平成 21 年 6 月三台目導入）
平成 22 年度 4407 回
平成 23 年度 4920 回
平成 24 年度 5055 回
平成 25 年度 5806 回　　計 40068 回

[治療方法]

・ 1 時間枠を設け治療時間 40 分 + 前後 10 分を準備時間
・体位は第一選択が仰臥位、第二選択が側臥位
・深部加温時の電極選択はφ 300 が第一選択
・浅部加温時の電極選択は、病名・部位によりマニュアル化
・浅部加温時のみ温度センサー（IT-18）で皮膚表面温度を測定
・オーバーレイボーラスは使用しない
・エコーゼリーと置きパッド（SP-300）を使用
・出力の設定は施行者の状況判断で決める
・UASS の使用も同じく施行者の状況判断で決める

[教育]

・教育は独自のマニュアルを活用し、習得表で判断をする
・臨床工学技士と放射線技師が専門性を活かし治療・教育を行っている

[まとめ]

他職種が一緒に治療に当たる事で、多くの人員を治療に従事させることができる。それにより最大限の治療枠の利用を可能とし、多くの患者が治療を受けられている。今後もガン難民とされる患者の受け皿になると共にハイパーサーミア治療の普及に努めていきたい。

September 5th 12:00-14:00 Room 2

サーモトロンユーザーズミーティング

ハイパーサーミア治療における心理学的側面の応用について

森 信二

医療法人あいん会 温熱治療センター センター長

【はじめに】

当院では、神経症に対する精神分析療法の基本技法である、S. フロイトにより創案された自由連想法を基本にして、サーモトロンにおける実際の治療環境を構築しています。

もともとの自由連想法は、患者をソファに横臥させ、分析者はその背後に座ります。分析者は患者を見ることができるが、患者は分析者を見ることができません。このように治療状況を設定した上で、治療者は患者の心の中に浮かんだ一切のことを言語化することを要求します。つまり、関係がない、重要でない、無意味だ、話すことは不愉快だといった取捨選択を患者にまったく停止してもらい、頭の中に浮かんだことをまとめようとはせず、そのままに自由に連想してもらいます。

実際のサーモトロンの治療は、約 50 分間であり、その時間は治療者と患者が時間を共有することが出来ます。通常、この治療時間はテレビを観たり、治療者との相談等の会話で消化されますが、当院では、この治療時間を患者の心のケアーにあて、より有効な時間にすることを目的とし、その可能性を検討し、取り入れているので、その現状を報告します。

【治療方法】

患者が抱える心の負担、つまり心に溜まっている膿を吐き出してもらうことも目的として、フロイドが神経症の治療として考案した、自由連想法を基本とした治療方法を検討しました。

治療環境は、治療中は部屋の電気を消し、明かりは窓明かりだけにして、患者の心のケアーを中心に傾聴に徹し、心と身体を癒す空間を構築することを目指しました。

【結果】

ハイパーサーミア治療という特殊な空間で治療者が積極的に患者の心と向き合うことにより、患者は安心して自分自身が抱えている種々の不安や家族への思いと向き合うことが出来るようになり、治療者との信頼関係の中で安定した治療が受けられるようになっていきました。

また、治療者との信頼関係が深まる中で、サーモトロンによる継続的な治療が出来る土台が構築されました。

サーモトロンユーザーズミーティング

温熱療法室における取り組み及び技術的工夫

佐藤 光幸[1]、武田 力[1]、武田 和[1,2]、中野 義人[1]、辻本 はずき[1]、中村 華奈[1]、
武田 寛子[1]

[1]協林会 大阪ガン免疫化学療法センター
[2]国立病院大阪医療センター 外科

当院では癌治療において樹状細胞・リンパ球・ペプチドワクチンを中心とした免疫療法と、抗癌剤・分子標的治療などの化学療法に温熱療法をあわせた集学的治療を行っている。サーモトロン RF8 は 2 台稼働し今年の 7 月末で温熱療法開始丸 9 年となり、これまでに 2000 人以上、25000 回以上の温熱療法を施行してきた。温熱療法が免疫療法・化学療法・放射線療法の効果をあげることは今回の他の演題でも発表しているが、この発表ではサーモトロンユーザーミーティングの目的である治療の技術的な標準化（ガイドラインの作成）に向けて我々の経験が一助になればと考え、現在当院温熱療法室で行っている取り組みや技術的工夫等をまとめたのでこれを報告する。

サーモトロンユーザーズミーティング

りんくう出島クリニックでの温熱療法ハイパーサーミアの取組みと工夫

大木 幸治
りんくう出島クリニック

当院 2011 年 10 月開業から治療患者数 333 名、治療件数のべ 4554 件を行った。
当院の特徴として血管内治療を併用した温熱療法ハイパーサーミアを行っており、局所の治療成績向上をはかるため、効果的な加温方法を探るべく体位や照射方法を試行錯誤しており、ファントム実験等も積極的に行ってきた。

① 座位での温熱治療
肺・縦隔腫瘍の患者は呼吸状態が悪化していることが多く、従来の臥位でのセッティングは圧迫に伴う負担が大きく、治療継続が困難なことが多い。
患者の希望で始めた座位での治療は、治療機器への乗降や治療時の座位姿勢保持に問題があった。そこで DIY で座面を安定させる支柱やアームレスト、フットレストを作成し患者の安全を確保した。従来位置決め等に時間を要したが、それら補助具によりセッティング時間の短縮も可能となった。また座位治療の有用性はボーラスの圧迫感が軽減され、呼吸が容易となり患者の治療負担が軽減した。さらに加温時の疼痛が減少し、高出力での治療が可能となった。

② オフセット加温・サイド加温
寒天ファントム実験を行った結果、加温中心部と辺縁部での加温効率はそれまで認識していた以上に隔たりがあり、加温中心部をいかに治療目的腫瘍部に合わすかが重要である。また意図的にボーラスを体幹部中心からオフセットさせセッティングすることにより、肝右葉に限局するような病変の場合には効率よく加温でき、実際の治療にも積極的にオフセット加温を行っている。一方で体幹部を両サイド方向からボーラスで挟み込むセッティングは、ファントム実験の結果から前後からの加温と比べて全体てきには大きな差異はなく、ターゲットとなる腫瘍の位置によっては効率よく加温できるセッティングとなることがわかった。
治療のターゲットとなる腫瘍の位置を把握することが大切であり、CT や MRI などの画像評価は不可欠である。当院では画像診断専門医の指示のもと、臨床症状と検査画像を照らし合わせて治療計画を立てている。また、RF-8 コンソール上部に電子カルテ、画像ビュアー、治療録を表示するために、2 面モニターを備え、治療時に患者情報が容易に把握できるよう工夫している。

③ 予約システムの開発
当院では温熱治療の予約を一般的な予約ソフトを用いて行っていたが、複数回にわたる予約を行う際には予約空き状況の把握に時間を要していた。予約業務の短縮やダブルブッキングなどインシデントを回避するために、カレンダー機能を有する専用ソフトを開発した。結果として予約業務の短縮が可能となった。

サーモトロンユーザーズミーティング

－ 座長 －

今田 肇

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がん治療センターセンター長
日本ハイパーサーミア学会指導医

りんくう出島クリニックでの温熱療法ハイパーサーミアの取組みと工夫

大木 幸治
医療法人龍志会りんくう出島クリニック
放射線技師
ハイパーサーミア担当技師

温熱療法室における取り組み及び技術的工夫

佐藤 光幸
医療法人協林会　大阪がん免疫化学療法センター
温熱療法室　主任

ハイパーサーミア治療における心理的学側面の応用について

森 信二
医療法人あいん会　あいん常澄医院
センター長
日本ハイパーサーミア学会認定技師

新札幌恵愛会病院におけるハイパーサーミアの現状

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WS3-5　ワークショップ３

術中温熱腹膜還流hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC)の有効性のエビデンスと世界の保険支払いの状況

米村　豊

NPO 法人腹膜播種支援機構　理事長

腹膜播種の治療は過去 20 年間に劇的な変化を遂げた。全身化学療法による 5 年生存率は大腸癌・胃癌の播種では 5 %以下で、8 年以内にほぼ全例死亡する。一方、Peritoneal Surface Malignancy International が 1998 年腹膜切除による肉眼的播種の完全切除と周術期化学療法を組み合わせた包括的治療を開発した。この方法で従来は治癒することがないと考えられていた腹膜播種の永久治癒例が報告されるようになった。周術期化学療法では術前腹腔内化学療法（Neoadjyuvant intraperitoneal/systemic chemotherapy; NIPS, bidirectional intraperitoneal systemic induction chemotherapy; BISIC）, hyperthermic intraoperative intraperitoneal chemotherapy (HIPEC), early postoperative intraperitoneal chemotherapy (EPIC) がある。これらの方法は多くの randomized controlled study (RCT) で生存率改善に対する有効性が示されている。

過去に行なわれた HIPEC の有用性を検証する RCT では、オランダ癌センターの大腸癌腹膜播種、Wuhan 癌センターの胃癌腹膜播種で HIPEC の有効性が示された。さらに Coccolini F は Meta-analysis で HIPEC が胃癌腹膜播種の生存率を改善すると報告した [1)]。虫垂癌・腹膜義粘液腫・卵巣癌・中皮腫では RCT は行なわれていないが、Meta-analysis で HIPEC が生存率を改善させると報告されている。特に、中皮腫・虫垂癌・腹膜義粘液腫では HIPEC ＋ cytoreductive surgery (CRS) は、ヨーロッパ、アメリカ、カナダ、オーストラリアでは標準治療として腹膜播種治療センターで広く行なわれている。現在、ヨーロッパで 160・USA 120,Canada5, Mexico 5 箇所に治療センターがある。この包括的治療で重要な予後因子は、1) 手術による完全切除 2) 腹膜播種係数が閾値以下であること 3)HIPEC 施行 4) 術前抗がん剤有効などが上げられている。

イギリス・ドイツ・フランスではこの包括的治療は保険で包括払いとなっている。USA では外科医に支払う費用は 4000-20000$、病院への支払いは Medicare, Medicaid, あるいは私的な保険から支払い可能である。しかし日本では手術や HIPEC の保険点数はないのが現状である。早急に保険診療可能にするよう学会一丸となって働きかけなければならない。

[1)]Coccolini F, Cotte E Glehen O, et alo. Intraperitoneal chemotherapy in advanced gastric cancer. Meta-analysis of randomized trials. EJSO.2013;.doi.org/10.1016/j.ejso.2013.10.019

WS3-4　ワークショップ３

松山西病院における温熱療法治療の現状

俊野 昭彦

結和会松山西病院　院長理事長

私は平成 21 年 4 月に医療法人結和会松山西病院の院長理事長として病院の運営を引き継ぐことになり、同時に温熱療法の診療も引き継ぐこととなった。当時の問題点としては、患者や周辺の医療施設での癌診療に携わる医師の温熱療法に対する認知度が低いことであり、温熱療法を希望する患者は主治医の理解を得られないまま治療を受けることとなり、主治医から離れて治療を受けるため病状悪化時の治療に困窮するケースもみられた。そこで、当院での温熱療法を維持するために温熱療法の治療経験のある医師を大学病院より招聘し、診療に当たっては主治医との連携をとり共診することにより温熱療法に対しての主治医の理解を得ることとした。このことにより温熱療法を知る医師も徐々に増加していき、抗癌剤治療や放射線治療を受けながら温熱療法を行うことも可能となり、また新たに医師よりの紹介が得られるようにもなってきた。このため平成 22 年 7 月よりハイパーサーミア 2 基による診療体制とることとなった。

温熱療法の診療に関しては、保険診療として一連の治療を 1 クール 10 回の治療とし 3 か月に 1 回の保険請求を行ってきた。しかし平成 25 年夏に一部の保険者より一連の治療に関しての疑義がかかり、3 か月に一度の保険請求が認められないケースがみられるようになった。これを機に県内で 3 か月毎の保険請求を認めない保険者が拡大し、社会保険においては平成 26 年 1 月より初回請求のみしか認めないとの通達があり 5 月より温熱療法の保険治療を全面中止し自費診療での治療を行うこととなった

WS3-3　ワークショップ３

保険適応後に蓄積されたハイパーサーミアの臨床試験から得られたエビデンス

大栗 隆行

産業医科大学　放射線科学

本邦では 1990 年より放射線治療併用時にのみ電磁波温熱療法は健康保険適応となり、1996 年以降は保険適応の拡大により全面収載された。以降、改定なく一連につき深在性悪性腫瘍に対するもので 9,000 点、浅在性悪性腫瘍では 6,000 点と設定されている。しかしながら、電磁波温熱療法は週に 1~2 回の治療を何度も継続することで効果が発現されることが多く、経済的・運営面の悪さから本療法が敬遠され普及が阻まれているものと思われる。

保険適応となった後にエビデンスレベルの高い臨床試験が報告されており、対象となった疾患群に対して診療報酬の増点を目指す形が合理的と思われる。健保改定委員会では高いエビデンス（Level I）のある疾患、また、治療成績の改善が強く望まれる進行、再発・転移癌で有望な Phase II　study の結果が出ている疾患群に関して診療報酬の改定を目指し、主に保険適応後に蓄積された治療効果のエビデンスを集積した。

メタアナリシスまたはランダム化比較試験に基づく Level I エビデンスとして、放射線治療との併用で頭頸部癌、乳癌、肺癌、食道癌、子宮頚癌、膀胱癌、悪性黒色腫と多くの疾患群において局所制御率や腫瘍完全消失率の有意な改善が確認されている。化学療法との併用では、高悪性度軟部肉腫や肝臓癌において同様の改善が Level I エビデンスとして認められる。特に子宮頚癌や高悪性度軟部肉腫では生存率においても有意な改善が得られている。また、主に全身化学療法に温熱療法を併用した進行、再発・転移癌に対する有望な Phase II study の認められる疾患として、非小細胞肺癌、膵癌、卵巣癌、癌性腹膜炎、子宮頚癌、高悪性度軟部肉腫が挙げられた。

本発表では、診療報酬改定の根拠となりうる上述の温熱療法の臨床試験の概要や、現在進行中の温熱療法の臨床試験に関し概説する。

WS3-2 ワークショップ３

我が国のハイパーサーミアと診療報酬の現状

寺嶋 廣美

原三信病院放射線科

1980 年代から始まった我が国のハイパーサーミアは、1990 年に保険収載されたこともあって徐々に普及してきた。近年は治療施設や対象疾患は大きな変化を来たし、診療報酬の問題も大きくなっている。日本ハイパーサーミア学会、健保・保険点数改定委員会は、診療報酬の改定に向けて作業を続けてきた。2011 年 10 月、委員会は温熱療法の適正な使用と保険診療における「一連につき」の解釈に対するガイドラインを作成し、2012 年３月、日本ハイパーサーミア学会誌にて公表した。しかしその後も各都道府県の国民健康保険、社会保険の審査委員の間では、一連の治療解釈がまちまちで混乱は続いている。

ハイパーサーミア学会は 2013 年４月に「内保連」を通して医療技術再評価提案書を日本放射線腫瘍学会との共同提案として提出した。しかし、2014 年４月からの改定には至らず、現状の混乱は続いている。多くの申請の中から改定案件に採択されるためには 800 題以上の他の学会からの申請課題に勝るエビデンスが求められる。今後、放射線腫瘍学会などの他学会とも共同しつつ、次期診療報酬の改定を目指して対策を練って行くことが重要である。今までの確かなエビデンスを基に、新たなエビデンスが必要である。

その一つに「費用対効果評価」がある。国際的に認められた QALY(Quality-adjusted Life Year):質調整生存率）などの調査も考慮にいれる必要があり、ハイパーサーミア学会・会員の総力を挙げて取り組んで行きたいと考えている。

WS3-1　ワークショップ３

社会医療診療行為別調査からみる日本のハイパーサーミアの現状

黒崎 弘正
JCHO 東京新宿メディカルセンター　放射線治療科

（はじめに）

長年、ハイパーサーミア治療の保険点数の少なさが問題となっている。今回、厚生労働省の社会医療診療行為別調査を使用して日本でのハイパーサーミアの現状を把握することを目的とした。

（方法）

1996 ～ 2011 年の社会医療診療行為別調査を用いて、ハイパーサーミア診療について検討した。

（結果）

2008 年 6 月分のデータをみると、ハイパーサーミア診療は 153 件 1377000 点（1377 万円）であり、放射線治療（コード M）の 0.3%を占めていた。全例で深在性治療であった。44 歳以下と 80 歳以上の患者はなく、55-59 歳で 118 例と集中していた。病院で 118 例、有床診療所で 35 例、無床診療所で 0 件であった。年次推移では 96 年 15 件 90000 点、99 年 80 件 655500 点、2002 年 204 件 1836000 点、2005 年 41 件 369000 件、2008 年 153 件 1377000 点、2011 年 589 件 4955400 点であった。

（結語）

社会医療診療行為別調査で見る限り、ハイパーサーミア診療が廃れつつあるとは言えず、むしろ盛んになっていると考えられた。診療報酬的には放射線治療の中でも極わずかであり、保険点数が上がっても医療費の高騰を招かないと考え、日本放射線腫瘍学会と連携して保険点数を上げていく必要性があると考えられた。

ワークショップ 3
ハイパーサーミア診療報酬の現状と問題点
－その改定に関する経緯と今後の活動について

－ 座長 －

田中　良明

川崎幸病院副院長・放射線治療センター長

WS3-1　社会医療診療行為別調査からみる日本のハイパーサーミアの現状

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WS3-2　我が国のハイパーサーミアと診療報酬の現状

寺嶋　廣美

原三信病院放射線科

WS3-3　保険適応後に蓄積されたハイパーサーミアの臨床試験から得られたエビデンス

大栗　隆行

作業医科大学　放射線科学

WS3-4　松山西病院における温熱療法治療の現状

俊野　昭彦

結和会松山西病院　院長理事長

WS3-5　術中温熱腹膜還流hyperhermic intraoperative intraperitoneal chemotherapy(HIPEC) の有効性のエビデンスと世界の保険支払いの状況

米村　豊

NPO 法人腹膜播種支援機構 理事長

EL-3 教育講演

ハイパーサーミアにおける物理･工学の基礎

伊藤 公一

千葉大学 フロンティア医工学センター

ハイパーサーミアを用いたがん治療では、患部全体を残すことなく、的確に加温することが重要であることは言うまでもない。この目的を達成するため、これまでに、物理・工学的側面から、主として加温技術および測温技術に関して様々な検討が行われてきた。

本講演では、まず、電磁エネルギーを用いる加温法について、その原理を説明した後、代表的な RF(Radio Frequency) 誘電加温およびマイクロ波加温について、それぞれ加温装置の概要を解説し、効率的な加温を行う上での注意点を述べる。また、現在研究が行われている新しい加温技術についても簡単に紹介する。
次に、的確な加温が行われたかどうかを客観的・定量的に評価するためには欠かせない測温技術について、最近の話題も含めて概説する。
最後に、ハイパーサーミア治療を行う際に、医師・看護師などの医療従事者が、加温装置より発生する電磁界にさらされる機会を低減するための電磁界防護の考え方についても簡単に説明する。

EL-2 教育講演

ハイパーサーミアの生物作用:温熱誘導分子損傷

高橋 昭久
群馬大学先端科学研究指導者育成ユニット

温熱による細胞生物学は 1970 年代に確立され、細胞培養技術の発展とともに、その定量性の優れた実験方法 (コロニー形成法) を利用して、温度依存性、pH 依存性、温熱耐性、細胞周期依存性などを明らかにしてきた。さらに、最近では分子レベルでの研究がすすんでいる。温熱は生体分子（例えばタンパク質，脂質と DNA）に損傷を誘発することが知られているが、温熱に対する細胞の生体応答の分子機構についてはまだまだ多くの不明な点が残されている。例えば、温熱による細胞死の原因については、再考の余地があると考えている。従来の温熱による細胞死の原因がタンパク質変性と考える概念に対して、最近我々は新たな手法を用いて DNA 二本鎖切断 (DSB) こそが細胞死の原因とする実験結果を報告した。本講演では、温熱による細胞死の原因について、従来のタンパク質変性を主因とする論拠を概説し、次に DSB が細胞死の主因とする論拠を紹介する。さらに、温熱による DSB 生成機構について考察する。

今後の更なる研究により、温熱誘導 DSB と細胞死の関連が解明され、温熱生物学やがん温熱療法の学術的な理解がより深まることを期待している。

Westermann ら (11) は IIB, III, IVA 期の子宮頸癌に対して CDDP 併用温熱放射線治療の治療効果を報告し、2 年無病生存率は 71.6%、2 年全生存率は 78.5% と良好であった。しかし、観察期間が短く今後の報告を待ちたい。Plataniotis ら (12) は CDDP 併用温熱放射線治療の治療効果の可能性について報告し、CDDP 併用温熱放射線治療は比較的低い放射線感受性を有する癌には治療効果が期待できるかもしれないが、放射線抵抗性癌の予後を改善することは期待できないとしている。今後、進行期子宮頸癌の治療成績を向上させるためには、さらに放射線抵抗性癌の基礎と臨床の研究が重要であると考える。

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EL-1 教育講演

子宮頸癌の放射線温熱療法の臨床

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関西医科大学附属滝井病院放射線科

今回の教育講演では、子宮頸癌とはどういう癌なのか、その背景として発症のリスク要因、疫学を述べ、次に放射線治療、抗癌剤放射線治療、放射線温熱治療、抗癌剤温熱放射線治療について紹介する。

1．子宮頸癌とはどういう癌なのか

子宮頸癌は全世界で 50 万人が罹患し、27 万 5000 人が死亡したと報告されている（1)。わが国では上皮内癌を含めて毎年約 1 万 7000 人が子宮頸癌と診断され、2500 人が死亡するとの統計があるが、わが国ではがん登録がまだ十分でないので明確な発症数が把握されていないのが現状である。わが国では 2001 年度から急速に 20 ～ 30 代の若年層の子宮頸癌患者が増加していることが問題となっている。これは子宮頸癌のリスク要因として、低年齢での初交、性的パートナーが多い、他の性行為感染症が報告されているが、その多くはHPV (human papillomavirus, ヒトパピローマウィルス) 感染のリスク要因であることと関連がある。HPV の持続的な感染が発症の原因であることはよく知られている事実であり、実際、子宮頸癌患者の 90％以上から HPV が検出され、なかでもハイリスク・タイプ（16 型や 18 型など）で浸潤癌への進展がみられやすい。

2．子宮頸癌の治療

子宮頸癌の放射線治療の歴史は古く、治療方法は確立されていて、手術療法と同等の治療成績が得られている。欧米では全病期に放射線治療を施行しているが、わが国では I・II 期は手術、III・IV 期が放射線治療を基本とした治療を施行されていることが多い。病期別の 5 年全生存率は I 期で 80-90%、II 期で 60-70%、III 期で 40-50%、IV 期で 10-20% と報告されており、III･IV 期の治療成績は満足できるものではない。1999 年に New England Journal of Medicine 誌上で Cisplatin (CDDP) を含んだレジメでの子宮頸癌同時併用化学放射線治療と放射線単独治療の大規模無作為臨床試験結果が報告された (2,3,4)。CDDP を併用することで有意に良好な生存率を得たので一大センセーションを引き起こした。そして、1999 年に National Cancer Institute は子宮頸癌には CDDP 同時併用放射線治療を施行するべきであると警告し、わが国では日本婦人科腫瘍学会「子宮頸癌治療ガイドライン」2007 年版で子宮頸癌 III 期に対して CDDP 同時併用放射線治療が推奨されるに至った。しかし、ここで問題となるのは New England Journal of Medicine 誌上の 3 編の論文 (2,3,4) では III・IVA 期の症例数が少ないことである。また、I・II 期では同時併用化学放射線治療は放射線単独治療よりも有意に治療成績の向上を認めた (P=0.002) が、III･IVA 期では有意差を認めなかった (P=0.44) (3)。

一方、子宮頸癌に対する温熱放射線治療と放射線治療単独の無作為臨床試験結果について我々の論文 (5) を含めて 6 編の報告 (6-10) がある。1 編は中国語で書かれているので詳細は不明である (9)。4 編は温熱放射線治療の方が放射線治療単独よりも良好な治療結果を示した (5-8)。しかし、Vasanthan らの報告 (10) では温熱放射線治療の優位性を示さなかった。理由として、第 1 に腫瘍のボリュームにばらつきがあった。すなわち放射線治療単独では 49.5 cc であったのに対して、温熱放射線治療では 60.3 cc であり、温熱放射線治療群の方が大きな腫瘍であった。次に、この報告の半数を占める症例で腔内加温を用いていたので、十分な加温ができなかった。温熱放射線治療と放射線治療単独の無作為臨床試験で温熱の優位性を示した 4 編の論文 (5-8) では IIIB 期の症例が多く含まれていたのにもかかわらず、温熱放射線治療の方が放射線治療単独よりも良好な治療結果を示した。この点からも III・IVA 期の子宮頸癌に対しては温熱放射線治療の方が同時併用化学放射線治療よりも良好な治療効果が望める可能性がある。

教育講演

－ 座長 －

加藤 博和

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EL-1　子宮頸癌の放射線温熱療法の臨床

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EL-2　ハイパーサーミアの生物作用 : 温熱誘導分子損傷

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EL-3　ハイパーサーミアにおける物理・工学の基礎

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抄録

謝　辞

「アジアハイパーサーミア腫瘍学会第 6 回大会・日本ハイパーサーミア学会第 31 回大会 合同大会」の開催に際し、上記の団体、企業の多大なるご支援・ご協力をいただきました。ここに厚く御礼申し上げます。

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日 程 表

大会２日目　　9月6日（土）

	Room 1 AOSSA 8F 福井県県民ホール	Room 2 AOSSA 6F 601B-C	Poster AOSSA 8F リハーサル室
8:45			
9:00	9:00 – 10:00 **ワークショップ 1-1** Hyperthermia: Up to Date in Asia – オンコサーミア – 座長 : 近藤　隆 , Taesig Jeung	9:00 – 12:14 **Poster/Short-Oral Presentation** GSE1 - GSE43 GSJ1 - GSJ6 (日本語)	10:00 – 17:00 **ポスター閲覧**
10:00	10:00 – 12:00 **ワークショップ 1-2** Hyperthermia: Up to Date in Asia – 症例報告および生物 – 座長 : 櫻井　英幸 , 浅尾　高行		
11:00			
12:00			
13:00	12:15 - 13:15 **ランチョン 2** The Latest Therapy for Peritoneal Metastasis 座長 : 片山　寛次 (セーレン株式会社)		
14:00	13:30 - 15:30 **シンポジウム 1** Hyperthermic Effects of HIPEC on Peritoneal Surface Malignancies 座長 : 米村　豊 , Yan Li Mao-Chih Hsieh (セーレン株式会社)	13:30 – 15:26 **Poster/Short-Oral Presentation** GSJ: 7 - 35 (日本語)	
15:00			
	15:30 – 15:45　**閉会式**		
16:00	16:00 – 17:30 **市民公開講座** 司会 : 阿部　光幸	15:45 – 17 : 45 **HIPEC トレーニングコース**	15:45 – 16:45 **ポスター撤去**
17:00			
18:00			
19:00			

日 程 表

大会 1 日目　　9月5日（金）

	Room 1 AOSSA 8F 福井県県民ホール	Room 2 AOSSA 6F 601B-C	Poster AOSSA 8F リハーサル室	
8:45	開会		8:30 – 10:00 **ポスター貼付**	
9:00	9:00 – 11:00 **シンポジウム 2** Impact of HSPs – Revisit & Perspective – 座長 : 大塚　健三 , S. V. Chiplunkar			
10:00			10:00 – 17:00 **ポスター閲覧**	
11:00	11:00 – 12:00 **大会講演** 座長 : 大西　武雄 （山本ビニター株式会社）			
12:00	12:00 – 13:00 **ランチョン 1** オンコサーミア 座長 : Andras Szasz （立山マシン株式会社）	12:00 – 14:00 **サーモトロン ユーザーズ ミーティング** 座長 : 今田　肇 （山本ビニター株式会社）		
13:00	13:15 – 14:00 **日本ハイパーサーミア学会 活動報告会**			13:00 – 17:00 **エクスカーション（外国人研究者、同行者向け）**
14:00	14:00 – 15:00 **日本ハイパーサーミア学会 教育講演** 座長 : 加藤　博和			
15:00	15:00 – 17:00 **ワークショップ 2** Development of the New Modality in Hyperthermic Cancer Therapy 座長 : 黒田　輝 , Tzyy-Leng Horng	15:00 – 17:00 **ワークショップ 3** ハイパーサーミア診療報酬の現状と問題点 ーその改定に関する経緯と今後の活動についてー 座長 : 田中　良明		
16:00				
17:00	17:00 – 18:15 受賞講演（英語） **ASHO 学会賞** 古倉　聡　座長 : 桑野　博行 **JSTM 学会賞** 藤内　祝　座長 : 伊藤　公一 **JSTM 奨励賞** 齊藤　一幸　座長 : 伊藤　公一 **優秀論文賞** 鈴木　亮　座長 : 高橋　昭久			
18:00				
19:00	18:30 –　**全員懇親会** （ユアーズホテルフクイ）			

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   ポスター貼付　9月5日(金)　8：30　～　10：00
   ポスター撤去　9月6日(土)　15：45　～　16：45
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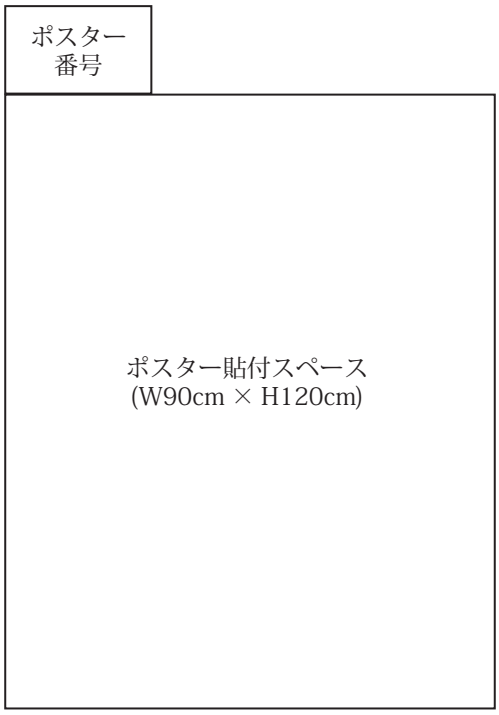

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5) PC 受付ではデータの修正はできません。
6) 必ずご自身でウイルスチェックのご確認を行ってください。
7) 持ち込まれるメディアには、当日発表のデータ（完成版）以外入れないようにしてください。
8) お持ち込みの CD-R には、氏名、機関、セッション名、演題番号をご記入ください。画面の解像度は XGA（1024 × 768、60H z限定）です。このサイズより大きい場合、スライドの辺縁部が切れたり、映らない場合がありますので、このサイズ以外の解像度のご使用はお控えください。
9) 受付時にコピーした発表データは、学会終了後、事務局にて責任を持って全て消去いたします。

パソコンを持ち込まれる方へ

1) OS は Windows（XP 以降）、Macintosh（Mac OS9 以降）が使用できます。
2) 使用可能なアプリケーションは Microsoft PowerPoint 2003 以降（Mac は Keynote を含む）のバージョンです。
3) 事務局では D-sub15 ピン（ミニ）のケーブルを用意します。
4) 一部の PC では本体付属のコネクタが必要な場合がありますので、必ず持参してください。
5) 事前に各自の PC から外部モニターに正しく出力できることをご確認ください。
6) 修正がない状態でお持ち込み下さい。
7) 画面の解像度は XGA（1024 × 768、60Hz）です。このサイズより大きい場合、スライドの辺縁部が映らない場合がありますので、このサイズ以外の解像度のご使用はお控え下さい。
8) スクリーンセーバーならびに省電力設定は事前に解除しておいてください。
9) 会場にて電源コンセントをご用意しております。PC 用 AC アダプターおよび電源コードも一緒にご持参ください。
10) 念のためバックアップデーターとして、USB メモリーもしくは CD―R をお持ちください。データ形式等は、上記の<データを持ち込まれる方へ>をご参照ください。
11) 動画の使用は可能ですが、本体の液晶画面に動画が表示されても PC の外部出力に接続した画面は表示されない場合があります。実際にお持ちいただく外部出力にモニターまたはプロジェクターを接続してご確認ください。

学術発表に関するご案内

【座長の皆様へ】

- 座長の方は来場されましたら、必ず**「総合案内」**にお立ち寄りください。
- 座長の方は担当セッション開始 20 分前までに各会場前方、次座長席までお越し下さい。
- シンポジウムの進行、各演者の発表時間、討論の有無等は座長一任としますが、所定の時間内に終了するようにご配慮ください。
- ワークショップの各演者の発表時間は 12 分 (講演 8 分＋質疑応答 4 分) です。所定の時間内に終了するように配慮ください。
- タイムテーブルに従って、各セッションをお進めください。開始の合図はありませんので、定刻通りの進行をお願いします。
- 座長の先生は限られた時間内に討論が円滑に進行するよう、「質問・討論を希望される参加者は、口演終了後、速やかにマイクの前にお立ちください。座長の指示に従い、所属・氏名を述べて発信してください。」とご指示ください。

【質問・発言者の方へ】

- 多くの参加者の活発な討論・発信を歓迎します。
- 質疑・コメントをされる方は、口演終了後、速やかにマイクの前にお立ちください。座長の指示に従い、所属・氏名を述べて発言してください。

【発表者の皆様へ】

1. 口演発表される方へ

- 発表はPowerPointによるPC発表のみとさせていただきます。フォトスライドによる発表はできません。
- 会場では各演者ご自身で演台上の機材を用いてスライドの操作をしていただきます。
- シンポジウムの発表時間はセッションによって違います。プログラムをご参照下さい。発表終了 1 分前に黄色ランプ、終了時赤ランプでお知らせします。所定の時間内に終了するようご配慮ください。
- ワークショップの発表時間は 12 分（講演 8 分＋質疑応答 4 分）です。発表終了 1 分前に黄色ランプ、終了時赤ランプでお知らせします。所定の時間内に終了するようご配慮ください。
- 一般演題のポスター紹介の発表時間は 3 分です。必ず所定の時間内に終了するようご配慮ください。また質疑応答はありません。
- 患者個人情報に低触する可能性のある内容は、患者あるいはその代理人からインフォームド・コンセントを得た上で、患者個人情報が特定されないように十分留意して発表してください。

2．発表データの受付について

場　所：　PC 受付　8 階　福井県県民ホール　ホワイエ
時　間：　9 月 5 日 (金)　8：30 ～ 17：00
　　9 月 6 日 (土)　8：30 ～ 16：00

- データ持込みの場合は、USB メモリーあるいは CD-R でデータをご持参され、PC 受付にて受付および登録と試写を行ってください。9 月 6 日 (土) に発表の方は発表日前日の 9 月 5 日 (金) でもデータの受付および登録ができます。
- パソコン持込の場合は、PC 受付にて受付と試写を行っていただき。その後、ご自身で会場内 PC デスク（発表演台付近）のオペレータ席までパソコンをお持ちください。パソコンは、発表終了後にオペレータ席にて返却します。PC 用 AC アダプターおよび電源コードも一緒にご持参ください。9 月 6 日 (土) に発表の方は発表日前日の 9 月 5 日 (金) でも受付および試写ができます。

受付時間

9月5日(金)　　8：30　～　17：00
9月6日(土)　　8：30　～　16：00
※9月4日(木)は、6階　福井市地域交流プラザ　601Aにて13:00～17:00まで受付を開設します。

大会参加費

会　員　10,000 円
非会員　15,000 円
学　生※　5,000 円　　※学生証の提示を求める場合があります。
同伴者　5,000 円

参加証

参加費と引き換えに参加証をお渡しいたします。氏名・所属をご記入の上、会期中はご着用ください。参加証を着用していない方は入場をお断りします。

プログラム・抄録集

すでにプログラム・抄録集を受理されている方は当日ご持参ください。追加希望の方、またはお忘れになった方は、当日総合案内にて 1 部 2,000 円で販売します。

新入会・住所変更など

日本ハイパーサーミア学会事務局までお申し付けください。

その他のご案内

学術ランチョンセミナー

日　程：　9月5日(金) 12：00～13：00　第 1 会場（8 階　福井県県民ホール）
　　9月6日(土) 12：15～13：15　第 1 会場（8 階　福井県県民ホール）

整理券：　開催当日の 8：30 より「総合案内」で整理券を配布しますので、参加希望の方はお受取りください。お 1 人様 1 枚とさせていただきます。尚、定員になり次第、配布を終了いたします。

ハイパーサーミア講習会

本大会は教育講演をもってハイパーサーミア講習会とします。

企業展示

大会期間中、企業展示を行いますので是非ご覧ください。
場　所：　8 階　福井県県民ホール　ホワイエ

ドリンクコーナー

場　所：　8 階　ポスター会場 (リハーサル室)

クローク

場　所：　8 階　福井県県民ホール　ホワイエ
時　間：　9月5日（金）8：30　～　18：30
　　9月6日（土）8：30　～　18：30

その他

・お呼び出し
会場内でのお呼び出しは原則として行いません。
総合受付付近の掲示板をご利用ください。

・写真撮影等
会場内での写真撮影、VTR 撮影、録音は禁止します。

・喫煙
AOSSA は全館禁煙です。AOSSA の館内での喫煙はお断りします。

お知らせ

会　期

平成 26 年 9 月 5 日 (金)　～　6 日 (土)

会　場

AOSSA (〒 910-0858　福井県福井市手寄 1-4-1)

- 福井県県民ホール (8 階)　　Tel, 0776-87-0003;　Fax, 0776-87-0303
- 福井市地域交流プラザ (6 階)　Tel, 0776-20-1535;　Fax, 0776-20-1536

大会公用語

英語 (一部の JCTM の特別なセッションは日本語も可)

公式行事

全員懇親会

会　場：　ユアーズホテルフクイ（http://www.yours-hotel.co.jp/）
〒 910-0006　福井県福井市中央 1 丁目 4-8
Tel, 0776-25-3200
日　程：　9 月 5 日 (木)　開場 18：00　開宴 18：30
参加費：　無料
形　式：　立食
服装規制：　カジュアル

各種会議

アジアハイアパーサーミア腫瘍学会カウンシラー会議	9月4日(木)	14:00 ～ 15:00	6階 602
日本ハイパーサーミア学会理事会	9月4日(木)	15:15 ～ 16:15	6階 602
日本ハイパーサーミア学会代議員総会	9月4日(木)	16:30 ～ 17:30	6階 601B/C
日本ハイパーサーミア学会活動報告会	9月5日(金)	13:15 ～ 14:00	8階 第1会場

各種委員会

会場 : AOSSA (大会会場)

認定委員会	9月5日(金)	12:00 ～ 12:50	6階 604
代議員評価委員会	9月5日(金)	12:00 ～ 12:50	6階 603
健保・保健点数改定委員会	9月6日(土)	12:00 ～ 12:50	6階 603
編集委員会	9月6日(土)	12:00 ～ 12:50	6階 604

会場 : ユアーズホテルフクイ

〒 910-0006　福井県福井市中央 1 丁目 4-8
電話　0776-25-3200

将来計画委員会	9月6日(土)	8:00 ～ 8:50	2階 桜の間

大会参加受付

場　所

8 階　福井県県民ホール　ホワイエ

運営組織

主　催

アジアハイパサーミア腫瘍学会 (ASHO)
日本ハイパーサーミア学会 (JSTM)

共　催

NPO 法人　腹膜播種治療支援機構

後　援

一般社団法人　福井県医師会

大会運営委員

大会長	片山　寛次（福井大学）
実行・準備委員長	松本　英樹（福井大学）

プログラム委員会（敬称略、五十音順）

委員長	片山　寛次（福井大学）
委員	浅尾　高行（群馬大学）
	伊藤　公一（千葉大学）
	上田　公介（はちや整形外科病院）
	大塚　健三（中部大学）
	加藤　博和（岡山大学）
	黒田　輝　（東海大学）
	黒田　昌宏（岡山大学）
	古倉　聡　（京都学園大学）
	近藤　隆　（富山大学）
	高橋　昭久（群馬大学）
	藤内　祝　（横浜市立大学）
	播磨　洋子（関西医科大学）
	米村　豊　（腹膜播種治療支援機構）
	松本　英樹（福井大学）

大会事務局

福井大学　腫瘍病態治療学講座
〒 910-1193　福井県吉田郡永平寺町松岡下合月 23-3
Tel：0776-61-8857；　　Fax：0776-61-8196
E-mail：eternal@u-fukui.ac.jp
事務担当：宇野　真理

運営事務局

株式会社日本旅行　国際旅行事業本部　ECP 営業部
〒 105-0001　東京都港区虎ノ門 3 丁目 18-19　虎ノ門マリンビル 11 階
Tel：03-5402-6401 Fax：03-3437-3955
E-mail：jstm_31@nta.co.jp
担当：山岸　浩史、楠見　早和子、新井　麻祐子

大会ホームページ

http://web.apollon.nta.co.jp/jstm31/index.html

ISSN 1882-2576

Vol. 30
Supplement, 2014

Thermal Medicine

アジアハイパーサーミア腫瘍学会第 6 回大会・
日本ハイパーサーミア学会第 31 回大会合同大会

ハイパーサーミア – がん治療の鍵 –

プログラム・抄録集

大会長　片山　寛次

福井大学医学部附属病院　がん診療推進センター　教授

平成 26 年 9 月 5 日（金）・6 日（土）
AOSSA（福井市）

Japanese Society for Thermal Medicine

本邦初、
アセトアミノフェン
静注液。

解熱鎮痛剤　薬価基準収載
アセトアミノフェン静注液

アセリオ®静注液1000mg

acelio® Intravenous Injection 1000mg

“疼痛領域”に可能性の花を

劇薬・処方せん医薬品　注意—医師等の処方せんにより使用すること

【警告】
(1)本剤により重篤な肝障害が発現するおそれがあることに注意し,1日総量1500mgを超す高用量で長期投与する場合には,定期的に肝機能等を確認するなど慎重に投与すること(「2.重要な基本的注意(8)」の項参照). (2)本剤とアセトアミノフェンを含む他の薬剤(一般用医薬品を含む)との併用により,アセトアミノフェンの過量投与による重篤な肝障害が発現するおそれがあることから,これらの薬剤との併用を避けること(「8.過量投与」の項参照).

【禁忌】(次の患者には投与しないこと)
(1)重篤な肝障害のある患者[重篤な転帰をとるおそれがある.] (2)本剤の成分に対し過敏症の既往歴のある患者 (3)消化性潰瘍のある患者[症状が悪化するおそれがある.] (4)重篤な血液の異常のある患者[重篤な転帰をとるおそれがある.] (5)重篤な腎障害のある患者[重篤な転帰をとるおそれがある.] (6)重篤な心機能不全のある患者[循環系のバランスが損なわれ,心不全が増悪するおそれがある.] (7)アスピリン喘息(非ステロイド性消炎鎮痛剤による喘息発作の誘発)又はその既往歴のある患者[アスピリン喘息の発症にプロスタグランジン合成阻害作用が関与していると考えられる.]

■効能又は効果　経口製剤及び坐剤の投与が困難な場合における疼痛及び発熱
〈効能又は効果に関連する使用上の注意〉経口製剤及び坐剤の投与が困難で,静注剤による緊急の治療が必要である場合等,静注剤の投与が臨床的に妥当である場合に本剤の使用を考慮すること.経口製剤又は坐剤の投与が可能になれば速やかに投与を中止し,経口製剤又は坐剤の投与に切り替えること.

■用法及び用量　下記のとおり本剤を15分かけて静脈内投与すること.
＜成人における疼痛＞通常,成人にはアセトアミノフェンとして,1回300～1000mgを15分かけて静脈内投与し,投与間隔は4～6時間以上とする.なお,年齢,症状により適宜増減するが,1日総量として4000mgを限度とする.ただし,体重50kg未満の成人にはアセトアミノフェンとして,体重1kgあたり1回15mgを上限として静脈内投与し,投与間隔は4～6時間以上とする.1日総量として60mg/kgを限度とする.＜成人における発熱＞通常,成人にはアセトアミノフェンとして,1回300～500mgを15分かけて静脈内投与し,投与間隔は4～6時間以上とする.なお,年齢,症状により適宜増減するが,原則として1日2回までとし,1日最大1500mgを限度とする.＜2歳以上の幼児及び小児における疼痛及び発熱＞通常,2歳以上の幼児及び小児にはアセトアミノフェンとして,体重1kgあたり1回10～15mgを15分かけて静脈内投与し,投与間隔は4～6時間以上とする.なお,年齢,症状により適宜増減するが,1日総量として60mg/kgを限度とする.ただし,成人の用量を超えない.＜乳児及び2歳未満の幼児における疼痛及び発熱＞通常,乳児及び2歳未満の幼児にはアセトアミノフェンとして,体重1kgあたり1回7.5mgを15分かけて静脈内投与し,投与間隔は4～6時間以上とする.なお,年齢,症状により適宜増減するが,1日総量として30mg/kgを限度とする.
〈用法及び用量に関連する使用上の注意〉(1)本剤の投与に際しては,投与速度を厳守すること(本剤の有効性及び安全性は本剤を15分かけて静脈内投与した臨床試験において確認されている.【臨床成績】の項参照).なお,本剤の投与速度及び投与量により,循環動態に影響を及ぼすことが明らかに予想される患者には投与しないこと.(2)乳児,幼児及び小児の1回投与量の目安は下記のとおり.(「1.慎重投与」及び「2.重要な基本的注意」の項参照)

体重	5kg	10kg	20kg	30kg
アセリオ静注液1000mg	3.75mL	7.5～15mL	20～30mL	30～45mL

(3)乳児,幼児及び小児に対する1回あたりの最大用量はアセトアミノフェンとして500mg,1日あたりの最大用量はアセトアミノフェンとして1500mgである.

■使用上の注意　1.慎重投与(次の患者には慎重に投与すること)(1)アルコール多量常飲者[肝障害があらわれやすくなる(「3.相互作用」の項参照).](2)絶食・低栄養状態・摂食障害等によるグルタチオン欠乏,脱水症状のある患者[肝障害があらわれやすくなる.](3)肝障害又はその既往歴のある患者[肝機能が悪化するおそれがある.](4)消化性潰瘍の既往歴のある患者[消化性潰瘍の再発を促すおそれがある.](5)血液の異常又はその既往歴のある患者[血液障害を起こすおそれがある.](6)出血傾向のある患者[血小板機能異常が起こることがある.](7)腎障害又はその既往歴のある患者[腎機能が悪化するおそれがある.](8)心機能異常のある患者[症状が悪化するおそれがある.](9)過敏症の既往歴のある患者(10)気管支喘息のある患者[症状が悪化するおそれがある.](11)高齢者(「2.重要な基本的注意」及び「5.高齢者への投与」の項参照)(12)小児等(「2.重要な基本的注意」及び「7.小児等への投与」の項参照) 2.重要な基本的注意　(1)本剤の使用は,発熱,痛みの程度を考慮し,最小限の投与量及び期間にとどめること.(2)解熱鎮痛剤による治療は原因療法ではなく,対症療法であることに留意すること.原因療法があればこれを行うこと.(3)投与中は患者の状態を十分観察し,副作用の発現に留意すること.本剤の投与直後には経口製剤及び坐剤に比べて血中濃度が高くなることから,過度の体温下降,虚脱,四肢冷却等の発現に特に留意すること.特に高熱を伴う高齢者及び小児等又は消耗性疾患の患者においては,投与後の患者の状態に十分注意すること.(4)高齢者及び小児等には副作用の発現に特に注意し,必要最小限の使用にとどめるなど慎重に投与すること.(5)感染症を不顕性化するおそれがあるので,感染症を合併している患者に対して用いる場合には適切な抗菌剤を併用し,観察を十分行い慎重に投与すること.(6)他の消炎鎮痛剤との併用は避けることが望ましい.(7)アセトアミノフェンの高用量投与により副作用として腹痛・下痢がみられることがある.本剤においても同様の副作用があらわれるおそれがあり,疼痛又は発熱の原疾患に伴う消化器症状と区別できないおそれがあるので,観察を十分行い慎重に投与すること.(8)重篤な肝障害が発現するおそれがあるので注意すること.1日総量1500mgを超す高用量で長期投与する場合には定期的に肝機能検査を行い,患者の状態を十分に観察すること.高用量でなくとも長期投与する場合にあっては定期的に肝機能検査を行うことが望ましい.また,高用量で投与する場合などは特に患者の状態を十分に観察するとともに,異常が認められた場合には,減量,休薬等の適切な措置を講ずること. 3.相互作用　併用注意(併用に注意すること) 薬剤名等:アルコール(飲酒),クマリン系抗凝血剤/ワルファリン,イソニアジド,カルバマゼピン/フェノバルビタール/フェニトイン/プリミドン/リファンピシン 4.副作用　国内において,本剤の有効性,安全性を検証する臨床試験は行われていない. (1)重大な副作用 **1)ショック,アナフィラキシー**(頻度不明):ショック,アナフィラキシー(呼吸困難,全身紅潮,血管浮腫,蕁麻疹等)があらわれることがあるので,観察を十分に行い,異常が認められた場合には投与を中止し,適切な処置を行うこと. **2)中毒性表皮壊死融解症(Toxic Epidermal Necrolysis:TEN),皮膚粘膜眼症候群(Stevens-Johnson症候群),急性汎発性発疹性膿疱症**(頻度不明):中毒性表皮壊死融解症,皮膚粘膜眼症候群,急性汎発性発疹性膿疱症があらわれることがあるので,観察を十分に行い,異常が認められた場合には投与を中止し,適切な処置を行うこと. **3)喘息発作の誘発**(頻度不明):喘息発作を誘発することがある. **4)劇症肝炎,肝機能障害,黄疸**(頻度不明):劇症肝炎,AST(GOT),ALT(GPT),γ-GTPの上昇等を伴う肝機能障害,黄疸があらわれることがあるので,観察を十分に行い,異常が認められた場合には投与を中止し,適切な処置を行うこと. **5)顆粒球減少症**(頻度不明):顆粒球減少症があらわれることがあるので,観察を十分に行い,異常が認められた場合には投与を中止し,適切な処置を行うこと. **6)間質性肺炎**(頻度不明):間質性肺炎があらわれることがあるので,観察を十分に行い,咳嗽,呼吸困難,発熱,肺音の異常等が認められた場合には,速やかに胸部X線,胸部CT,血清マーカー等の検査を実施すること.異常が認められた場合には投与を中止し,副腎皮質ホルモン剤の投与等の適切な処置を行うこと. **7)間質性腎炎,急性腎不全**(頻度不明):間質性腎炎,急性腎不全があらわれることがあるので,観察を十分に行い,異常が認められた場合には投与を中止し,適切な処置を行うこと.

●その他の使用上の注意等につきましては、製品添付文書をご参照ください。

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2014年6月作成

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2013年10月作成