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ONCOTHERMIA JOURNAL

Introduction of Clifford Hospital

*Oncothermia activity and case reports in Clifford Hospital, Panyu,
Guangzhou, China*

Case reports

*Oncothermia-Booster (Targeted Radiofrequency) treatment – in some non-
oncological diseases as special physiotherapy*

*Connections between Warburg's and Szentgyorgyi's approach about the
causes of cancer*

*Why modulated electrohyperthermia (mEHT) destroys the rouleaux formation
of erythrocytes?*

Personalised dosing of hyperthermia

Editorial



Dear Readers,

in 2013 we were lucky to experience an exciting, large and professional conference in Guangzhou, China: The yearly meeting of the International Clinical Hyperthermia Society (ICHS) organized by Prof. Dr. Clifford LK Pang.

Prof. Pang manages a very successful hospital. The patient as a whole is in the center of his philosophy, and this is the clue of his medical success. Over the years we built up a personal friendship, and I am more than happy that this year he is president of the ICHS again and will host the annual conference. We are very much looking forward to this event.

Prof. Pang contributed a lot to this issue of the Oncothermia Journal and kindly provided information about his hospital. He also wrote an article on their Oncothermia activity and especially mentioned several case reports showing the wide range of treatment areas and the remarkable success even for advanced cases.

We are happy to share other case reports as well with the Oncotherm community: two doctors from Pakistan sent us case reports and we are proud to see their results.

This volume of our Journal also provides articles on the topics of the Booster treatment, Warburg's and Szentgyorgyi's approaches, the destruction of the rouleaux formation of erythrocytes by modulated electrohyperthermia and the personalized dosing of hyperthermia.

hope you enjoy reading, and could use the Journal in your everyday practice!

Sincerely yours,

Prof. Dr. Andras Szasz

Liebe Leserinnen, liebe Leser,

Im Jahre 2013 hatten wir das Glück eine spannende, große und professionelle Konferenz in Guangzhou, China zu erleben: Das jährliche Treffen der Internationalen Klinischen Hyperthermie Gesellschaft (International Clinical Hyperthermia Society - ICHS), organisiert von Prof. Dr. Clifford LK Pang.

Prof. Pang leitet ein sehr erfolgreiches Krankenhaus. Der Patient als Ganzes steht im Mittelpunkt seiner Philosophie und diese Haltung ist das Geheimnis seines medizinischen Erfolgs. Im Laufe der Jahre haben wir eine persönliche Freundschaft aufgebaut und ich bin überglücklich, dass er dieses Jahr wieder Präsident der ICHS ist und die jährliche Konferenz veranstalten wird. Wir freuen uns sehr auf diese Veranstaltung.

Prof. Pang hat viel zu dieser Ausgabe des Oncothermia Journals beigetragen und gab uns freundlicher Weise Informationen über sein Krankenhaus. Er hat auch einen Artikel über die Oncothermie-Behandlungen in China geschrieben und einige Fallberichte zur Verfügung gestellt, die das breite Spektrum der Therapiemöglichkeiten und den bemerkenswerten Erfolg auch bei fortgeschrittenen Erkrankungen zeigen.

Wir freuen uns, auch andere Fallberichte mit der Oncotherm-Gemeinschaft zu teilen: Zwei Ärzte aus Pakistan haben uns Case Reports geschickt und wir sind stolz darauf, ihre guten Ergebnisse vorstellen zu dürfen.

Diese Ausgabe unserer Zeitschrift bietet auch Artikel über die Themen der Booster-Behandlung, Warburgs und Szentgyorgyis Ansätze, die Zerstörung der Rouleaux Bildung von Erythrozyten durch die modulierte Elektrohyperthermie und die personalisierte Dosierung der Hyperthermie.

Ich wünsche Ihnen viel Freude beim Lesen und hoffe, Sie können die Informationen aus dem Journal in Ihrem Alltag nutzen!

Mit freundlichen Grüßen,

Prof. Dr. Andras Szasz

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As the editorial team we are committed to a firm and coherent editorial line and the highest possible printing standards. But it is mainly you, the author, who makes sure that the Oncothermia Journal is an interesting and diversified magazine. We want to thank every one of you who supports us in exchanging professional views and experiences. To help you and to make it easier for both of us, we prepared the following rules and guidelines for abstract submission.

Als redaktionelles Team vertreten wir eine stringente Linie und versuchen, unserer Publikation den höchst möglichen Standard zu verleihen. Es sind aber hauptsächlich Sie als Autor, der dafür Sorge trägt, dass das Oncothermia Journal zu einem interessanten und abwechslungsreichen Magazin wird. Wir möchten allen danken, die uns im Austausch professioneller Betrachtungen und Erfahrungen unterstützen. Um beiden Seiten die Arbeit zu erleichtern, haben wir die folgenden Richtlinien für die Texterstellung entworfen.

1. Aims and Scope

The Oncothermia Journal is an official journal of the Oncotherm Group, devoted to support them, making a collective for using the results and making it common for general use. The Oncothermia Journal has an open-minded character, expecting the complete study-papers, case-reports, reviews, hypotheses, opinions, and all the informative materials which could be helpful for the international Oncotherm community. Advertisement connected to the topic is also welcome.

- *Clinical Studies*: Regional or local or multilocal oncothermia or electro cancer therapy (ECT) treatments, case-reports, practical considerations in complex therapies, clinical trials, physiological effects, Oncothermia in combination with other modalities, and treatment optimization.
- *Biological Studies*: Mechanisms of oncothermia, thermal-or non-temperature dependent effects, response on electric fields, bioelectromagnetic applications for tumors, Oncothermia treatment combination with other modalities, effects on normal and malignant cells and tissues, immunological effects, physiological effects, etc.
- *Techniques of oncothermia*: Technical development, new technical solutions, proposals.
- Hypotheses, suggestions, opinions to improve the oncothermia and electro-cancer-therapy methods, intending the development of the treatments.

Further information about the Journal, including links to the online sample copies and content pages can be found on the website of the journal: www.Oncothermia-Journal.com.

1. Selbstverständnis und Ziele

Das Oncothermia Journal ist das offizielle Magazin der Oncotherm Gruppe und soll diejenigen unterstützen, die ihre Ergebnisse der Allgemeinheit zur Verfügung stellen möchten. Das Oncothermia Journal ist neuen Inhalten gegenüber offen, sollte aber vor allem Studienarbeiten, Fallstudien, Hypothesen, Meinungen und alle weiteren informativen Materialien, die für die internationale Oncotherm-Gemeinschaft hilfreich sein könnten, enthalten. Werbung mit Bezug zum Thema ist ebenfalls willkommen.

- *Klinische Studien*, regionale, lokale oder multilokale Oncothermie oder Electro Cancer Therapy (ECT) Behandlungen, Fallstudien, praktische Erfahrungen in komplexen Behandlungen, klinische Versuche, physiologische Effekte, Oncothermie in Kombination mit anderen Modalitäten und Behandlungsoptimierungen.
- *Biologische Studien*. Mechanismen der Oncothermie, thermale oder temperaturunabhängige Effekte, Ansprechen auf elektrisches Feld, bioelektromagnetische Anwendungen bei Tumoren, Kombination von Oncothermie und anderen Modalitäten, Effekte auf normale und maligne Zellen und Gewebe, immunologische Effekte, physiologische Effekte etc.
- *Oncothermie-Techniken*. Technische Entwicklungen, neue technische Lösungen.
- Hypothesen, Meinungen, wie die Oncothermie- und ECT-Methoden verbessert werden können, um die Behandlung zu unterstützen.

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All submissions should be made online at the Oncothermia Journal by email Oncothermia-Journal@oncotherm.org.

2. Manuskripte einreichen

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3. Preparation of Manuscripts

Manuscripts must be written in English, but other languages can be accepted by special reasons, when it has an English abstract.

Texts should be supplied in a format compatible with Microsoft Word for Windows (PC). Charts and tables are considered textual and should also be supplied in a format compatible with Word. All figures (illustrations, diagrams, photographs) should be supplied in JPG format.

Manuscripts may be any length, but must include:

- *Title Page*. Title of the paper, authors and their affiliations, 1-5 keywords. At least one corresponding author should be identified, whose email address has to be provided with full contact details.
- *Abstracts*. Abstracts should include the: Purpose, Materials and Methods, Results, Conclusions.
- *Text*. Unlimited volume.
- *Tables and Figures*. Tables and figures should be referred to in the text. (numbered figures and tables). Each table and/or figure must have a legend that explains its purpose without reference to the text. Figure files will ideally be supplied as jpg-file (300dpi for photos).
- *References*. Oncothermia Journal uses the Vancouver (Author-Number) system to indicate references in the text, tables and legends, e.g. [1], [1-3], [1-3]. The full references should be listed numerically in order of appearance, and presented following the text of the manuscript.

3. Manuskripte vorbereiten

Manuskripte müssen in englischer Sprache vorliegen. Andere Sprachen können in Ausnahmefällen akzeptiert werden, wenn ein englisches Abstract vorliegt.

Texte sollten in einem mit Microsoft Word für Windows (PC) kompatiblen Format eingereicht werden. Tabellen sollten in einem Word-kompatiblen Format eingefügt werden. Alle Graphiken (Illustrationen, Diagramme, Photographien) sollten im jpg Format vorliegen.

Manuskripte können jede Längen haben, müssen aber die folgenden Punkte enthalten:

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- **Abstracts.** Abstracts müssen enthalten: Zielsetzung, Material und Methoden, Ergebnisse, Fazit.
- **Text.** Beliebige Länge.
- **Abbildungen und Tabellen.** Abbildungen und Tabellen sollten im Text erläutert werden (nummeriert). Jede Abbildung / Tabelle muss eine erklärende Bildunterschrift haben. Bilder sollten als jpg verwendet werden (300 dpi).
- **Zitate.** Das Oncothermia Journal verwendet die Vancouver Methode (Autornummer), um Zitate auszuweisen, z.B. [1], [1-3], [1-3]. Die Bibliographie erfolgt numerisch in Reihenfolge der Erwähnung im Text.

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8. Legal responsibility

Authors of any publications in the Oncothermia Journal are fully responsible for the material which is published. The Oncothermia Journal has no responsibility for legal conflicts due to any actual publications. The Editorial Board has the right to reject any publications if its validity is not enough controlled or the Board is not convinced by the Authors.

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Die Autoren aller im Oncothermia Journal veröffentlichten Artikel sind in vollem Umfang für ihre Texte verantwortlich. Das Oncothermia Journal übernimmt keinerlei Haftung für die Artikel der Autoren. Der redaktionelle Beirat hat das Recht, Artikel abzulehnen.

9. Reviewing

The Oncothermia Journal has a special peer-review process, represented by the Editorial Board members and specialists, to whom they are connected. To avoid personal conflicts the opinion of Reviewer will not be signed, her/his name will be handled confidentially. Papers which are not connected to the scope of the Journal could be rejected without reviewing.

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Contents

CONTENTS

Contents.....	6
Introduction of Clifford Hospital	7
Oncothermia activity and case reports in Clifford Hospital, Panyu, Guangzhou, China	21
Case reports	77
Oncothermia-Booster (Targeted Radiofrequency) treatment – in some non-oncological diseases as special physiotherapy	83
Connections between Warburg’s and Szentgyorgyi’s approach about the causes of cancer	89
Why modulated electrohyperthermia (mEHT) destroys the rouleaux formation of erythrocytes?	103
Personalised Dosing of Hyperthermia	112
Advertisement	122

Introduction of Clifford Hospital

Clifford L. K. Pang, Professor, MD, PhD*

* President (2013) of ICHS, President of WFCMS-SCNT, President of Clifford Hospital

Clifford Hospital

- Integrative approach to treatment that combines Traditional Chinese Medicine, Western Medicine and Natural Medicine
- An exceptional JCI accredited hospital in China
- China's Level A Tertiary Hospital of Traditional Chinese Medicine and Western Medicine (advanced level in China's hospital grading system)
- Member of World Federation of Chinese Medicine Societies - Specialty Committee of Natural Therapy
- Designated Hospital for International Medical Services
- Designated Hospital for Government Medical Care and Medical Insurance



About Us

JCI Accreditation

Joint Commission International (JCI) is a global accreditation organization which evaluates health care quality. It is an academic body recognized by World Health Organization. The accreditation commission holds the highest standards in hospital accreditation in the world. Their evaluation team comprise of experts from 18 countries. Once accreditation certification is granted, a triennial reassessment for reaccreditation is ongoing.

Clifford Hospital was successfully accredited by JCI in 2003, the first JCI accredited hospital in China which has fully adopted JCI hospital management standards; Clifford Hospital was successfully reaccredited by JCI in 2006, 2009, 2012, and 2015; Clifford Hospital remains the only hospital in China with five consecutive accreditations high evaluation grade.

As an integrated hospital in China that combines Traditional Chinese Medicine, Western Medicine and Natural Medicine, Clifford Hospital succeeded in 5 consecutive JCI accreditations. This achievement is a testament to Clifford hospital's full compliance with international health care standards in hospital management and quality of patient care.

An International General Hospital

Founded in 2001, Clifford Hospital covers an area of 90,000 square meters, with a capacity of 650 licensed inpatient beds. The hospital serves 3000 outpatient visits per day. Currently, the phase II building is under construction, to be fully operational in 2017. The total number of inpatients beds will increase to 3,000, and outpatient visits will increase to 12,000 per day.

Clifford Hospital presents a hotel-like environment which complies with international hospital management standards. The hospital utilizes state-of-the-art medical technologies and equipment. For more than 1,000 health care professionals poised to provide quality patient-centered care. Patients from over 120 countries have visited Clifford Hospital for treatment and preventive health care.



Hospital mission: Commitment to highest quality patient-focused care with dedication, compassion and a profound respect for human life

Hospital vision:

- Clifford Hospital’s effective integrative approach to treatment and prevention to serve as the universal standard for all health care practitioners
- To continually deliver comforting, safe and time/cost efficient care to patients
- A modern comprehensive general hospital that upholds exemplary national and international health care standards
- To provide an advanced physical facility that promotes calm healing in combination with state-of-the-art technology in treatment and prevention

Non-toxic integrative cancer treatment, targeting both causes and symptoms

Clifford Hospital is a general hospital with a full range of health care services, supported by a team of specialists in Western Medicine, Chinese Medicine, and Natural Medicine. Based on the “non-toxic” principle, the multidisciplinary team conferences address both the symptoms and causal pathogenesis.

A general hospital with multi-specialty medical and health services

As an institution of health care services, education and research, disease prevention and management, Clifford Hospital is an integrated general hospital in China with outpatient and inpatient departments and emergency unit. It has more than 40 clinical and technical departments and approximately 200 outpatient consultation rooms.

Multi-specialty clinical and technical support services:

Oncology Center, Cardiology, Neurology, Endocrinology, Gastroenterology & Hepatology, Respiratory Medicine, Nephrology, Gynecology and Obstetrics, Pediatrics, General Surgery,

Orthopedics, Cardiothoracic Surgery, Urology, Neurosurgery, Colorectal, Dermatology, Dentistry, E.N.T., Ophthalmology, Emergency Center, ICU, Acupuncture and Massage Therapy, Rehabilitation Clinic, Children's Rehabilitation Clinic, TCM Rehabilitation Clinic, Nutrition, Preventive Medicine, Hyperthermia Center, Medical Ozone Center, Chelation, Physical Checkup Center, Radiology, Ultrasound, Laboratory, Pathology, Functional Testing Department, Anesthesiology, Operating Theatre, Endoscopy, Hemodialysis, and pharmacy.

Multidisciplinary team collaboration to prescribe the most effective treatment plan

Clifford Hospital has a competent and professional team of specialists consisting of over 1,000 health care professionals specializing in Chinese medicine, western medicine and natural medicine. 50 of the practitioners hold titles of excellence in national and provincial Chinese Medicine, with doctoral and post graduate credentials. In addition, overseas visiting physicians provide outpatient consults on a regular basis.

Our integrative medicine team jointly assess and evaluate each patient to formulate an effective individualized protocol. Each protocol integrates Traditional Chinese Medicine, Western Medicine and Natural Medicine, aiming to maximize treatment success, to reduce side effect, and to accelerate recovery.



Unique patient care combining Western Medicine, Chinese Medicine and Natural Medicine
Clifford Hospital is staffed by specialists with extensive experience and knowledge in Western Medicine, Traditional Chinese Medicine and Natural Medicines. Guided by the Non-toxic principle and philosophy, our treatment focuses on both symptoms and causation of the disease.

A general hospital with a diversity of health care services

Since its inception, Clifford Hospital stays committed to developing a patient focused care model combining western medicine, Chinese medicine, and natural medicine. The following distinct specialty programmes allow patients access to safe, appropriate and efficient care.

Oncological Integrative Treatment Center

Non-toxic integrative approach to cancer treatment developed by Clifford Hospital's Oncological Integrative Treatment Center is growing recognition by international health care communities as a successful cancer therapy combining western medicine, Traditional Chinese medicine, and natural medicine. At Clifford Hospital, TCM and Natural Medicine are indispensable treatment components in conjunction with conventional surgery, radiotherapy, and chemotherapy in cancer treatment.

Integrative cancer treatment adopts a holistic approach to treat symptoms and root causes of the disease. An individual care plan is formulated through collaborative effort of a team of specialists in Western Medicine, TCM and Natural Medicine. Modern techniques in natural therapies such as hyperthermia, chelation, medical ozone therapy, etc. are combined with TCM and practices, some

of which include acupuncture, herbal medicine, nutritional therapy, medical Qigong, etc. They serve to remove patient's internal disease causing toxins, to maintain balance, and to boost immune system, preventing relapses and metastases.

International Natural Medicine Center



Over 180 types of domestic and international therapies derived from natural elements such as light, sound, water, cold, heat, magnet, etc. are utilized in treatment. Natural medicine is a non-invasive form of treatment which activates the bodies' self healing potential to achieve the goal of prevention and cure.

Patients receive individualized care through multidisciplinary team consultation involving an integrative approach to diagnostics and treatment by combining Western Medicine, TCM and Natural Medicine.

Advanced medical facilities of international standard

Clifford Hospital is equipped with state-of-the-arts medical technology of international standard. This enables accuracy and precision in diagnostic assessments, to achieve optimal treatment outcome. It is by incorporating an integrative approach and up-to-date technology which enables Clifford Hospital to gain its distinct reputation.

An elegant, peaceful and healing environment to enhance patient's experience

Clifford Hospital is known for its unique therapeutic setting. The hotel-like outpatient lobby, clinics and wards convey a clean, spacious and comfortable environment.

The botanical garden on the 6th floor of Clifford Hospital has an array of more than 100 species of flowers, Chinese medicinal herb and exotic trees. This healing garden creates an idyllic surrounding for patients to relax, exercise and rehabilitate.



Ambience

Our dedicated and attentive staff at your service

Clifford Hospital is committed to patient-centered care to meet the different needs of our patients and their families. Some of the services include health and wellness center, VIP services, international customer service (translate and interpret), facilitate insurance claims and reasonable hotel-like accommodations for families.

The health and wellness center provides patients a respite from their daily treatment routine

Some of the amenities include reading room, billiard room, painting, calligraphy room, card room, etc. This facility provides a tranquil place for patients to mingle, relax, exercise and convalesce. A sacred space is available for prayer and meditation.

Serviced Apartment

An optimal choice of accommodation for patient's family and friends, easy walking distance from Clifford Hospital

Featured Services

1. Restaurants serve Chinese and Western cuisine and complimentary nutritious breakfast.
2. Every apartment has a private balcony and fully equipped kitchen for meal preparations.
3. A serene lake surrounded by well maintained gardens where guests can enjoy leisurely walks.
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Service Hotline: (8620) 3990 2292

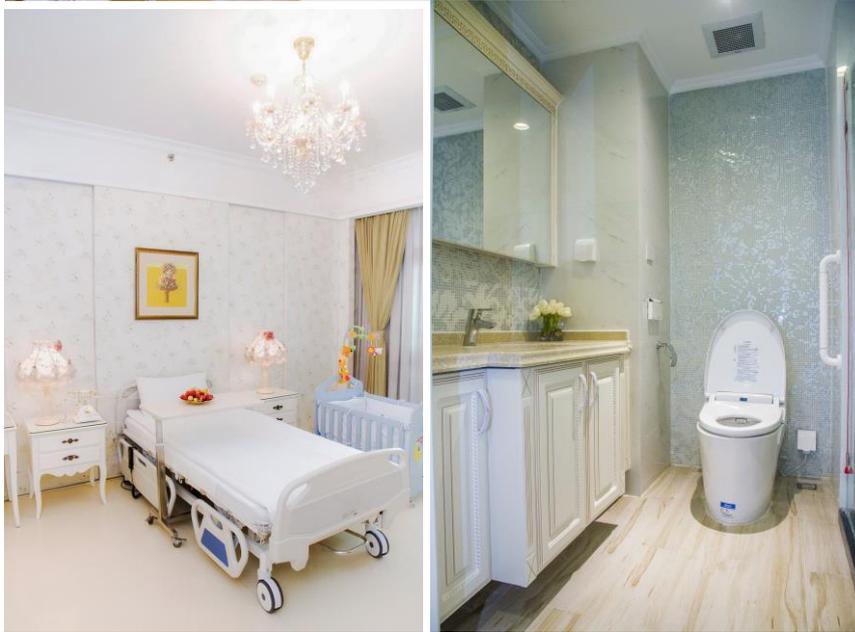
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Commitment to education and research

Over the years, Clifford Hospital has partnered with academic institutions in clinical teaching and research, accepting students for academic study and exchange.



Education and research

Partnership with many well-renowned academic institutions in clinical education and research. As a teaching hospital, select Clifford Hospital professors and physicians provide mentorship, training and guidance to medical school graduates from academic intuitions and medical universities throughout China and abroad. Education and research include the 3 specialty areas of integrative treatment, Western Medicine, Traditional Chinese Medicine and Natural Medicine.

We strive to surpass yesterday

Clifford Hospital's medical team attaches great importance to academic exchange. It is by means of facilitating platforms for domestic and international conferences or regular participation as guest speakers on their specialty and expertise both domestically and abroad.

Academic Exchange

- Fourth International Academic Conference on Traditional Chinese Medicine
- Third World Integrative Medicine Congress (WIMCO)
- First International Medicine Forum on Oncology and Hyperthermia
- The Inaugural Meeting of World Federation of Chinese Medicine Societies-Specialty Committee of Natural Therapy (WFCMS-SCNT) and 1st International Academic Conference on Natural Medicine
- The 2nd Academic Meeting of World Federation of Chinese Medicine Society-Specialty Committee of Natural Therapy(WFCMS-SCNT)
- The 32nd Annual Conference of the International Clinical Hyperthermia Society (ICHS) and the 3rd Annual Conference of The World Federation of Chinese Medicine Societies-Specialty Committee of Natural Therapy (WFCMS-SCNT)
- Clifford Hospital Successfully Held a National Academic Seminar on Traditional Chinese Medicine and Natural Medicine on Cancer Treatment
- The 33rd Annual Conference of the International Clinical Hyperthermia Society (ICHS)
- The 34th Annual Conference of the International Clinical Hyperthermia Society (ICHS)



Hyperthermia center in Clifford Hospital

Founded in 2005, Clifford Hospital Hyperthermia Center is the largest hyperthermia center in the world, equipped with advanced German Heckel-HT2000M Infrared Whole Body Hyperthermia machine, Hungarian OncoTherm EHY-2000 Local RF Hyperthermia machine and NRL-002 Radiofrequency Field Thermo-Therapeutic machine. It is also equipped with advanced centralized patient monitoring system and good medical treatment facilities. Training program and academic seminars by domestic and foreign hyperthermia specialists are held regularly. And this Center, which has excellent domestic hyperthermia professionals, applies the integration of Traditional Chinese and Western medicine therapies for both whole body (general) and local hyperthermia. World (National) renowned hyperthermia professors offer consultations regularly.



What is Hyperthermia?

Hyperthermia is a method of combining modern medical high-technology and ICU technology with the assistance of various heat sources to heat body tissues to treat cancers and other diseases. Hyperthermia has a long history. Due to its new development avenues with modern high-technology, it creates a new system of modern hyperthermia medicine, which has reliable therapeutic effects and minimal side effects. So hyperthermia is also named 'Green Therapy'. Hyperthermia has the following functions: Speeding up the metabolism rate; removal of endotoxin; improve microcirculation; facilitate the recovery of normal physiological activities and activate the body's immune system. It has the function of anti-inflammation, antibacterial effect and enhancement of other therapeutic effects. The treatment is mainly used in the following fields: Cancer treatment, gynecological diseases, rheumatism, detoxification and beauty-building, etc. It is safe and effective.

The Mechanism of Cancer Treatment

The mechanism of cancer treatment is as follows:

1. Killing Cancer Cells

Hyperthermia can change the fluidity of biomembrane, leading to destruction of cell membrane that may result in the death of cancer cells.

2. Inhibiting the Metastasis Trend of Tumor

Hyperthermia can inhibit the synthesis and repair of cell DNA, RNA and protein to stop cancer cells' reproduction, and inhibit the gene expression and synthesis of tumor matrix metalloproteinase to inhibit the metastasis trend of tumor.

3. Enhancing the Curative Effect of Chemotherapy

Hyperthermia can change the permeability of cell membrane to increase the concentration of anticancer drugs in cytoplasm, which are sensitive to chemotherapy.

4. Improving the Curative Effect of Radiotherapy

Hypoxic cells and the cells in the S stage are sensitive to heat but resistant to radiation, this compensates the other. This is why heat may increase the curative effect of radiotherapy.

5. Inhibiting the Formation of Tumor Blood Vessels

Experiment showed that whole body hyperthermia can inhibit gene expression and synthesis of vascular endothelial growth factor (VEGF) excreted by cancer cells to prevent the formation of blood vessels in cancer, which destroys the basic condition for growth and development of cancer metastasis.

6. Marrow Protection

Whole body hyperthermia can induce bone marrow to produce cytokine, stimulate and increase peripheral blood and marrow to produce various cytokine (Colony Stimulating Factor CSF, various Interleukin, Tumor Necrosis Factor- α , etc.) which can induce the differentiation of peripheral blood and hematopoietic stem cells in bone marrow. Clinical practices showed that whole body hyperthermia will not increase marrow suppression by radiation or chemotherapy, but strengthens these therapeutic effects.

7. Hyperthermia improves the function of Immune System

Whole body hyperthermia can stimulate and reinforce the function of body's immune system, whole body hyperthermia (41.8 °C) can activate long acting T-lymphocyte and whole body hyperthermia (39.8 \pm 2 °C/6h) can increase the activity of T- and B-lymphocyte and the anti-tumor activity of natural killer cells (NK), and can facilitate the redistribution of body's white blood cells to improve the monitoring function of body's immune system.

Treatment Scope

Hyperthermia is basically divided into 3 types: Whole body hyperthermia, local hyperthermia and regional hyperthermia. Because of the different routes and different range of heating temperature, the treatment scopes are also different.

I Whole Body Hyperthermia

1. Cancer Treatment

1.1 High-temperature whole body hyperthermia: With extremely high technology, it is a method which can effectively cure many kinds of cancer and can greatly improve the curative effect of other treatment methods. It may be applied to the following cancers: Lung cancer, esophageal cancer, stomach cancer, liver cancer, colon cancer, ovarian cancer, breast cancer, soft tissue

sarcoma, osteosarcoma, malignant melanoma, malignant lymphoma and lymph node metastasis, etc. High temperature whole body hyperthermia has all the functions of medium - low temperature whole body hyperthermia.

1.2 Medium-low temperature whole body hyperthermia: It is an easily acceptable hyperthermia therapy by most patients, and its treatment scope is as follows:

1.2.1 Combined with chemotherapy and radiotherapy, it can cure various kinds of malignant tumor applicable to high-temperature whole body hyperthermia and can improve their effect. The curative effect of this combination is more than the total of each treatment alone.

1.2.2 It can activate body's immune system and increase body's anti-tumor immune mechanism.

1.2.3 It has special curative effect on relieving pain of advanced cancer patients.

2. Treatment on Benign Diseases

With high safety, medium-low temperature whole body hyperthermia can cure many kinds of benign diseases and has effect on health care, cosmetics and beauty-building, detoxification, and weight lost etc. Curative diseases include:

2.1 Gynecological diseases: Chronic pelvic inflammatory disease, chronic salpingitis, endometritis, dysmenorrhea and infertility caused by chronic inflammation, etc.

2.2 Other chronic inflammations: Chronic cholecystitis, prostatitis, rheumatic arthritis, and chronic rhinitis, etc.

2.3 Detoxification: Eliminate all toxin absorbed by any reason in vivo and repair tissue injury caused by poisoning.

2.4 Cosmetology and beauty-building: Because it can facilitate facial blood circulation, open facial sweat glands and micro-channels, and excrete metabolic waste and colored particles of facial tissues, it has better effects in combination with other cosmetics treatments. It has good results on acne.

2.5 Functional recovery treatment: It can facilitate the recovery of body's automatic function, ease muscle cramps, allay tiredness, quicken neurotransmitter transmission and improve body's response ability. It has special curative effect on muscle strain, low back pain, and bone and joint degenerative diseases.

2.6 Losing weight: It can reduce weight because it can quicken metabolism in the body, burn body fat when the temperature rises and reduce fat storage.

2.7 Improving body's immune system: It can improve body's disease prevention capability because it can activate body's immune mechanism.

II Localised Hyperthermia

1. Malignant Tumor Treatment

1.1 Superficial tumor: Basal cell carcinoma, cervical lymph node metastasis carcinoma, supraclavicular lymph nodes metastasis carcinoma, melanoma and breast cancer.

1.2 Many kinds of advanced tumors that relapsed after chemotherapy, radiotherapy or surgery.

1.3 Remaining tumor that cannot be removed by surgical procedures

1.4 Intractable pain of advanced cancer.

2. Many kinds of benign diseases

Treatment of chronic inflammation: Chronic pelvic inflammatory disease, chronic salpingitis, endometritis, urinary system chronic inflammation, chronic cholecystitis, chronic prostatitis and rheumatic arthritis, etc.

Hyperthermia - New weapon for treatment of malignant tumors

Hyperthermia is currently the most effective method of tumor treatment after surgical operations, radiotherapy and chemotherapy. It may be divided into whole body hyperthermia, local hyperthermia and regional hyperthermia. It is mainly applicable to the following situations:

1. Hyperthermia may be applied in the treatment of many cancers: Lung cancer, esophageal cancer, gastric cancer, brain cancer, liver cancer, colon cancer, ovarian cancer, breast cancer, soft tissue sarcoma, osteosarcoma, malignant melanoma, malignant lymphoma,

- lymph node metastasis carcinoma, basal cell carcinoma and skin cancer, etc.
- 2. Residue cancer after surgery.
- 3. Many kinds of advanced cancer that relapsed after chemotherapy, radiotherapy or surgery.
- 4. It has special curative effects on intractable pain of advanced cancer.
- 5. It can reduce the incidences of metastases and recurrence of cancers.
- 6. It can reduce the side effects of chemotherapy and radiotherapy.

Hyperthermia - New nemesis for gynecological diseases and chronic inflammation

It is safe and reliable and with good effect in using medium - low temperature wholebody hyperthermia, local hyperthermia and regional hyperthermia to treat various kinds of gynecological diseases and chronic inflammation.

1. Gynecological diseases: Chronic pelvic inflammatory disease, chronic salpingitis, endometritis, dysmenorrhea and infertility caused by chronic inflammation, etc.
2. Other chronic inflammations: Cholecystitis, prostatitis, rheumatic arthritis, rhinitis, etc.

Hyperthermia - New means of health care and function recovery

Medium-low temperature wholebody hyperthermia has the effect in improving body's functional recovery and body's immune system and health care, etc.

1. Functional recovery treatment: It can facilitate the recovery of body' s function, alleviate muscle spasms, allay tiredness and improve body's reaction ability. It has special curative effect on muscle strain, low back pain and bone joint degenerative diseases.
2. Improving body's immune system: Heating can activate body's immune system and improve disease prevention capability.

Hyperthermia - New concept of cosmetology, skin care, detoxification and beauty-building

Medium-low temperature wholebody hyperthermia can speed up metabolism; improve blood circulation, immediately remove the metabolic waste and endotoxin in body; and repair injured tissues. It has also effect on detoxification, cosmetology, beauty-building, weight lost, etc.

Characteristic Hyperthermia - German Whole body Hyperthermia System and Process

Whole body hyperthermia has its special effect. In the past, because it was with some danger that its use was very restricted when applied to human beings. During heating, it needs to be done under general anesthesia, and multidisciplinary physicians are involved during treatment, which led to restriction of application of whole body hyperthermia in many hospitals. Clifford Hospital has introduced advanced German Heckel-HT2000M Infrared Whole body Hyperthermia Unit in China, and has acquired unprecedented effect and significant hyperthermia data when performing whole body hyperthermia under the control of moderate and deep anesthesia after German hyperthermia specialists' training. Now, patients have no need to perform intubation and anesthesia and the therapy can be safely conducted during sleep. This has been performed in hundreds of patients over 3 years, without major complications. Under whole body hyperthermia, good effects are achieved when used in combination with chemotherapy, radiotherapy, hyperthermic perfusion or with Traditional Chinese Medicine, etc, especially for intraperitoneal hyperthermia perfusion.

Characteristic Hyperthermia - Hungarian OncoTherm EHY-2000 RF Local Hyperthermia System

Clifford Hospital has introduced advanced Hungary OncoTherm EHY-2000 RF Local Hyperthermia System in China. In the past, local radio-frequency hyperthermia did not allow application to the head region. However, the Hungary OncoTherm EHY-2000 RF Local Hyperthermia System not only conducts local hyperthermia in various parts of the body, but it can also conduct local hyperthermia for intracranial tumor non-invasively. It has better curative effect when combined with chemotherapy or radiotherapy. During the past 3 years, we have not recorded

any side effects on hundreds of patient treatments. This has opened up a new field for hyperthermia.

For advanced intraperitoneal and pelvic malignant tumor, traditional therapies such as surgery, radiotherapy and whole body chemotherapy are not effective. However, in recent years, by the continuous efforts of domestic and foreign hyperthermia specialists and the development of high-tech hyperthermia devices, we have created a very effective treatment method in using hyperthermia to treat medium and advanced abdominal and pelvic primary and metastasis lesions, which is intraperitoneal hyperthermic perfusion chemotherapy.

Peritoneum is a semi permeable membrane with bidirectional permeability which has great power for absorbing body fluid and micro-particles. Due to its absorption ability, the medication concentration of portal system is up to 10 times that of peripheral blood, which has good effect in treating hepatic and pancreatic tumor. The concentration of some anti-tumor drugs is 15 times higher in the abdominal cavity than in the plasma. The concentration of some immunodepressants is 4,000 times higher in abdominal cavity than in the plasma. The function of killing cancer cells of many anti-cancer drugs is dependent on its concentration, that is to say, the higher the concentration, the higher the lethality. After injection of drug into the abdominal cavity, because of the function of abdominal barrier, the intraperitoneal and pelvic drug concentration is higher than that in the plasma's, which makes it more effective. However, hyperthermia can directly kill cancer cells and at the same time, can increase the efficacy of drugs and improves body's immune ability. Among all hyperthermia, the technique and effect of whole body hyperthermia has more advantages. The most advanced hyperthermia technique in China is that of performing intraperitoneal hyperthermic perfusion chemotherapy under whole body hyperthermia, and this has achieved significant effect in clinical treatment in recent years. Intraperitoneal hyperthermic perfusion chemotherapy under whole body hyperthermia can achieve 41.8 °C after drug injection into abdominal cavity, and it can maintain 40 °C to 41.8 °C for 240 minutes, which goes beyond local or regional hyperthermia's capability of 39.5 °C to 40.5°C for 60–90 mins. This has made a big progress in hyperthermia.



**Dr. Clifford L. K. Pang,
MD, PhD, Founder, CEO and Hospital Director of Clifford Hospital**

For over a decade, Professor Clifford L. K. Pang worked on the theory and clinical practice of hyperthermia for cancer treatment. He pioneered Non-Toxic Integrative Cancer Treatment combining hyperthermia with natural therapies such as chelation, detoxification, ozone therapy, TCM, acupuncture & moxibustion, Qigong, and nutrition therapy. Widely recognized by his peers, his research findings have been presented in medical conferences in China and around the world.

He is a professor and mentor for doctoral students of Guangzhou University of Chinese Medicine; Director of 32nd Annual Conference of the World Clinical Hyperthermia Society; President of

World Federation of Chinese Medicine Societies - Specialty Committee of Natural Therapy (WFCMS-SCNT); Director of Soong Chingling Foundation; Director of the 2nd Session of Chinese Hospital Association; Standing Director of the 5th Session of the China Association of Chinese Medicine; Director of Continuing Education Base for National Clinical Tumor Prevention with TCM; Vice Director of the 4th Session of Tumor Committee of the Guangdong Association of Integrative Traditional and Western Medicine; and Vice Director of the 8th Committee of Guangdong Hospital Associations.

“Outstanding President of China TCM Hospitals”, and “China Top Ten Hospital Merit Award”, are among the many national awards granted for Professor Pang’s contributions.

Publications:

1. *Clifford LK Pang (2008) JCI Hospital Standards Practical Guidelines*. People's Medical Publishing House, USA
2. *A Study of Non-Toxic Integrative Cancer Treatments* edited by Professor Clifford L.K. Pang and published by China TCM Publishing House in 2008;
3. *Non-Toxic Integrative Cancer Treatments—a New Approach for Cancer Prevention and Treatments* edited by Professor Clifford L.K. Pang and published by Hong Kong Economic Journal Publishing House in 2011;
4. *Hyperthermia in Oncology* edited by Professor Clifford L.K. Pang (Chinese edition) published by People's Medical Publishing House in 2013
5. *Hyperthermia in Oncology* edited by Professor Clifford L.K. Pang (English edition) published by CRC Press in 2015.

**Oncothermia activity and case reports in Clifford Hospital,
Panyu, Guangzhou, China**

Editorial Note: written by Prof. Andras Szasz*

* St. Istvan University, Department of Biotechnics, Hungary

Clifford hospital is an eminent private medical center in China. It was founded in 2001 by Professor Dr. Clifford Pang. It is the first hospital in China accredited by [Joint Commission International](#) (JCI), and yearly reaccredited as well as it has been awarded China's Level A Tertiary Hospital.

Clifford Hospital covers an area of 90,000 square meters and has the capacity of 600 inpatients, and its enlargement to over 2,000 in-patient capacity is in progress, giving an enormous medical facility for Chinese and foreign patients. Presently it serves 3,000 outpatients per day, and its capacity will be extended remarkable anticipated to increase to 12,000 daily ambulance services. The hospital accepts both Chinese patients and patients from foreign countries, such as the US, Canada, Malaysia, India and the Philippines. It has more than 40 clinical departments, and equipped with the latest medical technology for diagnostics and curative applications. Oncotherm is proud to have more than 10 years working cooperation with Prof. Pang and with his medical complexes.

The Clifford Hospital is eminent not only for their excellent results but due to their research and eager to have the complex integrative approach of personalized medicine with top level of state-of-art knowledge of the international medicine and clinical practice. They amalgamate the high-level traditional medical knowledge with the most modern availabilities, providing the best processes and personalized attention for their patients in all the fields of the medical care.

Their results are frequently reported at conferences and published in scientific journals. The book written by Prof. Pang [1] became one of the reference-books of hyperthermia in oncology. Prof. Pang leads clinical trials like [2], and publishes it in international cooperation, [3]. His other papers [4], [5], [6] clearly show how effectively they cure even complicated and sometimes hopeless cases with the combination of the Traditional Chinese Medicine and modern Western Medical Processes. Prof. Pang does not satisfy with the local control of malignant diseases, but takes emphases on the elongation of the survival time together with the quality of life of the cancer-patients.

The below published case-reports well represent the dynamism and success of the professional staff of Clifford Hospital to cure cancer with oncothermia method. This publication could produce a valuable collection for the medical staff working with oncothermia worldwide. I hope, this shared knowledge will help for physicians and patients reaching the best available result of the curative processes.

Allergy asthma

Z1, male, 38 years old.

The patient had allergy asthma for about 10 years with outbreaks every winter and spring. After 12 sessions of wholebody high temperature hyperthermia (38–40.5°C/2-4 hrs), there was no recurrence for one year, gained weight and obvious improvement of general condition was seen.

Benign prostatic hypertrophy (BPH)

F1, male, 87 years old.

The patient had benign prostatic hypertrophy (BPH) for about 30 years with urination dysfunction. There was no improvement after medication for several years. He could not receive operation due to heart diseases, diabetes and other systemic diseases. Urination only can be made by installation of a catheter. The result is normal urination after one course of local Radiofrequency hyperthermia treatment. The catheter was removed.

H1, male, 81 years old.

The patient had benign prostatic hypertrophy (BPH) for nearly 20 years with difficulty in urination and chronic nephrosis. A bladder fistula was inserted. The symptom of prostatic hypertrophy was obviously improved after 15 local RF-hyperthermia treatments, CT showed that the diameter of prostate cancer diminished by 2 cm, urination returned to normal. The fistula was removed. The patient leads a normal life.

Bladder Cancer

K1, male, 62 years old.

The patient underwent bladder cancer electrocision 2 months ago and was admitted with hematuria for 1 day on July 15, 2013. A bladder mass was found during a health checkup in April 2013. A B-mode ultrasound scan of urinary system in Guangdong General Hospital revealed an iso-echogenic area, measuring 1.5cm×0.6cm in size and further examination suggested; and prostatic hyperplasia. On April 24, 2013, he was admitted to Guang General Hospital and received a series of assistant examinations. On April 28, 2013, transurethral resection of bladder lesion was performed smoothly and postoperative recovery went well. Postoperative pathology result was consistent with bladder cancer (pathology type and staging unknown). On May 2, 2013, the patient started weekly bladder instillation chemotherapy with Pirarubicin. Minor post-chemotherapy hematuria was noted and relieved without special treatment. He didn't experience any discomfort. On June 20, he received a follow-up cystoscopy and a biopsy test, revealing a negative result. Chemotherapy was then discontinued. At about 6 o'clock on the day of admission, he developed sudden fresh red blood in urine with minor blood clot accompanied by frequent, urgent urination and pain in urethral orifice.

He was then transferred to Urology Dept. After the transfer, his urinary catheter was found to be blocked and could not be unblocked by repeated flushing. As preoperative examinations showed no contraindication, he underwent transurethral bladder blood clot extraction. During the procedure, blood clot in large amount was seen and estimated blood loss was 1000 ml. Repeated irrigation and negative pressure suction were used to extract blood clot. Bleeding points were identified at trigone and left posterior wall of bladder. Following the procedure, treatments were administered for bleeding stoppage, fluid replacement, and anti-infection. At 11:30 am, July 18, 2013, the patient developed bladder bleeding and repeated flushing unblocked the urinary catheter. He was not responsive to verbal stimuli and presented with cold and wet extremities and BP 60/30mmHg at 12:55, suggestive of hemorrhagic shock resulting from bladder hemorrhage. Emergency treatment was provided, including rapid blood transfusion and fluid replacement. The BP measured 110/70mmHg at 13:10, indicating a successful emergency care outcome. When being stable, the patient was transferred back to Oncology Dept. on August 15, 2013. On August 24, 2013, urine culture test result was positive. The patient's urodynia subsided following the use of Imipenem and Cilastatin Sodium for Injection. Hyperthermic intravesical chemotherapy with mitomycin was provided on August 21 and 28 and September 4 and 11, 2013 respectively. The chemotherapy went well and he was discharged with an improvement after 60 days of stay as an inpatient.

Diagnosis: Status post bladder cancer electrocision.

Integrative treatment plan: Cystoscopy revealed no evidence of tumor or neoplasm on October 13, November 12, and December 12, 2013 and January 13 and June 18, 2014 respectively. With contraindication for chemotherapy excluded, the 12th, 13th, 14th, 15th, 16th, 17th, 18th, 19th, and 20th hyperthermic intravesical chemotherapy with mitomycin was successfully performed on Jan.13, Feb. 18, Mar.19, Apr. 15, May 16, Jun. 18, Jul. 16, Aug. 14, and Sept. 17 respectively. In addition, daily systematic biofeedback therapy and medical ozone were administered to boost immunity and healthy Qi and inhibit tumor. Traditional Chinese medicine was also provided based on syndrome differentiation.

Treatment outcome: The patient complied with outpatient and inpatient follow-ups. The follow-ups in the last 2 years showed he was in the course of recovery. Male tumor markers (5 items) on March 16, 2015 were unremarkable. Pelvic MR showed status post bladder cancer resection and chemotherapy and similar findings compared with those on September 15, 2014. On March 17, 2015, a transurethral cystoscopy revealed 2 mushroom-shaped masses at the neck and trigone of bladder. The masses protruded from bladder's mucous membrane and shared similar color with adjacent tissue. Bilateral urethral opening was unremarkable. A mushroom-shaped mass was sampled for pathology testing. The result reported minor fibrous connective tissue.

Follow-up examinations in June, 2016 showed no sign of cancer relapse. The patient is completely normal at present.

L1, born in 1947, Guangzhou citizen.

The patient was diagnosed with bladder cancer in December 2008 but presented with no bloody urine. After completing related examinations in our hospital, the patient underwent a transurethral resection of bladder tumor under epidural anesthesia on December 15, 2008. The procedure was successful. Mitomycin of 20mg was administered by intervesical instillation. Postoperative pathological analysis revealed bladder transitional cell carcinoma, stage I-II. The patient was transferred to Oncology Department.

Conditions on admission: The patient felt foreign body sensation of throat, with intermittent cough but no phlegm. He has always been sensitive to cold. There were no chills, fever, dizziness, headache, chest tightness, chest pain, nausea, vomiting, frequent urination, urgent urination or bloody urination. The tongue was light red with thin white coating. The pulse was thready.

Physical examination: There was tenderness at the lower abdomen, without rebound tenderness. No sign of tenderness over hepatic region. Hepatic dullness was normal. Liver and spleen were not palpable. Murphy sign (-), shifting dullness (-). No tenderness or percussion-elicited pain was noted on renal regions. Bowel sounds were normal, without vascular bruit.

Assistant examination: Postoperative pathological analysis revealed bladder transitional cell carcinoma, stage I-II.

Diagnosis: Bladder transitional cell carcinoma, stage I-II.

Integrative treatment plan: Completing cystoscopy after admission, the patient received fluid supplement intravenously and traditional Chinese medicine and acupuncture. In TCM treatment plan, this senile patient lost vital qi when suffering serious illness. Kidney-yang is the most vital yang essence in the body. Insufficiency of kidney-yang could not strengthen the exterior so that the patient was sensitive to cold. Tongue and pharynx located between kidney Channels of Foot-Shaoyin. Since there is kidney qi insufficiency, discomfort in pharynx and throat is induced. Withal, tongue and pulse expressed insufficiency of the kidney-yang.

With a method of warming and invigorating kidney yang, Jinkui Shenqi Wan was adopted orally. Three doses of the detailed prescription included Radix Rehmanniae Preparata (Shu Di Huang) 18g, Fructus Corni (Shan Zhu Yu) 18g, Rhizoma Dioscoreae (Shan Yao) 18g, Cortex Moutan (Mu Dan Pi) 12g, Poria (Fu Ling) 30g, Herba Cistanche (Rou Cong Rong) 15g, Semen Cuscutae (Tu Si Zi) 18g, Rhizoma Alismatis (Ze Xie) 12g, Cortex Cinnamomi (Rou Gui) 6g, and Radix Aconiti Lateralis Praeparata (Fu Zi) 5g. One dose of the listed herbs was decocted with water for oral administration once daily. Treatment with acupuncture: The acupoints of BL 13, LU

1, LU 5, ST 36, LI 11, ST 40, SP 10, LR 3, SP 3 were selected for acupuncture with mild reinforcing and attenuating method, with the needle remained for 20minutes, once a day, and a 2-day interval after 5 needling sessions. Nutritionist instructed body conditioning with herbal cuisine. Local endogenous hyperthermia was given once weekly in combination with bladder hyperthermic intravesical chemotherapy with Mitomycin (30mg) once weekly. Chemotherapy was changed into once monthly with Pharmorubicin RD (30mg) after 12 times bladder hyperthermic intravesical chemotherapy continuously.

Treatment outcome: Cystoscopy and CT scan performed in Clifford Hospital revealed unremarkable findings and no recurrence in March and July 2009, May 2010, and February 2011.

Laboratory findings in inpatient dept. in August 2012:

Interleukin 6: 44.30pg/ml

T lymphocyte subset analysis:

CD3+T cell/lymphocyte	32%
CD3+CD4+T cell/lymphocyte	16%
CD3+CD8+T cell/lymphocyte	13%
NK cell/lymphocyte	64%

Cystoscopy revealed no tumor recurrence in the bladder.

The patient returned for follow-up examinations in October 2013. Laboratory study showed normal results including whole blood count, biochemical test, urine and stool analyses, and no remarkable abnormality in pelvic MRI.

He has survived for 7 years and fully recovered.

L2, female, 72 years old.

The patient was admitted with “a two-day history of frequent, urgent and painful urination” on February 24, 2011. Two weeks before admission, the patient presented with unexplained frequent, urgent and painful urination, especially during daytime. But she denied macroscopic hematuria, difficulty urination, cough, sore throat, fever or lumbar pain. Urine analysis in other hospital revealed “WBC +++, RBC +”. She took some oral medication (name and dosage unknown) but gained no improvement. Therefore, she presented to Clifford Hospital. B-mode ultrasound at Outpatient Department revealed “hypoechoic structures in bilateral kidneys, suspicious of small cysts; multiple space-occupying lesions in the bladder, suspicious of tumor”. Further examination was suggested.

The patient stated a healthy history.

A contrast CT scan of the middle and lower abdomen after admission revealed:

1. Multiple nodules in the bladder, suggestive of possible bladder cancer.
2. Multiple small cysts in bilateral kidneys.
3. Multiple small cysts in the liver.

Cystoscopy report:

The scope was smoothly inserted. Mucosa of the bladder was smooth. Bilateral ureteral orifices were normal, with clear ureteral jet. Cauliflower-like neoplasms with peduncles of various sizes were noted in the dome, right trigone (1.5cm away from the ureteral orifice) of the bladder and left side of internal urethral orifice. Those tumors were about 2×2cm, 2×1cm and 1×1cm, without bleeding, necrosis or erosion on their surfaces. Congestion was seen in the trigone and base of the bladder, with follicular hyperplasia noted. Pathological diagnoses were consistent with transitional cell papilloma and chronic mucosa inflammation.

In a joint consultation on March 1, 2011, oncologists suggested the greatest possibility of bladder cancer and total cystectomy which was rejected by the patient. The alternative plan suggested included a “partial cystoectomy” and bladder instillation chemotherapy, medical ozone therapy, chelation and hyperthermia therapy after surgery. Because the patient refused “total cystectomy”, a “transurethral resection of bladder tumor” under combined spinal and epidural anesthesia was performed on March 3, 2011. Postoperative pathology report was consistent with low-grade invasive urothelial carcinoma.

Dr. Yao Yousheng, head of Urology Department of Sun Yat-sen Memorial Hospital, Sun Yat-sen University, was invited to attend the consultation on March 7, 2011. Dr. Yao suggested close observation of the patient, administration of bladder instillation chemotherapy, and cystoscopy every three months. On day 5 after surgery, the patient was transferred to Oncology Department for further treatment and a joint oncologist consultation was held to decide a treatment plan. The patient successfully received 8 cycles of hyperthermic intravesical chemotherapy with mitomycin respectively on March 10, March 29, April 6, April 13, April 20, April 27, May 4, and May 13, 2011. A follow-up cystoscopy showed no sign of new neoplasm. Hyperthermic intravesical chemotherapy with mitomycin was performed once monthly on June 13, July 13, August 13, and September 14, 2011. A cystoscopy on September 14, 2011 showed no evidence of tumor recurrence or metastasis. A contrast CT scan of the middle and lower abdomen on September 15 also showed no tumor recurrence or metastasis.

Bladder instillation chemotherapy with Mitomycin 20mg was successfully performed on October 13, November 13, December 13 of 2011, and January 13, February 13 of 2012. A cystoscopy on January 12, 2012 showed no tumor recurrence and a color ultrasound scan of urinary system disclosed cysts in bilateral kidneys (possible pyelogenic cyst in the left kidney).

Hyperthermic intravesical chemotherapy was applied on March 26, 2012. A contrast MR scan of the pelvic cavity on April 25, 2012 revealed changes after bladder cancer surgery but no sign of cancer recurrence. Abnormal signal intensity was noted in the cervix. A cystic lesion was noted in sacral nerve root, which was probably a cyst. Cystoscopy showed normal findings. The 19th hyperthermic intravesical chemotherapy with Mitomycin 20mg was successfully applied on April 27, 2012. Follow-up gynecological ultrasound showed unremarkable finding and TCT result was also normal. The 20th hyperthermic intravesical chemotherapy with MMC 20mg was smoothly applied on May 29. The patient returned to Clifford Hospital for follow-up regularly and no cancer relapse or metastasis was found.

Diagnosis: Status post chemotherapy after transurethral resection of bladder tumor (low-grade infiltrating urothelial carcinoma pT₂N₀M₀ stage II)

Integrative treatment plan: Hyperthermic intraperitoneal chemotherapy was totally applied for 20 times; local deep hyperthermia once the other day, extracorporeal blood oxygenation and ozonation once to twice weekly, 30g chelation therapy once every other day, systemic biofeedback therapy once daily, acupuncture once daily and oral traditional Chinese medicine once daily.

Treatment outcome: After the hyperthermic intraperitoneal chemotherapy accomplished, the patient complied with outpatient and inpatient follow-ups every 3-6 months for 5 years. There is no evidence of cancer recurrence or metastasis.

The patient is fully recovered currently.

Brain Glioma

L3, female, 30 years old.

In 2006, the patient presented with unexplained intermittent headache, which was intermittently dull, tolerable and more significant on the left side and each episode lasted for 4-5 days and then subsided on its own. The patient visited Hainan People's Hospital and underwent a Brain MRI, which revealed a space-occupying lesion in the right brain (details unknown). As the lesion was small, it was left untreated and observation suggested.

But she experienced strong headache again in November, 2008, accompanied by nausea and vomiting. So she presented to Hainan People's Hospital again and a brain CT revealed masses in the right thalamus and parietal lobe, possible glioma; and abnormal signal intensity in the left parietal lobe, raising the possibility of edema lesion. She underwent a "lumpectomy of the right brain", and postoperative pathology indicated grade 2 oligoastrocytoma. She recovered well after surgery. She later continued her care in Clifford Hospital and received 4 cycles of chemotherapy with oral temozolomide capsules respectively on January 5, 2009, February 3, 2009, March 3,

2009 and March 31, 2009 (the first cycle: temozolomide capsules 150mg, qd, d1-d5; the last three cycles: temozolomide capsules 200mg, qd, d1-d5). Combined with chemotherapy, other therapies were also applied, including medical ozone, chelation and TCM therapies. The patient presented with chemotherapy side effects like leucopenia, nausea and vomiting, but those effects were relieved by symptomatic treatment.

In April 2009, she visited General Hospital of Guangzhou Military Command of PLA for gamma knife therapy (details unknown). Since the second half of 2009, annual brain MRI scan revealed no evidence of tumor recurrence or metastasis. At the end of 2012, she suddenly presented with unexplained headache and limb weakness, but no consciousness disturbance or limb cramp. The episode lasted about 5-8 minutes and subsided without any intervention. She visited Hainan People's Hospital where she was diagnosed with secondary epilepsy and given "sodium valproate sustained-release tablets 0.1g po bid" to fight against epilepsy. But there was no improvement. Since February 2013, she started to experienced paroxysmal dizziness, consciousness disturbance, limb jerking, and foaming at the mouth, but no urinary or fecal incontinence or injury. Each seizure lasted for about 30 minutes and subsided on its own. When she regained her consciousness, she felt week, unable to recall the event. The epilepsy occurred once every month. But the onset frequency changed into every 10 days since July. The patient experienced the same symptoms as before, and was again given "sodium valproate sustained-release tablets 0.1g po bid" to fight against epilepsy. Treatment outcome turned out unsatisfactory and therefore she visited Clifford Hospital for further treatment. A brain MRI with contrast on September 19, 2013 indicated, compared to MR findings on May 4, 2009, lesions in left temporal and parietal lobes significantly increased in size, suggestive of recurrence of astrocytoma in the right parietal lobe. After admission, topiramate tablets 50mg bid and oral sodium valproate 0.5g qd were administered for anti-epilepsy and dehydration. On September 26, 2013, the patient went to 421 Hospital of PLA and underwent brain gamma knife therapy: 50% isodose curve surrounding the gross tumor volume and accumulated dose around the tumor of 1500cGy/3F. In September, 2013, she presented to Clifford Hospital to received non-toxic integrative cancer treatments.

The patient had a healthy history and underwent "cesarean section" in June 2010.

Assistant examination: A brain MRI with contrast in Clifford Hospital on September 19, 2013 indicated, compared to MR findings on May 4, 2009, lesions in left temporal and parietal lobes significantly increased in size, suggestive of recurrence of astrocytoma in the right parietal lobe.

Diagnoses: 1. Relapse of grade 2 oligoastrocytoma after gamma knife surgery, radiation therapy and chemotherapy. 2. Secondary epilepsy.

Integrative treatment plan: Stereotactic gamma-ray radiation therapy was applied to treat the brain tumor relapse, combined with brain hyperthermia once every other day, chelation therapy once every day, and major ozonated autochemotherapy once every other day. According to traditional Chinese medicine (TCM) system, the patient suffered stagnation of blood stasis and therefore Naoliu Decoction + Sanleng Jianwan was prescribed: Rhizoma Sparganii (San Leng)15g, Fructus Polygoni Orientalis (Shui Hong Hua Zi)10g, Rhizoma Curcumae (E Zhu)15g, Radix Paeoniae Rubra (Chi Shao)15g, Poria (Fu Ling)15g, Semen Coicis (Sheng Yi Yi Ren)30g, Scorpio (Quan Xie)5g, Scolopendra (Wu Gong)5g, Herba Hedyotis Diffusae (Bai Hua She Cao)30g, Liuwei Dihuang Pills (bag)12g. The TCM was one dose daily for oral administration and should be decocted with water.

Acupoints for acupuncture therapy: EX-HN5, DU 20, DU 14, GB 20, LI 4, DU 23, ST 36, Triple Points (Sanchongxue) and Outer Three Passes (Waisanguan). Acupuncture adapted a "even reinforcing and reducing" method and the needles remained in the points for 20 minutes. The therapy was administered once daily for 5 days a week, followed by a 2-day rest.

Moxibustion therapy: CV 4, DU 20, ST 36, DU 14 were selected for moxibustion therapy. Method: each session of moxibustion was applied to 2 acupoints for 10 minutes respectively in the frequency of once a day, and there was a 2-day interval after 5 sessions.

Auricular therapy: acupoints selected were as follows: TF 4, AH 6a, AT 4, AH 6a, TF 4, LO 5 6i, AT 1, CO 12, and TG2P. Method: auricular therapy alternated once a week between two ears.

Cowherb Seeds were applied to the auricular points and the patient was instructed to press each acupoint 3 to 5 times per day, with each press lasting for 3 to 5 minutes. In addition, head hyperthermia was also employed once every other day with chelation therapy; Anti-Tumor Mixture one dose daily and major ozonated autochemotherapy once every other day (employed during the interval of chelation therapies).

Treatment outcome: The patient remained inpatient for 52 days without seizure. She was good in spirits and normal in limb strength and tone. She continued outpatient follow-up visits for 6 years and there was no evidence of remarkable change. Follow-up brain CT scan in other hospital revealed a stable tumor status.

Breast cancer

F2, 52-year-old.

The patient noticed a non-tender, broad bean-sized lump under areola of right lateral breast without nipple discharge or hemorrhage in April, 2011. The lump enlarged before menstruations and shrank after. Since 2012, the lump enlarged progressively that she consulted doctor in our hospital. Color ultrasound scan of the breasts on May 30, 2012 indicated mild hyperplasia of bilateral breasts and a nodule near the right nipple with possibility to be excluded. She was admitted with initial diagnosis of unexplained lump in the right breast and diagnosed with right breast cancer through related examinations in Inpatient. On June 16, 2012, lumpectomy of right breast was performed under local anesthesia and frozen pathological section during operation reported invasive ductal carcinoma of the right breast, at the same time, modified radical mastectomy of right breast cancer was done under general anesthesia successfully. Postoperative pathological analysis revealed breast fibrosdenosis and residual invasive ductal carcinoma in part of tissue. Skin of the nipple and deep fascia were not involved. Lymph nodes were metastasized (5/18, with maximal diameter of 0.5cm at nests). Immunohistochemical test (3 items) showed negative HER2, but positive ER and PR. The patient with a history of lumpectomy of right breast 20 years ago (it was benign without unknown pathological report) was transferred to Oncology Department after operation.

Physical examination: 20cm-long surgical scar was in the chest wall. Neck was soft without resistance, and no jugular varicosity or abnormal carotid pulsation. A soft and non-tender nodule of 1cm*1cm in the left thyroid was palpable, which moved up and down following swallowing movements. The chest without deformity was symmetric. Right breast was resected and left breast lump was impalpable.

Assistant examination: Lumpectomy of right breast was performed under local anesthesia on June 16, 2016 and frozen pathological section during operation reported invasive ductal carcinoma. Postoperative pathological analysis revealed breast fibroadenosis and invasive ductal carcinoma residual locally. Skin of the nipple and deep fascia were unremarkable. There were lymph node metastases (5/18, maximal diameter of cancer nests of 0.5cm). Immunohistochemical test (3 items) revealed negative HER2 but positive ER and PR.

Diagnosis: status postoperative change of right breast invasive ductal carcinoma, stage III.

Integrative treatment plan: This middle-aged woman with reduction of hormone function was in poor emotion. That was caused by dysfunction of liver in regulating and spleen in transport. Retention of water-dampness obstructed channels and collaterals that phlegm and stasis were accumulated. Sen Mai Fu Zheng Zhu She Ye was applied for supplementing qi and strengthening body resistance. In TCM theory, traditional Chinese medicine was used to relieve depressed liver, remove phlegm and boost qi of spleen and stomach. The prescription named "Six Gentlemen Decoction" was administered based on the patient's response. The detailed prescription included Radix Codonopsis (Dang Shen) 15g, Radix Scutellariae (Huang Qin) 15g, Radix Astragal (Huang Qi) 30g, Fructus Crataegi (Shan Zha) 30g, Rhizoma Atractylodis Macrocephalae (Bai Zhu) 30g, Fructus Hordei Germinatus (Mai Ya) 30g, Endothelium Corneum Gigeriae Galli (Ji Nei Jin) 20g,

Fructus Ligustri Lucidi (Nv Zhen Zi) 15g, Herba Ecliptae (Mo Han Lian) 20g, Fructus Corni (Shan Zhu Yu) 20g, Fructus Amomi (Sha Ren) 10g, and Fructus Aurantii (Zhi Ke) 10g. One dose of the above herbs was decocted with water for oral administration twice daily.

Since July 26, 2012, the patient was given systemic chemotherapy following AC-T plan, concurrently with deep hyperthermia on chest every other day, and intravenous medical ozone therapy and electro-magnetic biofeedback therapy once a day respectively. Acupuncture was adopted with principle of neutral supplementation and draining, with the needle retained for 20 minutes, once a day, and 2 days interval after 5 sessions. Moxibustion was applied to 2 acupoints for 10 minutes respectively in the frequency of once per day and a 2-day interval after 5 sessions. Auricular points included breast, AH10, CO4, CO12, CO18, AT4, TG2p, AT2,3,4i, and AH6a. Method: Cowherb Seed was applied to auricular points and the patient was instructed to press it 3 to 5 times per day.

Treatment outcome: Decrease of WBC after chemotherapy indicated the appearance of myelosuppression. Treatment to elevate WBC was adopted in combination with chelation therapy and ozone administration intravenously for effect-enhancing and toxicity-reducing. Follow-up complete blood test and liver and kidney function were normal. The patient has followed outpatient and intermittent inpatient treatment. Her illness is in stable conditions in 5 years' follow-ups.

The patient returns for inpatient treatment every 6 months. There is no recurrence or metastasis.

H2, female, 49 years old.

The patient felt a mass in her right breast on April 21, 2013 and she presented to Clifford Hospital for medical care. The mass was of about 1.0×2.0cm, ill-defined, and non-tender, with moderate hard texture, unsmooth surface and limited mobility.

A color ultrasound in Clifford Hospital on April 21, 2013 showed: Bilateral mammary hyperplasia. There was a nodule in the right breast, suspicious of breast tumor and biopsy recommended. A hypoechoic nodule was detected in the right axilla, probable lymphadenopathy.

Mammography revealed heterogeneously dense breasts, with the right breast consistent with BI-RADS Category IV (a MRI with contrast suggested) and the left breast consistent with BI-RADS Category II. The patient was admitted to the Surgery Department and underwent a lumpectomy + modified radical mastectomy under local + general anesthesia on April 28, 2013. Postoperative pathology was consistent with invasive ductal carcinoma of the right breast, with the largest diameter of 2.0cm and metastasis to the lymph nodes (3/13). Immunohistochemical analysis: P53 (4+), Ki67 (4+), EGFR (-), HER2: (1+, negative). ER (-), PR (-). After the surgical incision healed, the patient was transferred to Oncology Department.

Conditions on admission: There was mild referred pain along the thoracic incision when the patient moved her right upper limb. There was no restricted limb motion. Appetite was general.

Physical examination: A longitudinal and well-healed surgical scar of about 20cm was noted in the right chest. The right breast was absent. The left breast developed well with its nipple free of retraction. Nothing abnormal was palpated in the left breast. No enlarged lymph node palpated under bilateral axillae or above the collarbone.

Assistant examination:

Postoperative examination revealed invasive ductal carcinoma of the right breast, with the largest diameter of 2.0cm and metastasis to the lymph nodes (3/13). Immunohistochemical analysis: P53 (4+), Ki67 (4+), EGFR (-), HER2: (1+, negative). ER (-), PR (-).

Diagnosis: Status post lumpectomy + modified radical mastectomy & chemotherapy of right breast invasive ductal carcinoma (pT1N1M0 stage II).

Integrative treatment plan: The patient was a middle-aged female with a depressed nature. After she developed the disease, she suffered mental stress, which caused liver Qi disorder and Qi stagnation. Because "Qi transformation promotes blood circulation and Qi stagnation results in

blood stasis and pain”, the patient presented with pain in the right breast. “Liver Wood restrains Spleen Earth, causing spleen dysfunction and transformation failure of essence of water and grain”. The patient’s liver had been long-term depressed and fluid and wetness stagnated inside her body, leading to formation of phlegm and mass in the breast. She also occasionally experienced nausea and loose stool, which indicated she was deficient in spleen.

Traditional Chinese medicine “Xiaoyaosan Decoction” was employed to relieve the depressed liver, regulate Qi and tonify the spleen, including the following herbs: Radix Bupleuri (Chai Hu)15g, Radix Angelicae Sinensis (Dang Gui)15g, Radix Paeoniae Alba (Bai Shao)15g, Radix Glycyrrhizae (Gan Cao)6g, Rhizoma Atractylodis Macrocephalae (Bai Zhu)15g, Poria (Fu Ling)15g, Radix Codonopsis (Dang Shen)15g, Spica Prunellae (Xia Ku Cao)15g, Radix Curcumae (Yu Jin)10g. The TCM was one dose daily and should be drunk warmly after meals.

Chemotherapy with cyclophosphamide + epirubicin was planned. Chest local deep hyperthermia was applied every other day; EBOO therapy once a day and chelation therapy every other day. Such integrative therapies were employed to promote chemotherapy and reduce toxic effects.

Treatment outcome: The patient has been keeping outpatient and intermittent inpatient visit. During the 2-year follow-up, chest CT scans and whole body bone scans show no cancer recurrence or metastasis. Currently she is still on follow-up.

H3, female, 38 years old.

The patient was admitted on July 28, 2011 due to "space-occupying lesions in bilateral breasts for half a month".

On July 10, 2011, a color ultrasound scan performed during a health checkup showed:

1. A solid space-occupying lesion with calcification in the right breast, suggestive of a further examination;
2. A cystic-solid nodule in the left breast with possibility of a space-occupying lesion not excluded;
3. Bilateral mammary hyperplasia with multiple nodules;
4. Lymphadenopathy in the right axilla;
5. A lymph node in the left axilla.
6. Hypo-echogenic masses in the right breast, with the largest having well-defined margin measuring 31.0mm*19.5mm in size at the 10 o'clock position;
7. A cystic and solid echogenic mass with ill-defined margin at the 8 o'clock position of the left breast, approximately 34.0mm*14.0mm in size.

A subsequent mammography showed:

Bilateral breasts contained more fibrous and glandular tissue. The right breast was consistent with BI-RADS Category IV with solid lymph nodes in the axilla. The left breast was consistent with BI-RADS III suggestive of a periodic follow-up.

For further diagnosis and treatment the patient was admitted to Oncology.

On admission, the patient was conscious and alert and in good spirit. Appetite and sleep were good. Urination and bowel movement were normal. He denied discomfort all over the body.

After admission, she underwent nipple conserving lumpectomy of bilateral breasts and right-sided modified radical mastectomy under general anesthesia in General Surgery Department on August 6, 2011. Post-operative pathology revealed: The right breast: invasive ductal carcinoma (45%), ductal carcinoma in situ (40%) and papillary carcinoma (15%); the tumor was 5.5*3.5*2cm in size and 1cm from the nearest surgical margin; no cancer embolus was noted in blood or lymphatic vessels; margins of subcutaneous tissue of nipple, skin above tumor, and deep fascia were free from cancer invasion; and lymph nodes were unremarkable (0+/8). The left breast lesion was fibroadenoma. After removal of most stitches and wound healing, the patient was transferred to Oncology for non-toxic integrative cancer treatments such as wound dressing, hyperthermia

therapy, medical ozone therapy, and TCM (traditional Chinese medicine). After oncologists excluded chemotherapy contraindications, the patient received AC→T chemotherapy with Doxorubicin (90mg) and Cyclophosphamide (0.9) by IV (on 09/14/2011, 09/30/2011, 10/14/2011, 10/29/2011), and then intravenous chemotherapy with Paclitaxel (270mg) (11/13/2011, 11/29/2011, 12/15/2011, 12/31/2011).

Integrative treatment plan: Chemotherapy was combined with non-toxic integrative cancer treatments, including chest deep hyperthermia therapy each other day, intravenous medical ozone therapy once per day, magneto-electric biofeedback therapy once per day and acupuncture therapy. Acupuncture was administered in the principle of neutral supplementation and draining, with the needle retained for 20 minutes, once a day, and a 2-day interval after 5 needling sessions.

As to moxibustion therapy, acupoints included BL26, DU14, ST36, SP6, BL18, BL20, BL23. Each session of moxibustion was applied to 2 acupoints for 10 minutes respectively in the frequency of once a day and there is a 2-day interval after 5 sessions.

Cowherb seeds were applied to the auricular points and the patient was instructed to press the auricular points on her own 3-5 times per day. And the auricular points included RUXIAN, AH10, CO4, CO12, CO16, AT4, TG2p, AT2·3·4i, NAODIAN, AH6a.

With principle of clearing away heat and toxic materials, dispersing stasis and removing swelling, traditional medicine named "Wu Wei Xiao Du Decoction" was adopted for accumulation of heat-toxic based on her current conditions and comprehensive analysis by four diagnostic methods. The detailed herbs of the decoction included:

Lonicera Japonica (Jin Yin Hua)30g

Dandelion (Pugongying)15g

Herba Violae (Zihuadiding)15g

Begonia Fimbristipula (Zibeitiankui)15g

Peach seed (Taoren)10g

Flos carthami (Honghua)10g

Nidus Vespae (Lufengfang)6g

Spina gleditsiae (Zaojiaoci)10g

One dose of the herbs were decocted with water and administered once a day.

Treatment outcome: The patient has been followed for 5 years and receives periodic examinations and non-toxin integrative cancer treatments. There is no evidence of cancer recurrence or metastasis.

K2, aged 59, female, American.

The patient was admitted on October 18, 2007 due to right breast invasive ductal carcinoma for more than 4 years, progressive lump enlargement with emaciation for 3 months and skin redness and swelling for one week.

With a history of estrogen replacement therapy for over 3 years, the patient found a peanut-sized, painless, hard lump in the right breast in October, 2003. Regional tissue biopsy result revealed breast invasive ductal carcinoma PR (+), ER (+), CerbB2(+++) in Carolina State Hospital, United States. But she preferred natural therapies like Vitamin C, medical ozone therapy, massage and hydrotherapy in local hospital rather than any invasive treatment such as operation, radiotherapy and chemotherapy. Her illness was in stable state; however, 3 months before admission to Clifford Hospital, the lump enlarged progressively and then the right breast appeared hard, red and swollen. She also experienced significant weakness, shortness of breath and palpitation after activities, and recurrent paroxysmal dry cough. She had lost about 10kg in 3 months before admission. She was not so energetic during inpatient stay, and had general appetite. Urination and bowel movement were normal.

Physical examination: The patient was conscious but looked ill and emaciated. Body weight was 51kg. Bilateral breasts appeared swollen and red with local ulcerations covered with pus. Retracted nipples looked like fragiform. Multiple lymph nodes could be palpable in armpits and

left supraclavicular fossa, of which the biggest one of 2.0×2.0×1.5cm in size was firm and hardly movable, but was well-defined from the surrounding tissue. One hard lump of 2.0×1.5×1.5cm in size with poor mobility was in the 6th intercostal space of the right posterior axillary line and ill-defined to the surrounding tissue.

HR was 112bpm and heart rhythm was normal without murmurs. Percussion dullness was noted from lower lungs to the 5th intercostal space and respiratory sounds significantly decreased. She was unable to lie on her right side. Pitting edema was noted in the right forearm and upper arm while mild edema appeared in lower limbs. KPS: 60.

Assistant examinations:

Pathology reported invasive ductal carcinoma of right breast, PR(+), ER(+), CerbB2(+++) in Carolina State Hospital, United States.

Complete blood count: Hb 93g/L.

Biochemistry: ALT 37U/L, AST 32U/L, TP 58g/L, ALB 27.3g/L, ALP 157U/L, GGT 88U/L, TBIL13.2umol/L, DBIt 5.0umol/L, Cr 35umol/L, Ua 335umol/L, BUN 5.3mmol/L, GLU 5.25mmol/L, TG0.2 mmol/L, GHO3.46mmol/L, K⁺3.95 mmol/L, Na⁺ 141mmol/L, Cl⁻ 107mmol/L, Ca²⁺ 2.01mmol/L, while immunological test (5 items) and micro-element were normal.

CEA 48ng/ml, AFP 7.09ng/ml, CA12-5(OV) 34.99U/ml, CA199 35.94U/ml, CA153(BR) 238U/ml.

Chest and abdomen CT scan indicated cancer metastases to lungs, liver and chest cavity, one tumor of 5×4.5×4cm with pedicle in the left pleural cavity connected to parietal pleura, and bilateral pleural effusion, particularly in the right side.

Whole body bone scan revealed no bone metastasis.

ECG indicated sinus rhythm, HR 115bpm and right bundle branch block.

Diagnosis: Right breast invasive ductal carcinoma in stage IV with metastases to left breast, lungs, liver, chest cavity and skin.

Integrative treatment plan: At admission, the patient suffered cancer metastases to liver, lungs, chest cavity, skin and lymph nodes, moderate malnutrition, ulceration and infection on breast surface, and bilateral pleural effusion. Right upper limb edema was probably due to lymphatic obstruction of chest wall, while bilateral lower limbs edema resulted from hypoproteinemia. Debridement and local medical ozone therapy on breasts were provided for three days, which healed superficial ulceration and relieved swelling. After drainage of pleural effusion, Cisplatin 30mg plus Interleukin-II 4×10⁶U were injected once weekly and local hyperthermia of the bilateral chest every other day. Letrozole was administered orally once daily at a dosage of 2.5mg. Pleural effusion almost disappeared after 2 weeks treatment. Since then, general medium-high temperature hyperthermia was given every 10 days and chelation therapy every other day. Local hyperthermia (20 sessions in total) was given during intervals of general hyperthermia (4 sessions in total).

Nutrition support was administered. Extracorporeal Blood Oxygenation and Ozonation (EBOO) was adopted every other day, alternately with chelation therapy. Chinese herbal medicine and acupuncture therapy were given throughout the treatment. Tongue was dark red with yellow and greasy coating. Pulse was thready and uneven. The patient was diagnosed with accumulation of toxic heat in accordance with her symptoms. Chinese herbal medicine named “Wu Wei Xiao Du Yin” was used to clear away heat and toxic materials and disperse blood stasis and swelling.

The prescription was as follows:

Flos Lonocerae (Jin Yin Hua) 30g	Herba Tataxaci (Pu Gong Ying) 15g
Herba Violae (Zi Hua Di Ding) 15g	Begonia Fimbristipula (Zi Bei Tian Kui) 15g
Semen Persicae (Tao Ren) 10g	Flos Carthami (Hong Hua) 10g
Nidus Vespae (Lu Feng Fang) 6g	Spina Gleditsiae (Zao Jiao Ci) 10g

One dose of the above herbs was decocted with water for oral administration once daily.

Acupoints of ST 36, SP 6, RN 12, KI 3, CV4, RN 6, BL 23, BL 20, and San Chong Xue were selected for acupuncture with principle of neutral supplementation and draining. The needles

remained in place for 20 minutes. This procedure was performed once daily, and a 2-day interval after 5 needling sessions.

Moxibustion was applied to the following points: RN 4, DU 14, ST 36, SP 6, BL 14, BL 23, and BL 20. Methods: Each session was applied to 2 points for 10 minutes respectively in the frequency of once a day and there was a 2-day interval after 5 sessions.

Auriculotherapy alternated weekly between two ears. Cowherb Seeds were applied to the auricular points (breast, AH10, CO4, CO12, CO18, AT4, TG2p, AT2,3,4i, and AH6a) and the patient was instructed to press each acupoint 3 to 5 times per day, with each press lasting for 3 to 5 minutes.

Chinese herbal medicine and acupuncture were adjusted based on the patient's response to the treatment. She was discharged after 2-month hospitalization and continued traditional Chinese medicine.

Treatment outcome: Ulceration and swelling of breasts disappeared and mega lump at the right breast became soft and smaller (shown as pictures) after 60 days non-toxic integrative cancer treatment. Edema of limbs and weakness subsided. She did not complain of shortness of breath on climbing up and down stairs. Heart rate was 80-90bpm. Lymph nodes in bilateral armpits and left supraclavicular fossa were smaller, of which the biggest one measured 1cm×1.5cm×1.5cm in size and softened. Her weight increased to 62kg with good appetite. She could lie on the supine position and lived a normal life. Follow-up CT scan of chest and abdomen indicated lung and liver lesions became smaller than the prior findings and no new lesion, and the lesion in the left pleural cavity was 3.5cm×4.2cm×3.4cm in size.

Laboratory findings: RBC 4.2×10^{12} /L, Hb123g/L, ALB36.5g/L, CEA15ng/ml, AFP7.09ng/ml, CA12-5(OV)20U/ml, CA19930U/ml, CA153(BR)88U/ml. KPS was 90.

The patient kept in touch via email in the following 3 years after discharge and continued Letrozole 2.5mg once per day. Her condition was stable.

But she lost her life in a flight accident in 2011.

L4, female, 39 years old.

In 2010, the patient accidentally found a corn-sized lump in the lateral side of right breast. There was no galactorrhea or bleeding in the nipple and no evidence of rapid mass growth. At that time she also suffered periodic swelling and pain in bilateral breasts, which appeared more significantly before menstruation and alleviated after.

Therefore, she presented to the Outpatient Service of Clifford Hospital. Mammography was performed and indicated hyperplastic changes in bilateral breasts, which were consistent with BI—RADS Category II.

In June, 2010, the patient noticed the painless lump in right breast increased in size. She visited General Surgery and received a color ultrasound scan of bilateral breasts. The scan (by Clifford Hospital, 06/04/2010) indicated:

1. Bilateral breast hyperplasia;
2. Multiple nodules in the right breast, with the possibility of breast cancer to be excluded for larger ones. Surgery and biopsy were recommended;
3. Small nodules and fluid sonolucent areas in the left breast, suggestive of possible cystic hyperplasia or local ductal dilation.

On June 5, 2010, she was admitted to General Surgery and underwent a lumpectomy of right breast on June 9. Pathological examination of the intraoperative frozen section revealed right breast invasive ductal carcinoma. Modified radical mastectomy of the right breast was performed immediately afterwards.

Post-operative pathology: Invasive ductal carcinoma was noted in the upper outer quadrant of the right breast with lobules involved. The cancerous nodules were 2.0 cm and 1.8cm in diameter. Cancer emboli were seen in some small blood vessels. The cancer was histologically classified as Grade 3 (score: 8). No cancer involvement was noted in the nipple, areola, deep fascia or incisional

margins. Ductal epithelial and lobular hyperplasia was noted in tissue around the cancer. Lymph nodes in right axilla were unremarkable (+0/4). Immunohistological test revealed ER (+), PR (+) and Cerb2 (-).

History review was significant for congenital heart disease (atrial septal defect). On April 29, 2008, she underwent an atrial septal defect closure in Clifford Hospital. In 2005, she received a caesarean section.

Physical examination on admission: A surgical scar about 10cm in length was noted on right chest with good healing. Right breast was absent. The left breast was normal in development without nipple retraction, but was positive for a painful, palpable, rice-sized nodule in the upper outer quadrant.

Assistant examinations:

Color ultrasound scan of bilateral breasts: Mild hyperplasia of the left breast; small nodules in the left breast, suggestive of possible hyperplastic nodules.

Color ultrasound scan of axillary lymph nodes: A nodule in the right axilla, suggestive of an enlarged lymph node, with other possibilities to be excluded.

Diagnoses:

1. Status post right mastectomy; stage 1 invasive ductal carcinoma (PT1N0M0);
2. Left breast hyperplasia.

Integrative treatment plan:

The patient was a middle-aged woman with menstrual dysfunction and emotional depression. Because of this, her liver failed to maintain the normal flow of Qi, resulting in Qi depression in the liver. The overwhelming excessive liver Qi therefore leaked and invaded the neighboring organ-spleen, and impaired the spleen's major function to transport water through the human body and maintain the water balance. Water and dampness were retained within the body and finally led to the stagnation of blood stasis in the arteries and veins, and further caused a vicious circle, the accumulation of phlegm and blood stasis. Since meridians and collaterals of liver and stomach passed through breasts, but now were blocked by the accumulation of phlegm and blood stasis, masses developed in the breasts and finally turned into cancer. Hence the TCM treatment targeted soothing the liver, regulating Qi, dissipating phlegm and resolving masses. "Xiao Yao Powder" was prescribed according to her symptoms and signs. Local hyperthermia of the left breast and intravenous ozone therapy once per day, and chelation every other day were administered. She also received TC chemotherapy (07/08/2010/, 07/29/2010, 08/19/2010, 09/09/2010, 09/30/2010, 10/23/2010) with Docetaxel Injection (120mg d1) + Cyclophosphamide Injection (1g d1). After chemotherapy, she experienced grade II gastrointestinal reaction and grade II myelosuppression, for which she received symptomatic treatment to inhibit gastric acid, protect stomach, stop vomiting, and increase white blood cells. She was discharged from hospital after improvement.

Treatment outcome:

The patient has been receiving regular outpatient treatment and intermittent inpatient care. Two years of follow-ups showed an ongoing recovery and no cancer recurrence or metastasis. The follow-up is still going on. Her follow-up chest and abdominal enhanced CT scan showed changes after the modified radical mastectomy of the right breast and no evidence of cancer recurrence or metastasis. Emission Computed Tomography also revealed no abnormal finding of whole body bones.

It has been more than six years with no cancer recurrence since the patient's operation. She now lives and works normally.

L5, female, 64 years old.

The patient underwent modified radical mastectomy of the right breast due to a right breast mass on May 16, 2000. Postoperative pathology result was consistent with invasive ductal carcinoma, ER2+, PR+, stage T2N1M0. Chemotherapy with Cyclophosphamide, Methotrexate, and 5-Fluorouracil (CMF) of 6 cycles and hormonal therapy with Tamoxifen of 5 years in duration were

provided. On February 3, 2010, she was admitted to Endocrinology in Clifford Hospital. A chest CT scan revealed breast cancer with metastases to lung and lymph nodes. She was then given hormonal therapy, non-toxic integrative cancer treatment, intermittent oral Capecitabine, deep hyperthermia, medical ozone and acupuncture. Regular examinations showed no sign of tumor progression.

History review was significant for hypertension, type 2 diabetes mellitus, diabetic peripheral neuropathy, diabetic nephropathy, osteoarthritis of knees and hyperthyroidism.

Diagnoses: 1. Status post modified radical mastectomy, with metastases to lung and hilar lymph nodes. 2. Type 2 diabetic nephropathy. 3. Type 2 diabetic peripheral neuropathy. 4. Arthritis of knees. 5. Grade 2 hypertension, extremely high risk group. 6. Coronary atherosclerotic heart disease.

Integrative treatment plan: During and after chemotherapy, non-toxic integrative cancer treatments were administered, including chelation (once a day), chest hyperthermia (every other day), EBOO (twice a week), and biofeedback therapy (once a day). Acupuncture was administered in the principle of neutral supplementation and draining, with the needle retained for 20 minutes, once a day, and a 2-day interval after 5 needling sessions. Moxibustion was applied to the following acupoints: CV 4, GV 14, ST 36, SP 6, BL 18, BL 20, and BL 23. Methods: Each session of moxibustion was applied to 2 acupoints for 10 minutes respectively in the frequency of once a day and there was a 2-day interval after 5 sessions. Auricular points included breast, AH 10, CO4, CO12, CO18, AT4, TG2P, AT2, 3 & 4i, and AH6a. Method: Auriculotherapy alternated once a week between two ears. Cowherb Seeds were applied to the auricular points and the patient was instructed to press each acupoint 3 to 5 times per day, with each press lasting for 3 to 5 minutes. Oral Chinese medicine decoction was ordered based on syndrome differentiation.

Treatment outcome: The patient complied with regular outpatient and inpatient follow-ups for 5 years. CEA and CA153 were normal, Chest x-ray on May, 2015 revealed status post modified radical mastectomy; similar lesions of right middle and upper lung fields compared with chest x-ray on January 30, 2015.

Currently, she suffers breast cancer with lung metastasis. She has been living with breast cancer for 16 years, with good quality of life at present. She continues weekly outpatient treatment with hyperthermia and Chinese medicine.

W1, female, 66 years old.

The patient presented with a mass in right breast without any cause 3 years ago. The mass measured in a size of a rice grain, without pain or discomfort, and was unattended. In the past 3 years, the patient received a color ultrasound of breasts every half a year and results showed no significant change of the mass, and no treatment was given. Over the last 2 months, the mass in right breast increased in size and number. A sequential ultrasound revealed a mass of right breast with malignant tendency and surgical treatment was recommended. Mammography of bilateral breasts showed: Bilateral mammary glands contained more fibrous and glandular tissue; a nodule was noted in the right lower quadrant; a nodular density was detected in the right upper quadrant with sand-like calcification, and biopsy suggested; the right breast was consistent with BI-RADS Category IV while the left breast consistent with BI-RADS Category II.

History review was positive for hypertension and subtotal gastrectomy due to gastric perforation 30 years ago.

After admission, she underwent lumpectomy of the right breast on June 17, 2011. As the neoplasm was confirmed as malignant during surgery, right-sided radical mastectomy was performed, with a drainage tube placed to right chest wall and axilla respectively. Postoperative treatment was ordered for anti-infection and hemostasis. Postoperative recovery went smoothly. Postoperative pathology results were consistent with invasive ductal carcinoma, intraductal carcinoma and mucinous adenocarcinoma of right upper breast (see pathology report). On July 4, 2011, the axillary drainage tube was removed as there was no discharge. On July 8, 2011, the

patient was transferred back to Oncology Department for integrative cancer treatment. On July 13, 2011, chest wall drainage tube was removed as there was no discharge. A chest CT scan with contrast excluded lung metastasis. Chemotherapy plan was dose-dense AC→T with Epirubicin Hydrochloride for Injection 60mg/m² and cyclophosphamide 0.6g/m², IV drips for 1 day (14 days as a cycle, 4 cycles in total). Four cycles of chemotherapy above were followed by sequential paclitaxel of 4 cycles. Epirubicin Hydrochloride for Injection 90 mg and cyclophosphamide 0.9 were administered intravenously. It was also combined with local deep hyperthermia, intravenous medical ozone, acupuncture and chelation. The patient stayed as an inpatient for 44 days and was discharged with an improvement.

Intravenous chemotherapy with Epirubicin Hydrochloride for Injection 90 mg and cyclophosphamide 0.9 was provided on July 15 and 28 and August 11 and 25 respectively in 2011. On September 10, sequential paclitaxel of 270 mg was administered. On September 24 and October 10 and 26, sequential paclitaxel of 210 mg was administered, with treatment for anti-allergy, anti-vomiting and stomach protection. Meanwhile, it was combined with local deep hyperthermia, intravenous medical ozone, acupuncture and chelation. The chemotherapy went successfully. On November 7, 2011, the patient started conformal radiotherapy for right chest wall, right supraclavicular area, and left and right axillae, which went smoothly. Following radiotherapy, she has been on Exemestane Tablets 25 mg daily.

Diagnosis: Status post chemotherapy and radiotherapy of right breast cancer; invasive ductal carcinoma, pT2N2aM0, stage IIIa.

Integrative treatment plan: During chemotherapy, deep hyperthermia was administered every other day; intravenous medical ozone daily; chelation every other day; acupuncture daily; and traditional Chinese medicine. Following the end of chemotherapy, the patient complied with outpatient and inpatient follow-ups and received integrative treatment once every 3 to 6 months, with each lasting for 15 to 30 days.

Treatment outcome: The patient followed up for about 6 years. Contrast CT scan of the chest on June, 2014 revealed status post right-sided mastectomy and chemotherapy without any sign of relapse; radiation pneumonia of right lung; similar findings compared with that on December 23, 2013. A color ultrasound scan of breasts indicated status post right mastectomy and a nodule of left breast (no significant enlargement compared with previous finding.)

It has been 5 years since surgery and the patient has fully recovered.

Bruise, sprain in lumbar

Y1, male, 52 years old.

Japanese businessman, had bruise and sprain in lumbar and back soft tissues caused by a traffic accident, bad sleep caused by pain. He gained obvious improvement from pain and slept well after one treatment of lumbar and back local RF-hyperthermia treatment. He was cured and discharged after 9 treatments.

Chronic cholecystitis

L6, male, 45 years old.

The patient had chronic cholecystitis for about 10 years, no good medication treatment effect and had lots of side effect. No resolution of subcostal pain because she refused surgery. After one course of local hyperthermia no recurrence of pain within one year.

Chronic salpingitis, pelvic inflammation

G1, 31 years old.

The patient had had chronic salpingitis and pelvic inflammation for many years. No pregnancy within 5-years even though she had received many kinds of fertility treatments. After undergoing abdomen hyperthermia therapy, she achieved pregnancy after 3 months and gave birth to a healthy baby boy.

Colon Cancer

F3, male, 75 years old.

The patient was admitted on January 2, 2014 due to "status post resection of colon cancer for 8 months and hepatic metastasis found for over 1 month".

On April 11, 2013, the patient was hospitalized to Surgery Department of Clifford Hospital because of "intermittent blood in stool for 5 months". Through assistant examinations he was definitively diagnosed with "sigmoid colon cancer" and underwent radical colectomy on April 15, 2013. Post-surgical pathology results: Consistent with Moderately differentiated adenocarcinoma of sigmoid colon, 5.0x3.3cm in size, infiltrating the full thickness of colonic wall. There was necrosis but no evidence of vascular or nervous invasion. Cancer tissue did not involve incisional margins. Lymphatic metastasis was noted (1/10, diameter of cancer nest was 0.2cm).

Immunohistochemistry revealed GAT π ++, ToPoI-, ToPoII+,>25%), PgP-, P53(+,>50%), Ki67(+,40-50%), MLH1+, MSH6+, MSH2+, PMS2+, indicative of stable microsatellite and relatively low possibility of HNPCC.

Stitches were removed as expected from the wound which healed well. The patient was therefore discharged after improvement and later he continued follow-ups and treatment in USA.

He later returned to Clifford Hospital for follow-up examination. CEA was 17.18ng/ml and CA19-9 was 295U/ml. And a CT scan on in November, of 2013 demonstrated two quasi-circular, annular enhanced lesion in the liver, suggestive of metastases. Therefore, the diagnosis was liver metastasis of colon cancer. On November 26, 2013, he was discharged after he underwent an interventional therapy in Clifford Hospital.

Past history:

The patient underwent subtotal gastrectomy because of "gastric antral ulceration" in 1975 and received intraoperative blood transfusion without transfusion reaction. He received left-sided orchiectomy in 2005 because of probable left-sided carcinoma of testicle. He was also given 6-month drug therapy in an American hospital for prolonged PSA elevation of 10 years in duration. He denied a history of hepatitis, tuberculosis, hypertension, diabetes or heart disease. His vaccination history was unknown.

Conditions on admission: The patient was conscious and alert with good spirit. There was no sign of spontaneous or night sweating, chills or fever, dizziness or headache, chest tightness or shortness of breath, abdominal pain or bloating, nausea or vomiting. Urination and bowel movement were normal. He had normal appetite and no significant weight gain or loss recently.

Physical examination: There were two well-healed longitudinal surgical scars, 5cm in length in upper abdomen and 15cm in length in lower abdomen, without oozing. No enlarged superficial lymph node was noted. Heart and lungs were normal in auscultation. Abdomen was non-distended and non-tender. There was no palpable liver and spleen or edema in limbs.

Assistant examinations:

A whole abdominal CT scan showed several findings:

1. Status post resection of sigmoid cancer without evidence of local recurrence; two quasi-circular, annular enhanced lesion in the liver, suggestive of metastases.

2. A sub-capsular nodule with abundant blood supply in the lateral region of left hepatic lobe was probably focal nodular hyperplasia, similar to the finding on March 28, 2013.

3. Prostatic hypertrophy.

A color ultrasound scan revealed the liver had increased in size with multiple nodules, suggestive of metastases. Suspicious embolus was noted in main portal vein with its nature undetermined.

Laboratory studies:

Tumor markers showed:

CA19-9	374.7U/ml	CEA	18.64ng/ml
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Complete blood count showed:

WBC	$3.43 \times 10^9/L$	HGB	105g/L
RBC	3.28	MCH	32.0pg
MCV	97.4fL	HCT	31.90%
Liver function I + II: CHE	4606U/L		

Electrolyte, liver function and glucose were normal.

CEA	17.34ng/ml	CA19-9	319.20U/ml
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HBV-DNA $<1.0 \times 10^3$ copies/ml

Hepatitis B Serologic Test (5 items): HBsAb (+), and others were negative.

CT scan of upper abdomen showed:

1. Right hepatic lobe: Two well-defined, hypodense masses measured about 42.6mm×37.2mm and 32.4mm×25mm in size respectively with CT value of 24Hu. The center of the two lesions saw spots of much lower density, without lipiodol deposit. Lesions were mildly enhanced after injection of lipiodol.

2. There was lipiodol accumulation in the left hepatic lobe, clear-structured porta hepatis and no dilated internal and external bile ducts. Gallbladder was not enlarged with smooth wall and homogeneous enhancement. No radiopaque calculus could be seen in the bladder.

3. Spleen was normal in appearance and size. No abnormal density or contrast enhancement was detected in the splenic parenchyma.

4. And pancreas was also normal in appearance, size and density with non-dilated pancreatic duct and clear peripancreatic space.

5. There was no retroperitoneal lymphadenopathy or peritoneal effusion. Poor lipiodol accumulation showed status post interventional therapy of liver metastasis.

Diagnoses: Status post operation of moderately differentiated adenocarcinoma of sigmoid colon; status post interventional therapy of liver metastasis.

Integrative treatment plan: In western medicine, treatment was given to protect liver, supply nutrition and boost immunity. Interventional therapy of liver metastases was also planned.

In Chinese medicine, "Shenqi Fuzheng Zhushenye" was given to boost Qi, reinforce the healthy Qi and boost immunity. The patient's symptoms and signs were attributed to spleen-kidney Yang deficiency. So traditional Chinese decoction named "Fu Zi Li Zhong Tang" combined with Chinese patent medicine "Si Shen Wan" were given to warm the kidney and fortify the spleen. Six doses of the above formula were given and included the following herbs:

Radix astragali (Huang Qi) 30g
Fried atractylodes macrocephala (Chao Bai Shu) 30g
Roasted ginger (Pao Jiang) 10g
Platycodon grandiflorum (Jie Geng) 10g
Roud cardamon seed (Bai Kou Ren) 10g
Fructus amomi (Sha Ren) 10g
Cinnamon (Rou Gui) 10g
Radix aconite lateralis preparata (Fu Zi) 10g
Fructus psoraleae (Bu Gu Zhi) 20g

Fructus alpiniae oxyphyllae (Yi Zhi Ren) 15g

Radix codonopsis (Dang Shen) 15g

Radix liquiritiae (Zhi Gan Cao) 10g

One dose of the listed herbs was decocted with water for oral administration once daily after meals in warm temperature.

Treatment outcome: The patient had been hospitalized for 5 days with significantly improved general conditions. Currently he was conscious and alert with good spirit. He denied spontaneous or night sweating, chills or fever, dizziness or headache, chest tightness or shortness of breath, abdominal pain or distention, nausea or vomiting. Urination and bowel movement were normal. The tongue was light red with thin-white coating and the pulse was thin. Consequently, he was discharged. Since then he complies with outpatient and inpatient follow-ups.

The patient has survived with colon cancer with liver metastasis for 3 years and 6 months by now although he didn't undergo chemotherapy. He has a good quality of life and is still on treatment.

Z2, male, 75 years old.

In 2013, the patient started to experience unexplained repeated blood in his stool, which was bright red or sometimes black in color. The bleeding was minor but present every day. Since he had no diarrhea, fever, abdominal distension or poor appetite, the problem was left unattended and he had never sought diagnosis or treatment. Not until October 2013 when the patient presented with increased amount of the bright-red blood in feces, weakness and weight loss, did he start a long-term treatment in Clifford Hospital.

A colonoscopy showed an annular, protruding mass in the sigmoid colon of about 25-29cm. It covered 1/2 of the colonic cavity and was superficially ulcerated and prone to bleeding. The nature of the sigmoid colon mass remained to be investigated: Colon cancer? Pathology revealed well-differentiated sigmoid colon adenoma. Surgery was indicated whereas the patient declined. So non-toxic integrative treatment like stopping bleeding and hyperthermia therapy were given to improve immunity and control tumor growth.

He stated a past history of coronary heart disease, atrial fibrillation, type II diabetes mellitus, chronic bronchitis, pulmonary emphysema, gastric ulcer, esophagitis, internal hemorrhoids and cerebral atrophy.

Conditions on admission:

The patient suffered abdominal distension and pain. He had 2-3 bowel movements per day with blood in the stool. He had poor appetite and painful shoulder with slightly limited motion, but no nausea, vomiting, fever, chills, chest tightness, shortness of breath, or edema in bilateral lower limbs. His sleep was normal but urination was weak. No significant weight loss was noted for the last one year. Physical examination revealed normal findings.

Assistant examination:

The colonoscopy (February 24, 2014) showed an annular, protruding mass in the sigmoid colon of about 25-29cm. It covered 1/2 of the colonic cavity and was superficially ulcerated and prone to bleeding. The nature of the sigmoid colon mass remained to be investigated: Colon cancer? Pathology reported well-differentiated sigmoid colon adenoma.

A test showed (May 7, 2014) CEA 2.97ng/ml. Stool analysis and occult blood test revealed positive findings. Urine analysis was unremarkable.

ECG: Abnormal heart rhythm and atrial fibrillation were noted, and ventricular rate was 84bpm. Left axis deviation by -51° .

Cervical spine X-ray (PA + LAT + bilateral oblique) showed: Left uncovertebral joint hyperplasia at C5/6, with corresponding narrowed intervertebral foramen. Intervertebral disc disease was noted at C6/7. Cervical vertebrae degeneration was shown.

Holter ECG: Ectopic cardiac rate and atrial fibrillation accompanied by long pause were shown. Occasional multifocal premature ventricular beats in four forms were noted and some occurred in pairs; ST-T was unremarkable.

Diagnoses:

1. Sigmoid colon cancer
2. Atrial fibrillation and flutter
3. Class II chronic cardiac insufficiency
4. Type II diabetes mellitus

Integrative treatment plan:

Non-toxic integrative cancer treatments were provided such as deep hyperthermia therapy three times per week and magneto-electric biofeedback therapy three times per week to improve immunology, CIK cell therapy and deep hyperthermia therapy once every other day, rod massage therapy and acupuncture to control the growth of the tumor.

TCM treatment:

The elderly patient had a history of hypertension, diabetes and colon cancer for many years which made the abdominal and collateral diseases become chronic without improvement. Thus, the pathogen entered the collaterals and led to blood stasis and obstruction. That was the reason he experienced abdominal bloating and pain. After a long period, there came spleen and stomach weakness, spleen Qi deficiency, and spleen failure to transport blood, and then the blood deviated from its normal path and overflowed to the colonic tract. That's why the blood was seen in stool. And also persistent diseases could injure kidney Yang, causing the kidney Yang declination. This also led to the malnutrition of viscera and collaterals. As a result, the patient suffered pain in the left shoulder with slightly limited motion and weak urination. He presented with signs of Qi deficiency including light white tongue, thin and white tongue coating, and knotted pulse. The patient's disease was located at the spleen and colon tract. Therefore, he was treated by "Ba Zhen Tang" was prescribed for boosting Qi and tonifying blood. Acupuncture and Tuina massage were also ordered.

Treatment outcome: After being hospitalized for 26 days, the patient was alert and conscious and with good spirit. His abdominal distension and pain were alleviated and the pain in the left shoulder was basically relieved as well. He had bowel movement twice per day with stool well-formed and light brown. He had normal appetite, sleep and urination. He visited our hospital periodically for examinations and non-toxic integrative treatment. On April 17, 2015, his whole abdominal and chest CT scans revealed status post sigmoid colon cancer treatment; posterior wall of sigmoid colon was thickened and clinical correlation was suggested.

In July 2016, the patient's follow-up examination showed significant alleviation of the posterior wall thickening of the sigmoid colon. The patient had never received any surgery for the sigmoid colonic cancer, but TCM and local hyperthermia therapy. The goal of remission was basically achieved.

Currently, the patient returns for a rehabilitation treatment every three months.

Z3, female, 95 years old.

The patient was admitted with status post sigmoidectomy due to colon cancer for 10 months on March 11, 2013. With a space-occupying lesion of sigmoid colon with hemorrhage, the patient underwent laparoscopic sigmoidectomy in Guangzhou First People's Hospital on May 17, 2012. Pathology result was consistent with sigmoid colon cancer. She presented to Clifford Hospital for follow-up examinations. She was then admitted to Oncology. History review was significant for hypertension.

Physical examination revealed an oblique surgical scar on left lower abdomen and 3 puncture scars of 1 to 1.5 cm on abdominal wall. Abdomen was non-distended, without visible outline of stomach and intestine or gastrointestinal peristaltic wave. Abdominal walls were free of viscosity. Abdominal respiration was not limited. Abdomen was soft in muscles, without tenderness or

rebound tenderness. Liver region was negative for tenderness. Hepatic dullness borders were normal and liver and spleen were impalpable. It was negative for Murphy sign and shifting dullness. Kidneys were free of tenderness and percussion-induced pain. Bowel sounds were normal. There was no vascular bruit heard.

Assistant examinations: Pathology result (Guangzhou First People's Hospital) was consistent with sigmoid colon cancer. Complete blood count: WBC: $4.81 \times 10^9/L$, Neu%: 66.5%, RBC: $3.65 \times 10^{12}/L$, HGB: 96g/L, PLT: $227 \times 10^9/L$. Liver and kidney profiles, electrolytes, fasting blood glucose, blood lipid, urinalysis and stool analysis were unremarkable.

Diagnosis: Status post sigmoidectomy

Integrative treatment plan: 1. Non-toxic integrative cancer treatment included chelation and hyperthermia, every other day, and intravenous medical ozone and biofeedback therapy, every day. 2. Given the fact of being elderly and physically frail after surgery, therapy focused on boosting Qi and nourishing blood. Prescribed Chinese herbs included Radix Codonopsis (Dang Shen) 30 g, Poria (Fu Ling) 15 g, Rhizoma Atractylodis Macrocephalae (Bai Zhu) 12 g, Radix Glycyrrhizae Preparata (Zhi Gan Cao) 9 g, Radix Rehmanniae Preparata (Shu Di Huang) 15 g, Radix Angelicae Sinensis (Dang Gui) 15 g, Radix Paeoniae Alba (Bai Shao) 15 g, and Rhizoma Chuanxiong (Chuan Xiong) 12 g. Later, the patient was diagnosed with Yang deficiency of spleen and kidney based on TCM syndrome differentiation. Therefore, the TCM prescription aimed to warm Yang and invigorate spleen and included the following herbs: Radix Codonopsis (Dang Shen) 15 g, dried ginger 15 g, Rhizoma Atractylodis Macrocephalae (Bai Zhu) 15 g, Licorice Root (Gan Cao) 10 g, Fructus Psoraleae (Bu Gu Zhi) 30 g, Semen Cuscutae (Tu Si Zi) 30 g, Fructus Lycii (Gou Qi Zi) 30 g, and Herba Epimedii (Yin Yang Huo) 30 g. Shenqifuzheng Injection was provided to boost healthy Qi. Acupuncture and dietary instructions were also combined into the treatment.

Treatment outcome: The patient stayed as an inpatient for 12 days and gained a significant improvement in her conditions, and was good in spirit. The patient complied with outpatient and inpatient follow-ups. Follow-ups in the last 2 years revealed an ongoing recovery. Assistant examinations on July 15, 2013, September 9, 2014, and March 6, 2015 revealed status post sigmoidectomy and no other evidence of tumor relapse.

The patient, aged 95 this year, has been living for 5 years since sigmoidectomy, and receives non-toxic integrative cancer treatment every half a year. Her quality of life scores 0 currently.

Follow-up examination in July, 2016 showed no evidence of tumor and good physical conditions.

Esophageal Cancer

H4, male, 49 years old.

He was admitted to Clifford Hospital on June 19, 2007 with a status post esophageal cancer resection for 20 months, progressive emaciation with hoarseness for over 2 months, and progressive dysphagia for 20 days.

The patient suffered repeated epigastric pain and vomiting in October, 2005 and underwent a CT scan which disclosed possible cancer of the lower esophagus. A gastroscopy revealed neoplasm in the lower esophagus and pathology reported moderately differentiated squamous carcinoma. Radical resection of esophageal cancer was successfully performed under general anesthesia. Pathology study indicated esophageal squamous cell carcinoma, which infiltrated muscular layer to serosal layer. Upper and lower surgical margins were negative for cancer invasion. There was no lymphatic metastasis. The patient recovered well after surgery and didn't receive any chemotherapy. In April 2007, he presented with emaciation (weight loss about 10kg in 2 months), hoarseness, poor appetite and occasional vomiting. Twenty days before admission, he experienced progressive dysphagia; therefore, he was admitted to the hospital for further treatment.

Physical examination: The patient was normal in physical development but was emaciated. He weighed 49kg and looked moderately anemic. There was no enlarged superficial lymph node. Heart and lung auscultation were normal. The abdomen was not distended, without tenderness.

Liver and spleen were impalpable. A surgical scar of 15cm in length was noted in the chest. Ecchymosis was seen in left abdomen and lower back. Karnofsky score was 70.

Assistant examination:

Tumor markers test: CEA 3.7ng/ml, AFP 6.6ng/ml, CA-125 12U/ml, CA-153 12U/l, CA19-9 27ml, TSGF 31.7U/ml. Immunology (5 items) and trace elements tests were normal. Ultrasound scan of the abdomen was unremarkable. Gastroscopy showed a red, swollen and erosive anastomosis and pathology study was consistent with canceration of the anastomosis, moderately differentiated squamous cell carcinoma. Esophageal barium swallow test showed postoperative change of the lower esophagus, and barium filling defect in the anastomosis. ECG and chest X-ray were normal. Fecal occult blood test: (++).

Diagnosis: Relapse after esophageal cancer surgery.

Integrative treatment plan: The patient suffered postoperative recurrence; his general conditions were poor, with a Karnofsky score of 70. He presented with nausea, vomiting, and significant emaciation, which were caused by eating difficulty from esophageal stricture after tumor recurrence and severe malnutrition due to tumor consumption. Therefore, nutritional support was given to the patient immediately after his admission, including total parenteral nutrition (TPN) and herbal cuisine.

For anti-tumor treatment, chest local hyperthermia was provided once every other day, together with chelation therapy. Intravenous medical ozone saline was employed once every other day at intervals of hyperthermia therapies, and systematic biofeedback therapy was also applied once every other day. Traditional Chinese medicine (TCM) and acupuncture therapies were combined during the whole treatment process.

The patient's tongue was dark-red, with white and greasy coating. Pulse was thready and thin. According to TCM syndrome differentiation, it was Phlegm Qi stagnation and TCM treatment was provided to remove the depressed Qi and Phlegm. Therefore Xuanfu Daizhe Decoction + Sinisan was prescribed: Flos Inulae (Xuan Fu Hua)15g, Haematitum (Dai Zhe Shi)15g, Radix Bupleuri (Chai Hu)15g, Fructus Aurantii (Zhi Ke)15g, Radix Curcumae (Yu Jin)15g, Pericarpium Citri Reticulatae (Chen Pi)10g, Rhizoma Pinelliae (Ban Xia)15g, Radix Sophorae Tonkinensis (Shan Dou Gen)10g, Rhizoma Paridis (Cao He Che)15g, Radix Paeoniae Alba (Bai Shao)15g, Gekko Japonicus Dumeril et Bibron (Bi Hu)6g, Nidus Vespae (Lu Feng Fang)10g. The TCM was one dose daily for oral administration and should be decocted with water.

In acupuncture therapy, the following acupoints were selected: BL 13, PC 6, RN 17, ST 36, RN 12, SP 6, KI 3, BL 18, RN 6, and Outer Three Passes (Waisanguan). The acupuncture adapted an "even reinforcing and reducing" method, and needles remained in the points for 20 minutes. This therapy was administered once daily, for 5 days, followed by a 2-day rest.

Moxibustion therapy: RN 12, RN 4, RN 8, and ST 36 were selected for moxibustion therapy. Method: each session of moxibustion was applied to 2 acupoints for 10 minutes respectively in the frequency of once a day, and there was a 2-day interval after 5 sessions.

Auricular therapy: acupoints selected were as following: CO 2, CO 4, CO 3, CO 12, AT 4, AH 6a, CO 13 and CO 1. Method: auricular therapy alternated once a week between two ears. Cowherb Seeds were applied to the auricular points and the patient was instructed to press each acupoint 3 to 5 times per day, with each press lasting for 3 to 5 minutes.

During the treatment, TCM therapy and acupuncture therapy (acupoints selected) were adjusted according to the patient's symptom. One week later, symptoms like nausea and vomiting disappeared. Therefore, chelation therapy increased in dosage, 3 times a week for 6 weeks successively. Ozonated saline and systematic biofeedback therapy were employed continuously for 2 weeks. TCM therapy and acupuncture therapy remained unchanged. Two weeks later, the patient was better in spirits and he gained more weight to 52kg. Intravenous ozonated saline therapy was changed into EBOO (18 sessions in total), while hyperthermia into whole-body moderate-high temperature hyperthermia (every two weeks, 4 sessions in total) + local hyperthermia (every other day, 3 sessions weekly, and 27 sessions in total). Systematic biofeedback was provided every other day, 3 sessions weekly, and 27 sessions in total. Chelation therapy and hyperthermia were applied

at the same time and acupuncture therapy remained the same as before. TCM therapy was adjusted based on the previous formula.

After 3-month treatment, a gastroscopy showed mildly red and swollen anastomosis and a significant shrinkage of the erosive lesion.

After discharge, the patient continued non-toxic integrative cancer treatments, including local hyperthermia, EBOO, chelation, TCM, acupuncture, systematic biofeedback and herbal cuisine. Local hyperthermia, systematic biofeedback, EBOO and chelation therapies were all administered once a week.

Treatment outcome: The patient received the integrative non-toxic cancer treatments (mainly hyperthermia therapy) for 3 months, which alleviated nausea, vomiting, poor appetite, emaciation and anemia. He was better in spirits and gained 9kg and returned to normal appetite and good sleep. Anemia was basically reversed. Karnofsky score was 100. In order to strengthen the treatment outcome and avoid cancer relapse and metastasis, he complies with one-week of the non-toxic integrative cancer treatments ever month.

Currently the patient leads a life with good quality and a ECOG PS score of 0.

Glioma

L7, 28 years old.

The patient was admitted on December 26, 2008 due to intracranial space-occupying lesion for over two years, headache and dizziness for over one month and aggravation for one day.

The patient found a left intracranial space-occupying lesion in a health checkup in December, 2006. Despite such a finding, she denied the presence of headache, dizziness, nausea, vomiting, blurred vision or hearing loss, and the lesion was left untreated. In early November, 2008, the patient experienced headache and dizziness, accompanied with intermittent nausea and vomiting. A head CT scan done at a local hospital revealed masses in the right-sided thalamus and parietal lobe, raising the possibility of glioma; abnormal signal intensity in the left parietal lobe with a significant edema zone. On November 5, 2008, she underwent resection of intracranial mass. Postoperative pathological analysis indicated oligoastrocytoma (grade 2). The patient recovered well after operation. But one month later, after being fatigued by a long journey, she experienced worsening headache and dizziness accompanied by nausea and vomiting. Therefore, she was admitted through emergency department to Clifford Hospital.

Conditions on admission: Headache, dizziness, nausea and vomiting affected walking. No complaint of tinnitus, limb numbness, or restricted motions. Appetite was poor. Sleep was good. Urination and bowel movements were normal. Tongue was light red with thin white coating and cyanotic sublingual veins. Pulse was weak and unsmooth.

Physical examination: General conditions were good. Two arc-shaped surgical scars of about 7cm in length were noted at the right parietal region. No enlarged superficial lymph nodes could be palpable. Neck was soft without resistance. Respiratory sounds were clear and free of dry or moist rales. HR was 72bpm. Cardiac rhythm was normal without any murmurs. Abdomen was soft and non-distended. Liver and spleen was impalpable. No tenderness or rebound tenderness was noted at the whole abdomen. Bowel sounds were normal. Limbs moved normally, without limited motions. There were physiological reflexes but no pathological reflex.

Assistant examinations: A head CT scan done in Hainan General Hospital on December 8, 2008 revealed status post resection of right parietal lobe glioma. Compared with prior study, there was edema and a small amount of blood at the surgical site. Left parietal lobe lesion remained unchanged. A small amount of fluid was noted in the right frontal, temporal and parietal regions. Subcutaneous blood buildup was noted at right occipital and parietal regions. Sphenoid sinusitis and right mastoiditis were indicated as well.

Diagnosis: Status post resection of brain astroglioma.

Integrative treatment plan: A joint consultation suggested the patient was in postoperative recovery phase and initial treatments should include intracranial pressure reduction, WBC elevation, nutritional supplement and symptomatic treatment. Oral chemotherapeutic agent (Temozolomide 150mg, qd×5/28d) was administered. Integrative treatments involved traditional Chinese medicine, acupuncture, local hyperthermia, chelation therapy, anti-tumor mixture and medical ozone therapy. As blood stasis and internal obstruction according to TCM syndrome differentiation, “Nao Liu Yin and San Ling Jian Wan” were prescribed to activate blood, remove stasis, and disperse mass. The prescription included the following ingredients: Rhizoma Sparganii (San Ling) 15g, Fructus Polygoni Orientalis (Shui Hong Hua Zi) 10g, Curcuma Zedoary (E Zhu) 15g, Radix Paeoniae Rubra (Chi Shao) 15g, Poria (Fu Ling) 15g, Semen Coicis (Sheng Yi Yi Ren) 30g, Scorpion (Quan Xie) 5g, Scolopendra (Wu Gong) 5g, Herba Hedyotidis Diffusae (Bai Hua She She Cao) 30g, and Liu Wei Di Huang Wan 12g. One dose of the above herbs was decocted with water for oral administration daily.

Acupuncture was applied to the acupoints including EX-HN 5, DU 20, DU 14, ST 8, GB 20, LI 4, DU 23, ST 36. It adopted principle of neutral supplementation and draining, with the needle retained for 20 minutes, once a day, and a 2-day interval after 5 sessions.

Moxibustion was applied to 2 acupoints for 10 minutes respectively in the frequency of once per day and a 2-day interval after 5 sessions.

Auricular points included AH10, CO4, CO12, CO18, AT4, TG2p, AT2,3,4i, and AH6a. Method: Cowherb Seeds were applied to auricular points and the patient was instructed to press them 3 to 5 times per day. Auriculotherapy alternated weekly between two ears. Local hyperthermia of the head was given every other day; chelation therapy every other day; one dose of anti-tumor mixture every day; and medical ozone therapy every other day (alternately with chelation therapy).

The patient was basically symptom free after one week of treatment. Hyperthermia, chelation therapy, EBOO, acupuncture and traditional Chinese medicine continued and her conditions improved to discharge one month later. She continued non-toxic integrative cancer treatments for over 3 months at outpatient department after discharge. The patient received 36 sessions of hyperthermia and 45 sessions of chelation therapy. Her condition was stable without presence of increased intracranial pressure.

Treatment outcome: All the symptoms were relieved after integrative treatment. On discharge, the patient’s appetite was normal and her weight increased by 3kg. Limbs moved normally and she could care for herself independently. One week after discharge, she returned for chemotherapy with oral Temozolomide and non-toxic integrative treatment including traditional Chinese medicine, chelation therapy, hyperthermia, medical ozone therapy, anti-tumor mixture and acupuncture. After she continued above therapies for 3 months, a follow-up head MRI revealed status post resection of right parietal lobe astrogloma. The lesion was smaller than the prior MRI finding on December 8, 2008. She was recommended to continue non-toxic integrative treatment. Follow-ups in the past 4 years showed no significant abnormality. Imaging reports showed continuous improvement. The patient has returned to normal life and work. She gave birth vaginally to a boy in 2011. She and her boy are healthy.

Hypothyroidism

L8 female, 36 years old.

The patient had hypothyroidism for many years; she had oral administration of thyroxin 75 mg a day, one wholebody low-temperature hyperthermia session a week for 10 weeks. After one wholebody low-temperature hyperthermia, 25 mg thyroxin can meet patient's daily requirement and the symptom caused by hypothyroidism disappeared or obviously improved.

Liver Cancer

L9 female, 82 years old, Mongolian.

The patient was admitted on March 9, 2014 with status post liver cancer surgery for 5 years and epigastric discomfort for over 2 years, which became severer in the past 3 weeks.

In April, 2008, she was hospitalized to Clifford Hospital for further investigation into abdominal discomfort. A CT scan of the epigastrium revealed multiple space-occupying lesions in anterior lower and posterior upper segments of right liver lobe, supportive of malignant liver tumor (cancer); and hypodense diffuse lesion in the liver, suggestive of liver damage.

On May 9, 2008, she underwent resection of liver cancer (segment V & VI), cholecystectomy and chemotherapy pump placement for portal vein. The surgery went successfully. Postoperative pathology result was consistent with hepatocellular carcinoma. She was then transferred to Oncology Dept. and received local chemotherapy (Epirubicin 10 mg + Fluorouracil 0.25 mg) and integrative treatments like medical ozone and chelation. The treatment course went smoothly and the patient was free of discomfort or post-chemotherapy side effect. Following the treatment, she stayed on long-term use of oral Chinese medicine, but didn't return for follow-up regularly due to her residency in Mongolia.

In 2013, the patient started to present with unexplained, repeated and intermittent epigastric discomfort, especially in middle and upper abdomen, which was not aggravated or relieved by any factor. She left the discomfort untreated; however, such symptoms were present 3 weeks ago including acid reflux, heartburn, and fatigue, which were more significant after meal and walking.

On February 24, 2014, she presented to outpatient office for medical attention. A color ultrasound scan of the epigastrium revealed a solid space-occupying lesion of the liver, supportive of liver cancer, and clinical correlation was suggested; and minor ascites. On February 25, 2014, a CT scan performed in outpatient department suggested: 1. Status post liver cancer surgery. Compared with CT findings on July 23, 2008, this scan showed multiple liver masses, indicating cancer relapse. 2. Multiple cysts of left kidney.

Outpatient treatment was administered for protecting stomach and liver, which yielded a poor outcome. She was then admitted to Oncology Department for further treatment with a diagnosis of relapse of liver cancer after surgery.

Conditions on admission: The patient was alert and energetic and complained of epigastric discomfort, acid reflux, heartburn, occasional pricking pain of left upper limb, weakness, and poor appetite. He denied significant abdominal pain and had normal nocturnal sleep and urination. His bowel movement frequency was about once every 1 to 2 days.

Physical examination: Patchy focal proliferation was noted on the skin all over the body, which was itchy and free of discharge. There was no sign of petechia. A well-defined mass with a moderate texture measuring 4*2 cm in size was palpated behind the neck. A surgical scar was seen along bilateral costal margins. Bilateral respiratory sounds were clear to auscultation, without any dry or moist rales. There was no sign of precordial bulge. Apex beat was noted at the left 5th intercostal space, about 2 cm medial to midclavicular line. Cardiac dullness borders were normal; heart rate 80 bpm; and heart sound and rhythm were normal. No murmur was auscultated in valves. Abdomen was non-distended, without visible outline of stomach and intestine or gastrointestinal peristaltic wave. Abdominal walls were free of viscosity. A surgical scar measured 10 cm on the left and 15 cm on the right. Abdominal respiration was not limited. Abdomen was soft in muscles, without tenderness or rebound tenderness. Liver region was negative for tenderness. Hepatic dullness borders were normal and liver and spleen were impalpable. It was negative for Murphy sign and shifting dullness. Kidneys were free of tenderness and percussion-induced pain. Bowel sounds were normal. There was no vascular bruit heard.

Assistant examinations:

In February, 2014, a color ultrasound scan performed in outpatient department revealed a solid space-occupying lesion of the liver, supportive of liver cancer, and clinical correlation was suggested; and minor ascites.

On February 25, 2014, a CT scan performed in outpatient department suggested: 1. Status post liver cancer surgery. Compared with CT findings on July 23, 2008, this scan showed multiple masses in the liver, cancer relapse considered.

Laboratory study: Complete blood test: WBC $2.35 \times 10^9/L$. Biochemistry test: LDL 2.17 mmol/L, HDL 1.00 mmol/L, ALP 225 U/L, ALT 76 U/L, AST 89 U/L, LDH-1 84 U/L, DBIL 9.3 $\mu\text{mol/L}$, PA 52.0 mg/L, GLB 41.6 g/L, ALB 25.8g/L, A/G 0.6. DIC profile: activated partial thromboplastin time: 36.1 seconds; thrombin time: 22.2 seconds; D-dimer: 1420.94ng/ml; and other findings were normal. Hepatitis B test: positive for hepatitis B virus surface antigen, hepatitis B e antigen, and hepatitis B core antibody.

ECG: 1. Sinus bradycardia. 2. Degree I atrioventricular block. 3. ST changes. Whole-body bone scanning: 1. Abnormal hypermetabolism of anterior portion of 7th right rib and follow-up suggested in 3 months. 2. Degenerative changes of right knee. 3. Degeneration of thoracic and lumbar vertebrae. 3. Whole body osteoporosis. These findings were suggestive of liver cancer with bone metastasis. CT scan results: 1. Status post liver cancer surgery. Compared with CT findings on July 23, 2008, this scan showed multiple masses in the liver, cancer relapse considered.

Diagnoses: 1. Relapse of hepatocellular carcinoma after surgery, with bone metastasis. 2. Ascites. 3. Prurigo nodularis. 4. Degree I atrioventricular block.

Integrative treatment plan: In western medicine, treatments included chemotherapy (arsenious acid 5 mg, 10 sessions) and supportive treatments like liver protection and nutrition support in combination with medical ozone and chelation.

In Chinese medicine, the patient was an elderly female with status post liver cancer surgery and suffered deficiency of Qi and blood of Zangfu. In addition, she was subject to emotional depression, internal injury caused by excess of seven emotions, and impaired dispersion of the liver and gallbladder. As liver and spleen interpromote and interrestrict each other, a depressed liver restricts spleen, resulting in abnormal transportation and transformation. A deficient spleen compromises nutritional absorption and generation of blood and Qi, which results in inadequate energy supply and weakness. The signs of fat tongue body with white coating and fine, stringy pulses were suggestive of stagnation of liver-Qi with deficiency of the spleen.

This was a cancer case and differentiation of syndromes also points to stagnation of liver-Qi with deficiency of the spleen. The treatment focused on reinforcing the spleen to replenish qi, relieving depression of the liver-qi and softening masses. In Chinese medicine, Kangai Injection and other anti-cancer treatment were administered to boost the healthy Qi. The patient suffered itchy proliferative lesions of full body skin, indicating damp toxin accumulation on the exterior. Chinese medicine compress was given to stop itching, remove toxin and expel wind.

During stay in hospital, the patient was provided with oral Chinese medicine, once a day and acupuncture, 5 sessions a week.

Treatment outcome: The patient stayed in hospital for 30 days. He was alert and in good spirit, with normal appetite, sleep, urination and defecation. He denied other discomfort. Physical examination: There was a fat tongue body with white coating and fine and stringy pulses. Liver palms of both hands were noted. Patchy and focal proliferation was scattered all over the body, with reduced itch and no oozing. A well-defined mass with a moderate texture measuring 4*2 cm in size was palpated behind the neck. Abdomen was soft, without tenderness or rebound tenderness. Liver and spleen were impalpable. It was free of shifting dullness and bilateral lower limb edema. The patient's conditions were stable and ascites was reduced, without any significant discomfort. Therefore, the patient was discharged.

The patient has been living with advanced liver cancer for more than 7 years and is still on maintenance treatment with Chinese medicine tablets.

L10, male, born in 1947, from Zhejiang Province.

The patient presented to a hospital in Dongyang city, Zhejiang province due to vague pain in the right upper abdomen with bad appetite in February, 2012, and was diagnosed with "liver cancer".

He received interventional therapy and radiofrequency ablation in the hospital. After such procedures, follow-up examinations like CT scan at Oncology Department in Clifford Hospital showed stable tumor lesion. He had been on long-term traditional Chinese medicine (TCM) (medication) treatment. A complete blood count in November 2013 revealed decreased white blood cell and platelet; and another complete blood count on April 12, 2014 revealed: WBC $3.25 \times 10^9/L$, PLA $53 \times 10^9/L$, but those problems were left untreated. On March 11, 2015, the patient presented with abdominal bloating and pain, which could be aggravated by food intake, and poor appetite. He was then admitted to Clifford Hospital for treatment. He stated a history of chronic hepatitis B for over 20 years and he had been on Entecavir tablets for a long time, and HBV-DNA was controlled around 1×10^3 /copy.

Conditions on admission: The patient was listless and could be worsened by activity. The abdomen was distended, with epigastric pain. Facial complexion was dark. He disinclined to talk much. Urination was normal but stool was yellow and loose.

Physical examination: There was no jaundice or nevus araneus on whole body skin or mucosae. Bilateral lungs were clear to auscultation, without dry or moist rales. Heart rhythm and sounds were normal. No pathological murmur was heard in cardiac valves. Abdomen was slightly distended, without varicose veins in the abdominal wall. Abdominal muscles were soft, with slight epigastric tenderness but no rebound tenderness. Liver and spleen were impalpable under the ribs. Shifting dullness was positive. Lower limbs were free of edema.

Assistant examination:

Blood count: WBC $3.24 \times 10^9/L$, PLT $71 \times 10^9/L$.

Blood transfusion test (4 items): HBcAb positive, HBsAg positive.

Blood biochemistry: TBIL $31.3 \mu\text{mol/L}$, PA 110.0mg/L , IBIL $25.3 \mu\text{mol/L}$.

Diagnosis:

1. Status post interventional treatment for primary liver cancer
2. Chronic Hepatitis B, positive HBsAg, HBeAg, HBcAb
3. Liver cirrhosis caused by hepatitis
4. Ascites

Integrative treatment included TCM, acupuncture, and CIK cells infusion treatment, etc. As the patient was an aged gentleman with a history of chronic hepatitis and excess alcohol consumption, his liver lost control of conveyance and dispersion, causing Qi transformation insufficiency and subsequently presented with Qi stagnation and blood stasis. According to TCM disease differentiation and syndrome differentiation, he had “liver cancer” and “a depressed liver and a deficient spleen”.

In TCM therapy, Xiaoyaosan Decoction was prescribed: Radix Angelicae Sinensis (Dang Gui)15g, Paeonia lactiflora (Shao Yao)30g, Radix Bupleuri (Chai Hu)30g, Poria (Fu Ling)20g, Rhizoma Atractylodis Macrocephalae (Bai Zhu)20g, Radix Glycyrrhizae (Gan Cao)10g, Rhizoma Zingiberis Recens (Sheng Jiang)10g, Herba Menthae Haplocalycis (Bo He)10g (added later), Fructus Aurantii (Zhi Ke)15g, Radix Astragali (Huang Qi)20g. The TCM was given one dose daily for oral administration and should be decocted with water.

Acupoints for acupuncture therapy: BL 18, LU 1, LU 5, ST 36, LI 11, ST 40, SP 10, LR 3, Spirit Bone (Linggu), SP 3 and Outer Three Passes (Waisanguan). Triple Points (Sanchongxue) and Outer Three Passes (Waisanguan). Acupuncture adapted an “even reinforcing and reducing” method and the needles remained in the points for 20 minutes. The therapy was once daily for 5 days a week followed by a 2-day rest. CIK cells infusion treatment was applied twice daily. In addition, intravenous diuretic was provided with albumin supplement and immunity boosting.

Treatment outcome: The patient had been hospitalized for 9 days. Abdominal distention and pain were relieved. He denied weakness and stated normal sleep, urination and bowel movement. Tongue was red, with thin white coating. Physical examination showed no jaundice or nevus araneus on whole body skin or mucosae. Bilateral lungs were clear to auscultation, without dry or moist rale. Heart rhythm and sounds were normal. No pathological murmur was heard in cardiac valves. Abdomen was slightly distended, without varicose veins in the abdominal wall. Abdominal muscles were soft, without tenderness or rebound tenderness in the epigastrium. Liver and spleen

were impalpable under the ribs. Shifting dullness was negative. Lower limbs were free of edema or varicosity. Follow-up liver function test was normal.

The patient has been living with advanced liver cancer for 4 and a half years. He only receives TCM and non-toxic integrative cancer treatments. Currently he recovers well with the cancer basically in remission.

The patient keeps periodic follow-ups in Clifford Hospital. Currently he is in stable condition and still on TCM treatment.

X1, 62 years old.

The patient was admitted on April 28, 2007 due to "yellowish discoloration of skin and sclera for 20 days and abdominal bloating with edema in bilateral lower limbs for 3 days".

More than 20 days before admission, the patient noticed yellow discoloration of sclerae and lacked strength. He then sought medical attention in a local clinic and was diagnosed with "hepatitis"; however, the patient paid no attention on doctor's suggestion for further examination. Three days before admission, the patient noted edema in bilateral lower limbs and suffered poor appetite and bloating abdomen. Therefore, he decided to seek medical care at Outpatient Department of Clifford Hospital.

A B-mode ultrasound scan of abdomen indicated multiple nodules in right hepatic lobe, of which the largest one was 4cm×5cm×5.5cm in size.

Later an abdominal CT scan revealed atrophic left hepatic lobe and hypodense lesion in the posterior-upper segment of right hepatic lobe with a sectional area of 5.4cm×6.2cm. A satellite nodule with a diameter of about 6mm was behind the lesion. These were suggestive of primary hepatic carcinoma, hepatic cirrhosis and ascites. He was subsequently hospitalized for further treatment.

At admission, he was in poor spirit and appetite, and felt whole-body weakness and mild abdominal bloating. Sleep was acceptable. Stool was dark-black occasionally.

Physical examination: There was medium yellowish discoloration all over the skin and mucosae. Several spider angiomas were noted in neck and upper chest, but no rash or subcutaneous hemorrhage or ecchymosis. The abdomen was soft in muscle and slightly distended, without venous engorgement tenderness or rebound tenderness. Hepatic region was not tender. Liver and spleen were impalpable. Murphy sign was negative, and shifting dullness was positive. Mild edema was noted in lower limbs. Karnofsky Performance Status Scale was 60.

Assistant examinations:

Complete Blood Count:	RBC	5.5×10 ¹² /L	Hb	125g/L
	WBC	5.3×10 ⁹ /L	PLT	224×10 ⁹ /L
Biochemistry test:	ALT	775U/L	AST	585U/L
	TBIL	217U/L	DBIL	154.5U/L
	ALB	26.7g/L	ALP	256U/L
	GGT	357U/L	Cr	12umol/L
	Ua	125umol/L	BUN	2.7mmol/L
	GLU	6.21mmol/L	TG	0.54mmol/L
	GHO	3.78mmol/L	K ⁺	3.5mmol/L
	Na ⁺	137mmol/L	Cl ⁻	101mmol/L
	Ca ²⁺	1.78mmol/L		
	Tumor markers:	CEA	3.7ng/ml	AFP
CA-125		12U/ml	CA-153	12U/ml
CA19-9		27ml	TSGF	31.7U/ml

Immunology test (5 items) revealed normal findings.

Micro-elements:

Copper 3.55mmol/L

Zinc, lead, mercury, cadmium, nickel were within normal limits.

NH 143umol/L

HBV(5 items): HBsAg (+)

HBsAb (-)

HBcA (-)

HBeAg (+)

HBeAb (+)

HBV-DNA 3.37×10^5 copies/ml

An abdominal CT scan revealed atrophic left hepatic lobe, an abnormal low-density lesion in the inferior-posterior segment of right hepatic lobe with a sectional area of 5.4cm×6.2cm, and a satellite nodule about 6mm in diameter behind the lesion. Therefore, the impression was primary hepatic carcinoma, hepatic sclerosis and ascites.

A gastroscopy showed varicosity of esophagus and gastric fundus.

A chest X-ray showed a small amount of right-sided pleural effusion.

An ECG was normal.

Diagnoses:

5. Primary liver cancer (T3N0M0);

6. Decompensated cirrhosis secondary to chronic hepatitis B.

Integrative treatment plan:

The patient suffered obviously abnormal liver function, massive ascites, hypoproteinemia and elevated blood ammonia at admission. Without medical management, it could develop into liver failure or even hepatic coma, hepatorenal syndrome, massive hemorrhage in upper gastrointestinal tract or other major diseases. Therefore, symptomatic treatment was given for detoxification, protecting liver and reducing enzyme, relieving jaundice, lowering blood ammonia, inhibiting gastric acid and reversing hypoproteinemia. And nutritional support included a rational combination of Compound Amino Acid Injection, medium/long-chain fat emulsion and glucose.

In syndrome differentiation of traditional Chinese medicine, the patient's primary symptoms (yellow discoloration of skin and sclerae, ascites, edema in lower limbs, poor appetite, red tongue with yellow-greasy coating, and wiry pulse) were attributed to "liver Qi depression and stagnation" and "water-dampness and retention". Accordingly, the patient should be treated to soothe the liver, regulate Qi, drain dampness and relieve icterus and TCM prescription included the following herbs:

Green tangerine Peel (Qing Pi) 10g

Radix curcumae (Yu Jin) 20g

Cyperus rotundus (Xiang Fu) 20g

Hovenia dulci (Zhi Ke) 10g

Angelica sinensis (Dang Gui) 15g

Radix notoginseng (Tian Qi) 6g

Concha margaritifera (Zhen Zhu Mu) 30g

Light wheat (Fu Xiao Mai) 60g

Prepared liquorice root (Zhi Gan Cao) 10g

Trichosanthes kirilowii maxim (Gua Lou) 30g

Allium macrostemon (Xie Bai) 15g

Acorus calamus (Chang Pu) 15g

Root of red-rooted salvia (Dan Shen) 20g

Root of kudzu vine (Ge Gen) 30g

Mint (Bo He) 6g

Radix curcumae longae (Jiang Huang) 10g

Radix Paeoniae Rubra (Chi Shao) 60g

Capillary worm wood Herb (Yin Chen) 30g

These herbs were decocted with water for oral administration once daily.

A local hyperthermia of abdomen was also given every two days and after 2 weeks of continuous treatment, skin and sclerae discoloration obviously subsided and ascites and edema in lower limbs were reversed. However, the patient developed paroxysmal palpitation and an ECG

indicated paroxysmal supraventricular tachycardia, and subsequently local hyperthermia was stopped.

According to TCM differentiation of symptoms and signs, the patient suffered Qi and Yin deficiency and was given "Si Jun Zi Tang" combined with "Sheng Mai San". Chelation or extracorporeal blood oxygenation and ozonation (EBOO) were administered alternately every other day.

After a week of treatment, the patient got rid of yellowish skin or sclerae, or palpitation, but with poor appetite. In TCM's perspective, symptoms were differentiated as spleen-stomach weakness. Xiangsha Liu Junzi Tang was prescribed to fortify the spleen and improve appetite as well as "Pei Yuan Tang" (1 bag per day).

Symptoms disappeared after the treatment, and the patient continued the local hyperthermia every other day.

Besides, acupuncture therapy was given with a neutral supplementation and draining method and some acupoints (in international codes) selected were as follows:

Ganshu (BL18), Qimen (LA14), Pishu(BL20), Shenshu (BL23), Zusanli (ST36), Taixi (KI3), Sanyinjiao (SP6), Taichong (LR3), Yinlingquan (SP9), and Waisanguan (GB34). Needles remained for 20 minutes and there was a 2-day interval after 5 sessions. Meanwhile, moxibustion was applied to 2 acupoints among Guanyuan (RN4), Zusanli (ST36), Ganshu (BL18), Shenshu (BL21), Pishu (BL20) for 10 minutes respectively in the frequency of once per day and a 2-day interval after 5 sessions. Auriculotherapy alternated weekly between two ears. Cowherb seeds were applied to the auricular points (CO12, CO13, HX1, GAN YAN DIAN, HX6,7i, CO18, TG2p, AT4, AH6a, TF4).

Typical symptoms of decompensated cirrhosis on admission were treated with western medicine for liver protection, gastric acid inhibition, albumin supplement, and reduction of enzymes and blood ammonia. Since he went through the critical days, treatment increased progressively and systematically in intensity.

Treatment outcome:

After 2 months of inpatient stay, the patient stated well improved spirit and normal appetite. Stool was yellow and soft. He was free of weakness, abdominal distension and edema in bilateral lower limbs. Physical examination revealed no yellowish skin or sclerae. In follow-up examination, space-occupying lesion in liver measured 5.4cm×5.5cm in size, which had shrank comparing with that before treatment. No evidence of ascites or lymphadenopathy.

Liver function test:

ALT	35U/L	AST	47U/L
TBIL	39U/L	DBIL	18.5U/L
ALB	20.5G/L	AFP	173UG/L

KPS was 100. The patient has good spirit, appetite and sleep in periodic follow-ups. He returned for 10 days of non-toxic integrative cancer treatment in inpatient department every 20 days and stayed on Chinese medicine after discharge. The follow-up treatment frequency was adjusted to 1 week per month after 3 months and three days per month after six months. A follow-up CT scan in outpatient department (1.5 year after discharge) showed stable lesions of unchanged size, and no evidence of new lesion. Liver function and AFP were normal.

The patient has a good quality of life currently and is still on non-toxic integrative cancer treatment.

Lung Cancer

C1, female, 64 years old.

The patient was admitted on August 27, 2014 with lung cancer for over 1 year, cough for over 1 month, and left chest pain for 3 days. In December 2012, the patient presented with cough,

shortness of breath, and chest distress, without hemoptysis or night sweat. Then she sought medical attention at Nansha Hospital of Chinese Medicine where she was diagnosed with lung cancer accompanied by pleural effusion. However, she didn't receive assistant examinations like pathology test. As patient family refused surgery, radiotherapy and chemotherapy, she only received Chinese medicine. From February 2013 until now, the patient was admitted to Clifford Hospital multiple times with chest pain, cough, shortness of breath and other discomfort. Chinese medicine and non-toxic cancer treatment helped relieve patient's symptoms. One month prior to admission, the patient presented with non-productive cough, which was not treated systematically. Three days ago, the patient developed paroxysmal chest pain, with each episode lasting for about 1 hour, which was relieved by oral analgesic.

Past history: History review was positive for rheumatic arthritis for over 10 years and cervical spondylopathy with repeated dizziness for over 5 years. She denied the history of hepatitis, tuberculosis, hypertension, diabetes mellitus, heart disease, surgery or trauma, or blood transfusion. Vaccination history remained unknown.

Conditions on admission: The patient was alert and in general spirit. She complained of non-productive cough and left chest pain. She denied chest distress, shortness of breath, chills or fever. Appetite, sleep, urination and bowel movement were normal. There was no recent weight loss. On physical examination, the patient was in an active posture and normal in development, poor in nutritional status, alert in consciousness, normal in gait, correct in response to questions, and cooperative in physical examination. The left lung presented with an inadequate respiratory movement and increased vocal fremitus as well as a flat percussion note. Significantly reduced respiratory sound was noted in the left lower lung. Right lung was clear to auscultation. Both lungs were free of dry or moist rale. There was no sign of precordial bulge. The apex beat was noted at the left 5th intercostal space, about 2 cm medial to midclavicular line. Cardiac dullness borders were normal; heart rate 77 bpm; and heart sound and rhythm were normal. No murmur was auscultated in valves.

Assistant examination: Chest CT scan: 1. Nodule has increased in size in lingular and apicoposterior segments of left lung. There were multiple new metastases in both lungs as well as left pleural metastasis. Lymphadenopathy was showed in left pulmonary hilus, mediastinum, and left supraclavicular region. There was an evidence of encapsulated pleural effusion. 2. Right thyroid had a space-occupying lesion, suggestive of adenoma.

Laboratory study: Liver function: DBIL: 7.4 $\mu\text{mol/L}$; complete blood count: $13.98 \times 10^9/\text{L}$, NEU#: $9.99 \times 10^9/\text{L}$, RP: 14.1mg/L.

Tumor markers (5 items): CEA: 86.82ng/ml, CA153:42.66U/ml, CA125:165.60U/ml. Other findings were normal.

Diagnoses: 1. Stage IV Lung cancer with metastases to lymph nodes and internal lung. 2. Pleural effusion. 3. Mixed cervical spondylopathy.

Integrative treatment plan: 1. Oral Dextromethorphan to stop cough and Esomeprazole Magnesium Enteric-coated Tablets to protect stomach. 2. Coenzyme Complex for Injection by IV for nutritional support. 3. Medical ozone to improve immunity. 4. Kangai Injection by IV to boost healthy Qi and inhibit cancer. 5. Cefoperazone Sodium and Sulbactam Sodium for Injection by IV drips (3 g, Q12 h) for infection. 6. Instruct the patient to stay positive, lead a regular life, keep good indoor ventilation, keep warm, and prevent secondary lung infection from pathogens. The patient was advised to minimize the intake of sticky, greasy, and spicy food and turn to food with anti-cancer properties, like mushroom, coix seed, and sea tangle.

The patient suffered deficiency of Qi and Yin in terms of syndrome differentiation. The Chinese medicine focused on supplementing Qi and nourishing Yin. Shashen Maindong Tang was prescribed, one dose a day orally, and included the following herbs: Radix Adenophorae (Sha Shen) 10 g, Ophiopogon Root (Mai Men Dong) 15 g, Fragrant Solomonseal Rhizome (Yu Zhu) 10 g, Radix Glycyrrhizae (Sheng Gan Cao) 6 g, Folium Mori (Sang Ye) 10 g, Radix Trichosanthis (Tian Hua Fen) 10 g, and Hyacinth Bean (Bian Dou) 10 g. Adenophorae (Sha Shen) and Ophiopogon Root (Mai Men Dong) serve to supplement Qi and nourish Yin. Fragrant Solomonseal rhizome (Yu Zhu) and Radix Trichosanthis (Tian Hua Fen) promote fluid production

to quench thirst. Folium Mori (Sang Ye) clears heat. Hyacinth Bean (Bian Dou) eliminates dampness.

Treatment outcome: After admission as an inpatient for 11 days, the patient was alert and energetic. A dragging sensation of left chest was noted, without pain, and discomfort below xiphoid process subsided. She coughed occasionally, but denied chest distress, shortness of breath, productive cough, chills or fever. Sleep, urination and defecation were normal. The tongue was red with a thin coating. The pulse was thready and rapid. Physical examination: There was no palpable enlarged superficial lymph node all over the body. Respiratory sounds of left lower lung weakened while that of right lung remained normal. Both lungs were free of dry or moist rale. The cough and chest pain subsided significantly, and the patient was discharged without obvious discomfort.

Currently, the patient continues treatment with Chinese medicine and local hyperthermia, without use of KTI treatment or chemotherapy. She has been living with lung cancer for more than 4 years with a stable quality of life.

D1, male, 64 years old.

On March 28, 2014, the patient was admitted with lung cancer for over 3 years and productive cough for 10 days. In October, 2010, the patient developed cough productive of excessive sputum with blood streak. A CT scan revealed a space-occupying lesion of left upper lung, suggestive of lung cancer accompanied by obstructive pneumonia. A follow-up CT scan in Clifford Hospital showed: 1. A space-occupying lesion of left upper lung, highly suggestive of lung cancer with metastases to lymph nodes of supraclavicular fossa and mediastinum; and hydropericardium and minor left pleural effusion. 2. Old lacunar infarction in left basal ganglia and thalamus. Sequential fiberoptic bronchoscopic pathology result was consistent with squamous cell carcinoma, stage IIIb, which was inoperable. Therefore, local hyperthermia and nontoxic integrative cancer treatment were administered and the patient improved and was discharged.

The patient presented with cough productive of sputum 10 days ago and was readmitted. On physical examination, the patient was in an active posture, moderate in nutritional status, normal in gait, correct in response to questions, and cooperative in physical examination. The full-body skin was free of yellowish discoloration, cyanosis, mucosal ulcer, or spider nevus. No evidence of superficial lymphadenopathy. The thorax was symmetrical without malformation. Both lungs were normal in respiratory movement. Vocal fremitus was asymmetrical. Auscultation of right lung revealed low-pitched respiratory sound. No respiratory sound was heard in left upper lung. There was no sign of dry or moist rale. There was no evidence of precordial bulge. The apex beat was noted at the left 5th intercostal space, about 2 cm medial to midclavicular line. Cardiac dullness borders were normal; heart rate 73 bpm; and heart sound and rhythm were normal. No pathologic murmur was auscultated in valves.

Conditions on admission: The patient looked tired and thin and suffered productive cough, chest distress, exertional dyspnea, and unclear speech. Diet intake, urination and defecation were normal. There was no sign of extremity edema. The tongue was red with thin and white coating. The pulse was stringy and thready.

Assistant examination: Complete blood count: WBC $8.49 \times 10^9/L$, Neu% 84.7%, HCT 38.7%, Lym% 9.9%. The remaining findings were normal. Liver function: ALT 43U/L, GLU) 18.13mmol/L, PA 134.0mg/L, GLB 35.7g/L, and S/L 0.5. Myocardial enzymes, renal function and electrolytes were unremarkable. HbA1C% 8.80%. FT4 1.80ng/dl. Urine analysis: Glucose 4+. Stool analysis: Weak positive (\pm) for occult blood.

Chest CT scan with contrast: Status post treatment of left upper lung cancer. Compared to CT scan findings on November 6, 2012, this CT scan revealed the following findings: lesion increased in size; atelectasis of left upper lobe; mediastinum displaced to the left; possibility of multiple metastases in left lower lobe to be excluded; small nodule in lateral segment of right middle lobe below pleura and regular follow-up suggested; minor left-sided pleural effusion; hydropericardium; and compensating emphysema of right lung.

Diagnoses: 1. Squamous cell carcinoma of the left lung with lymph node metastasis (T3N3M0, stage IIIb). 2. Obstructive pneumonia

Treatment plan: Non-toxic integrative cancer treatment was provided, involving Chinese medicine, acupuncture, hyperthermia, and medical ozone.

As a frail elderly, the patient suffered chronic lung disease, which consumed lung Qi and caused lung Qi deficiency. Lung Qi deficiency results in pulmonary dysfunction, impaired Qi activities, blood stasis, and interrupted body fluid circulation. Fluid accumulation forms phlegm while phlegm accumulation leads to Qi stagnation and block collaterals and subcollaterals. As a result, toxin accumulates and results in lung masses as time goes by. Impaired lung function and upward invasion of lung Qi result in cough productive of phlegm. Lung Qi deficiency induces chest tightness and exertional shortness of breath. Tongue and pulse showed signs of deficiency of both Yin and Qi. Therefore, Kangai Injection was administered to boost health Qi. Sha Shen Mai Men Dong Tang, a Chinese medicine formula, was prescribed, one dose per day after meal and heated before use, to nourish Yin and moisturize the lung and eliminate cough and sputum. The formula included Radix Glehniae (Bei Sha Shen) 15 g, Radix Ophiopogonis (Mai Dong) 10 g, Radix Trichosanthis (Tian Hua Fen) 15 g, Stir Fried White Hyaciath Bean (Chao Bai Bian Dou) 15 g, Folium Mori (Sang Ye) 10g, Fragrant Solomonseal Rhizome (Yu Zhu) 12 g, Radix Glycyrrhizae Preparata (Zhi Gan Cao) 6 g, Radix Codonopsis (Dang Shen) 15 g, Poria (Fu Ling) 15 g, Rhizoma Pinelliae (Fa Ban Xia) 12 g. The patient also received treatment to fight against infection and control blood pressure and glucose. Deep hyperthermia of the chest was ordered to inhibit tumor growth. Chinese medicine treatment focused on nourishing Yin and moistening lung while relieving cough and reducing sputum. With treatment given, patient's general conditions were good and productive cough subsided significantly.

During the 1-year follow-up, he presented regularly for outpatient and inpatient care. Assistant examinations after admission on August 2, 2014: liver function: LDL: 1.76mmol/L; HDL: 1.05mmol/L; ALT: 63U/L. Complete blood count, stool and urine analysis, glycosylated hemoglobin, lung cancer associated antigen (2 items), and TPSA were unremarkable. Chest CT scan results showed: Status post treatment of left upper lung cancer. Compared to CT scan findings on March 29, 2014, this CT scan revealed the following findings: mass shrank in size; foci were almost absorbed in left lower lobe; previous left-sided pleural effusion was almost absorbed. Small nodule in lateral segment of right middle lobe below pleura, hydropericardium; and compensating emphysema of right lung remained almost unchanged. The patient continued treatment as directed.

The patient with advanced squamous cell carcinoma of the lung did not receive chemotherapy, radiotherapy or targeted treatment. Treated with Chinese medicine and local hyperthermia, he survived for more than 5 years, with a significant outcome.

In July, 2016, the patient died of cardiovascular disease.

G2, male, 73 years old.

The patient was admitted on January 30, 2015 with status post lung cancer surgery for 4 years and shortness of breath and bilateral lower extremity edema for 1 month.

On December 2, 2010, he underwent right lower lobectomy and lymphadenectomy in Nanfang Hospital. Postoperative pathology result was consistent with moderately differentiated adenosquamous carcinoma of right lower lung (stage Ib), without evidence of lymphatic metastasis. The patient took long-term Chinese medicine after surgery, instead of chemotherapy. A PET-CT scan on December, 2013 revealed no sign of cancer relapse or metastasis. He complied with regular outpatient follow-up in Clifford Hospital. Past history: The patient received right liver resection and cholecystectomy as a result of suspected liver cancer in Zhongshan Hospital, Shanghai in 1991 and postoperative pathology result was consistent with nodular hyperplasia. History review was also significant for hypertension, coronary heart disease, lacunar infarction, diabetes mellitus, and pulmonary tuberculosis.

Conditions on admission: The patient stated shortness of breath, chest distress, bilateral lower extremity edema, and restricted motion range. He denied productive cough, hemoptysis, nausea or vomiting. His appetite, urination and defecation were normal, without recent weight loss or gain. The tongue was pink with thin and white coating. The pulse was stringy.

Physical examination: Bilateral respiratory sounds were clear to auscultation, without any dry or moist rales. There was no sign of precordial bulge. The apex beat was noted at the left 5th intercostal space, about 2 cm medial to midclavicular line. Cardiac dullness borders were normal; heart rate 84 bpm; and heart sound and rhythm were normal. No murmur or pathologic murmur was auscultated in valves. A 2cm surgical scar was noted on right chest and healed properly. A 20 cm surgical scar was seen on the abdomen and healed well. Moderate edema of bilateral lower extremities was noted.

Assistant examinations: Chest and abdomen CT scan revealed the following findings: 1. Status post right lower lobectomy due to lung cancer: minor organization foci in the right lung. A cystic lesion was seen at right heart margin. There was no significant interval change from CT results on June 28, 2014. 2. Fatty liver and small cyst in Segment 2 of liver. 3. Multiple cysts of bilateral kidneys, and bilateral adrenal gland thickening. 4. Multiple thyroid nodules. 5. Absence of gallbladder was noted. The findings remained similar to those on June 28, 2014. Prostatic hyperplasia and calcification were shown. CTA of coronary artery showed: Coronary heart disease; multiple calcifications of three coronary branches; mild to moderate luminal stenosis.

Laboratory study: Complete blood count and urinalysis were unremarkable. Biochemistry test: Uric acid 542 $\mu\text{mol/L}$. Glucose test result is 6.65mmol/L. Triglyceride 2.09mmol/L. Male tumor markers (6 items): Normal.

Diagnoses: 1. Lung cancer, status post adenosquamous lung carcinoma surgery. 2. Hypertensive heart disease with heart failure and class 3 heart function. 3. Grade 1 hypertension, extremely high risk group. 4. Type 2 diabetes mellitus. 5. Old cerebral infarction. 6. Benign nodular hyperplasia of the liver and status post right liver resection and cholecystectomy.

Integrative treatment plan: 1. In western medicine, deep hyperthermia of the lung was provided every other day to control cancer relapse and metastasis; cardiogenic and diuretic agents to control heart failure; and anti-platelet therapy and coronary artery dilator to prevent coronary event. 2. In Chinese medicine's perspective, the patient suffered deficiency of Qi and Yin and deficiency-excess complex. Sha Shen Mai Dong Tang, a Chinese medicine formula, was ordered to boost healthy Qi and nourish Yin, one dose a day (3 doses in total) and taken in the morning and evening. The formula included the following herbs: Radix Astragali (Huang Qi) 15g, Radix Adenophorae (Sha Shen) 15 g, Radix Ophiopogonis (Mai Dong) 15 g, Bulbus Lili (Bai He) 15 g, Radix Scrophulariae (Xuan Shen) 12 g, Fritillariae Thunbergii Bulbus (Zhe Bei Mu) 12 g, Semen Armeniacae Amarae (Ku Xing Ren) 12 g, Herba Scutellariae Barbatae (Ban Zhi Lian) 15 g, Poria (Fu Ling) 18 g, and Grifola (Zhu Ling) 15 g.

Treatment outcome: The patient stayed as an inpatient for 13 days and gained a significant improvement in his conditions. The patient was alert and in good spirit and chest tightness subsided. It was negative for expectoration, fever, nausea or vomiting, abdominal pain or bloating, lower extremity edema or restricted motions. Appetite, urination and defecation were normal. The patient complies with outpatient and inpatient follow-ups and is free of cancer relapse.

He has been living with lung cancer for 6 years, without use of chemotherapy, radiotherapy, targeted therapy or immunotherapy. The patient only received non-toxic integrative cancer treatment and led a completely normal life.

H5, female, 65, Hong Kong citizen.

The patient was admitted on August 29, 2014 with a 2-year history of adenocarcinoma of the left lung accompanied by multiple metastases. On September 14, 2012, she found unexplained enlarged lymph node in the left side of her neck, which was hard in texture, with limited mobility but no pain. She underwent an aspiration biopsy in a local hospital and was verbally informed that

the result revealed pulmonary adenocarcinoma with lymphatic metastases (detailed pathology report unknown). Later, as presence of pleural effusion resulted in shortness of breath, she underwent thoracentesis to remove the pleural effusion (pathology report of the pleural effusion unknown), which led to a minor relief in shortness of breath. Then she was transferred to Clifford Hospital for further treatment.

Conditions on admission: The patient was alert but in low spirits. Lymph nodes on left side of the neck were enlarged. There was no fever, cough, hemoptysis, chest tightness, nausea, vomiting, abdominal pain or diarrhea. She was poor in appetite and sleep, but was normal in urination and bowel movement. The tongue was dark red, with thin and white coating. Pulse was deep and thin.

Physical examination: The patient was emaciating, in bad nutrition and with dry body skin. Two enlarged lymph nodes of 0.4cm×0.4cm in size were noted on the left side of the neck, hard and hardly movable. Thoracic deformity was noted with significant shrinking of the left thorax. Respiratory sounds in the left lung weakened, but that was normal in the right lung. No dry or moist rale was auscultated in both lungs. A badly-circumscribed mass of 5×5cm was palpated in the left epigastrium, which was firm and unmovable. Other quadrants of the abdomen were flat.

Assistant examinations:

PET/CT on February 2014 revealed: 1. A mass was noted in the dorsal segment of the left lower lobe with increased glucose metabolism, consistent with lung cancer. Massive pleural effusion accumulated in the left chest, accompanied by left lung atelectasis. 2. Multiple nodules were detected in both lungs. Multiple nodules and masses were seen in left pleura, chest and abdominal wall, with increased glucose metabolism, suggestive of metastatic tumors. 3. Multiple lymph nodes with increased glucose metabolism were found in level V of the neck, mediastinum and abdominal wall, suggestive of metastatic tumors. 4. Multiple osteogenesis and osteolysis with partly increased glucose metabolism were noted in the whole body, suggestive of metastatic tumors. 5. Spinal degeneration.

Chest X-ray on September 7, 2014 revealed the following results: left lung cancer, pleural effusion in left chest, metastatic tumor in left upper lung and increased infection lesion in right lower lung.

Laboratory study: CRP: 17.8mg/L, WBC:17.12×10⁹/L, HGB:87g/L, PLT:441×10⁹/L. Liver function: ALB: 32.5g/L. Tumor markers for female (5 items): CEA: 9.19ng/ml, CA15-3: 147.80U/ml, CA19-9: 27.72U/ml, AFP and A12-5 (within normal range). 2014-09-09: Blood count: WBC: 14.10×10⁹/L, Neu#: 12.93×10⁹/L, HGB: 93g/L, CRP:69.0mg/L. Liver function and electrolytes: Na: 128.20mmol/L, Cl: 84.20mmol/L, ALB: 32.40g/L, Ca:1.91mmol/L, Mg: 0.60mmol/L.

Diagnosis: Adenocarcinoma of the left lung accompanied by lymphatic metastases in the mediastinum, supraclavicular fossa and multiple metastases to both lungs.

Integrative treatment plan: Non-toxic integrative cancer treatments were provided, including traditional Chinese medicine (TCM), acupuncture, chelation, hyperthermia and medical ozone therapies.

TCM: The patient was in older age and frail. Due to consumption and waste, lung Qi was deficient and obstructed, inducing chest tightness. Prolonged diseased status injured spleen and stomach and the spleen lost its normal function of transport, causing a bad appetite. Qi transformation was disordered and Qi was unable to transform into blood. Therefore, Qi and blood were too weak to ascend into the lungs, causing lung Yin deficiency. The tongue was red with scanty coating, together with thready and rapid pulse, suggestive of deficiency of both Qi and blood. In conclusion, the patient was diagnosed with lung cancer according to disease differentiation and deficiency in both Qi and blood according to syndrome differentiation.

Treatment focused on tonifying Qi and nourishing Yin. Shashen Maidong Decoction was prescribed and included the following herbs: Radix Ophiopogonis (Mai Dong) 12g, Radix Adenophorae (Sha Shen) 6g, Rhizoma Polygonati Odorati (Yu Zhu) 15g, Radix Glycyrrhizae (Gan Cao) 30g, Folium Mori (Sang Ye) 12g, Radix Trichosanthis (Tian Hua Fen) 15g, Semen Lablab

(Bian Dou) 9g. The prescription should be decocted in water for oral administration, one dose daily

Acupuncture was applied to acupuncture points: BL 13, LU 1, LU 5, ST 36, LI 11, ST 40, SP 10, LR 3, Spirit Bone (Linggu), SP 3, and Outer Three Passes (Waisanguan). The "even reinforcing and reducing" acupuncture method was adapted and the needles were remained in the acupuncture points for 20 minutes. The acupuncture therapy was administered once daily for 5 days a week, followed by a 2-day rest.

Moxibustion was applied to two acupoints selected from BL 13, DU 14, CV 4 and ST 36. The moxibustion therapy lasted 10 minutes each time with the frequency of once daily for 5 days, followed by a 2-day rest.

Auriculotherapy: Acupuncture points for auriculotherapy were as following: CO 14, AH 10, AT 4, TF 4, CO 16, CO 18 and AH 6a. Method: auricular therapy alternated once a week between two ears. Cowherb Seeds were applied to the auricular points and the patient was instructed to press each acupoint 3 to 5 times per day, with each press lasting for 3 to 5 minutes.

Intravenous nutrition and herbal cuisine were combined to strengthen nutrition. Local chest hyperthermia was applied together with chelation therapy 3 times weekly. EBOO was applied twice a week during the interval of hyperthermia therapy. In addition, intravenous medications were provided to fight against infection, protect the heart, promote urination, relieve spasm and supply nutrition (combined with herbal cuisine to regulate the body condition).

Treatment outcome: The patient has advanced lung cancer and presents with pleural effusion and dyspnea. By receiving TCM therapy and local hyperthermia, she has survived for more than 3 years with a good quality of life.

H6, female, 67 years old.

The patient developed rib pain secondary to an accidental bump of her right front chest during housework on August 24, 2013. On the following day, she sought medical care at Orthopedics in Clifford Hospital and underwent a chest X-ray. The X-ray demonstrated an abnormal nodule in the superior lobe of right lung, for which, further examination with contrasted CT scan was recommended. Anterior rib fracture (right 6th) was also suspected. The enhanced chest CT scan showed a well-defined lobular and spiculated soft tissue mass in the superior lobe anterior segment of right lung, measuring approximately 20.4mm*25.4mm, suggestive of a space-occupying lesion in the anterior segment of superior lobe of right lung. There was a high possibility of peripheral lung cancer. For a definitive diagnosis and treatment, she was admitted with outpatient diagnosis of "lung mass".

After admission, preoperative examinations showed no operative contraindications and patient's general conditions were acceptable. Following a multidisciplinary consultation, on September 3, 2013, a thoroscopic resection of right superior pulmonary mass was performed under tracheal intubation and general anesthesia.

The post-operative pathology revealed papillary adenocarcinoma in the right superior lung. No cancerous tissue was noted in pleura or bronchial stump. A lymphatic metastasis (1/3) was noted in right inferior lung and other lymph nodes remained unremarkable. There were congestion and bleeding in lung tissue spaces near the tumor. Immunohistochemistry result showed CEA (+), EGFR (+), Ki-67 (index of about 10%), P53 (+<5%), CK5/6 (-), TOPOII (10%+), GSTπ (80%) and PgP (-).

The patient was transferred to Oncology on September 16, 2013 after stitches were removed.

Her past medical history was significant for "cholecystectomy", "hepatic cyst resection", "left distal forearm fractures", "hyperlipemia", and "bile reflux gastritis".

Physical examination: A transverse, well-healed surgical scar about 5 cm in length was noted in the right front chest. No swollen superficial lymph node was noted. Bilateral respiratory movement was normal. There were symmetrical vocal fremitus, clear percussion sounds, and

normal respiratory sounds without dry or moist rales in auscultation. HR was 72 bpm, heart rhythm normal, heart sounds normal and there was no heart murmur in valve auscultation.

Assistant examination: The post-operative pathology revealed papillary adenocarcinoma in the right superior lung. No cancerous tissue was noted in pleura or bronchial stump. A lymphatic metastasis (1/3) was noted in right inferior lung and other lymph nodes were unremarkable. There were congestion and bleeding in lung tissue space near the tumor. Immunohistology result showed CEA (+) EGFR (+), Ki-67(index of about 10%), P53 (+<5%), CK5/6(-) TOPOII (10%+), GST π (80%), and PgP (-).

Integrative treatment plan:

The patient's symptoms and signs were attributed to Qi deficiency of lung and spleen. "Yangyin Qingfei Tang" was ordered to boost Qi and tonify Yin. The detailed herbal formula and their respective remedial effects were shown as follows:

To tonify Yin:

Radix rehmanniae recen (Sheng Di Huang)12g

Radix Rehmanniae Praeparata (Shu Di Huang)12g

Asparagus fern (Tian Dong)12g

Radix ophiopogonis(Mai Dong)12g

Radix scrophulariae (Xuan Shen)12g

Radix codonopsis(Dang Shen)12g

To clear heat and detoxify the body:

Houttuynia cordata (Yu Xing Cao)30g

Rhizoma cimicifugae(Sheng Ma)30g

To detoxify the body and dispel dampness:

Smilax glabra(Tu Fu Ling)30g

To tonify Qi and secure the exterior:

Radix astragali(Huang Qi)15g

To purge fire and detoxify the body:

Radix scutellariae(Huang Qin)10g

Gardenia(Zhi zi)10g

The decoction should be orally administrated when still warm, 1 dose per day in 2 separate times after meals.

In acupuncture, therapists used moxibustion and arranged needles on scalp.

The patient was also given ozonated autohemotherapy twice per week and deep hyperthermia therapy once every other day. In addition, standard chemotherapy was administered.

Treatment outcome:

The patient has been receiving outpatient treatment and intermittent inpatient care. Three years of follow-ups showed an ongoing recovery. She returned for follow-up every three months, which revealed no cancer recurrence and metastasis.

T1, 44-year-old, Malaysian.

The patient was admitted with "lung cancer for 1 month through Outpatient Department " on October 31, 2012.

In October, 2012, the patient underwent a CT scan in a local hospital in Malaysia secondary to the presence of low-grade fever and cough, which revealed a right bronchial nodule. Biopsy indicated poorly differentiated adenocarcinoma. Oral medication (details unknown) was given, but yielded a poor outcome. He sought further medical attention in Clifford Hospital in that month. A sequential CT scan showed space-occupying lesions in anterior mediastinum and right pulmonary hilum, suggestive of mediastinal lung cancer with metastasis to mediastinal lymph nodes. The right trachea and superior vena cava were compressed and narrowed. After patient's conditions became stable with treatment, he started radiotherapy 5 sessions weekly (35 sessions in total, 70Gy) on December 10, 2012 as well as chemotherapy with Paclitaxel Injection 90mg + Cisplatin

Injection 30mg once per week (9 sessions in total). Meanwhile, non-toxic integrative cancer treatments were also provided, such as pulmonary hyperthermia therapy, Chinese medicine, medical ozone therapy to reduce side effects of radiotherapy and chemotherapy. He was discharged after improvement. Since then he returned to Clifford Hospital for follow-ups and treatments. No cancer recurrence and metastasis were noted.

Conditions on admission: The patient was conscious and in good spirits. He stated thoracic dragging sensation and shortness of breath but denied chest pain, cough, expectoration, hemoptysis, chills or fever. There was normal sleep, urination and bowel movement. No significant weight loss was noted. Physical examination showed no yellow discoloration of skin and membrane, cyanosis, mucosal ulcer, spider angioma, or enlargement of superficial lymph nodes. Jugular vein was not distended and hepatojugular reflux sign was negative. The respiratory sounds were clear to auscultation without dry or moist rales. Heart rate was 85bpm with occasional premature beats; cardiac sounds normal; and no pathological murmurs auscultated at cardiac valves. The abdomen was non-distended without visible outline of stomach or intestines or gastrointestinal peristaltic waves. Abdominal wall was free of venous engorgement and abdominal breathing was not restricted. Right lower abdomen was positive for tenderness but was negative for palpable mass. There were free of hepatic tenderness, normal hepatic dullness, and impalpable spleen and liver. Murphy's sign and shifting dullness were negative. No tenderness or percussion pain in bilateral renal regions. Bowel sounds were normal without vascular murmurs. No edema was noted in bilateral lower limbs.

Assistant examinations:

A CT scan performed in Malaysia in November, 2012 showed a large nodule in right bronchus and a biopsy confirmed poorly differentiated adenocarcinoma. On November 28, 2012, the patient presented to our hospital and a CT scan indicated lung cancer.

Laboratory studies revealed no significantly abnormal findings in tumor markers (5 items), hepatic or renal functions, electrolyte, urine or stool analyses.

Diagnoses: 1. Stage IV pulmonary adenocarcinoma with metastasis to lymph nodes 2. Superior vena cava syndrome

Integrative treatment plan: Integrative treatment included chelation, vitamin B17 and deep hyperthermia therapy to enhance immunity and control cancer recurrence and metastasis. In TCM theory, lung cancer pathology is as follows: Lung cancer is phlegm-damp and stagnant blood coagulation as a consequence of yin-qi deficiency from long-term deficiency of lung yin and residue of smoke toxin remained in the body (particular in lungs and nose) blocking trachea due to chronic smoking. This deficiency originates from lack of vital qi and disorder of yin and yang. As a consequence, differentiation of disease was lung cancer, of which its syndrome was deficiency of lung-Yin. The disease was located in lung and was closely related to liver, spleen and kidneys. It was deficiency pattern in nature with good prognosis. Clinically, nourishing Yin and tonifying lung should be taken as the fundamental method.

The patient was given oral Chinese medicine one dose per day and acupuncture therapy, once daily and successively 5 times per week.

Treatment outcome:

The patient had been hospitalized for 7 days and he was conscious and oriented and in good spirit. His symptom of thoracic dragging sensation had been subsided and there was no chest pain, cough, expectoration, hemoptysis, chills or fever. Urination and bowel movements were normal. The general conditions were acceptable so he was discharged.

By August 2016, the patient has lived with cancer controlled for 4 years and returned to work. He had never received inhibitor treatment like TKI or ERGF. The next follow-up will be scheduled in this September.

Y2, born in 1938, from Jiangxi Province.

A chest X-ray done in Clifford Hospital (October 2011) indicated a space-occupying lesion in the lung.

A CT scan revealed soft tissue mass of 5.1cm×4.3cm×3.8cm in the right upper lobe. The mass's margin with long and short spicules was lobulated. Pleural indentation and upward oblique fissure indentation could be noted with significantly uneven enhancement after contrast medium injection. The lesion invaded right mediastinum. Enlargement of multiple lymph nodes were noted in the mediastinum, right hilum and bilateral supraclavicular fossae, and right superior diaphragmatic lymph nodes enlargement noted as well. A few patches of hyperattenuation were noted in the right middle lobe, without any solid lesions in the rest of lung. She was diagnosed with lung cancer with metastasis to lymph nodes.

The patient received aspiration biopsy guided by CT scan in New Zealand which revealed adenocarcinoma of lung. After then, she underwent 6 cycles of chemotherapy (details unknown) in New Zealand, but developed chest tightness, limb numbness and mobility limitation after chemotherapy. Even though the symptoms were relieved after related treatment, the patient still felt chest tightness and limb numbness. Therefore, she turned to Clifford Hospital for treatment.

Conditions on admission: The patient was in poor spirit. She complained of chest tightness, limbs numbness and restricted motions, but denied cough, shortness of breath, difficult breath, or hemoptysis. Appetite and sleep were poor. Urination and bowel movement were normal. Physical examination: No superficial lymphadenopathy. Normal respiratory motions. Respiratory sounds were clear to auscultation, without dry or moist rales. Heart and abdomen were unremarkable.

Assistant examination: Whole blood count and biochemistry test were normal. Tumor markers showed CEA 17.64ng/ml, and CA19-9 115.40U/ml. Urine analysis showed RBC 16/ul and WBC 10/ul. Stool test was unremarkable. Chest and head CT scan with contrast on November 23, 2013 indicated the lesion larger than the prior study on December 22, 2012, with metastasis to right hilar lymph nodes, and cystic lesion in the left frontal lobe with possibility of metastatic tumor. Head MRI with contrast on December 5, 2013 indicated likely metastatic tumor in the left frontal lobe and no remarkable change compared with prior CT finding (11/24/2013); and multiple small ischemic lesions in bilateral frontal lobes.

Diagnosis: Status post chemotherapy for lung adenocarcinoma with metastases to lymph nodes and brain.

Integrative treatment plan: Non-toxic integrative cancer treatment included traditional Chinese medicine, magnetic therapy, hyperthermia and medical ozone therapy. As the patient suffered chronic illness and weakness and Yin deficiency dominates in senile person, symptoms and signs were differentiated as Yin deficiency of lung and kidney and treatment focused on nourishing lung and kidney. Qingzao Jiufei Tang was administered once a day. The prescription included Radix Codonopsis (Dang Shen) 15g, Radix Scrophulariae (Xuan Shen) 10g, Radix Rehmanniae (Sheng Di) 10g, Radix Rehmanniae Preparata (Shu Di) 15g, Radix asparagi (Tian Dong) 15g, Radix Ophiopogonis (Mai Dong) 15g, Glabrous Greenbrier Rhizome (Tu Fu Ling) 30g, Rhizoma Cimicifugae (Sheng Ma) 30g, Herba Houttuyniae (Yu Xing Cao) 30g, Folium Mori (Sang Ye) 30g, Flos Chrysanthemi (Ju Hua) 10g, and Cortex Lycii (Di Gu Pi) 15g. The herbs were decocted with water for oral administration. Magnetic therapy 4 times a week and deep hyperthermia 3 times a week were provided alternately, and medical ozone therapy once daily. Intravenous nutrition supplement combined with herbal cuisine for body conditioning.

Treatment outcome: The patient stayed as an inpatient for 41 days. The patient was in improved spirit and her chest tightness and limb numbness subsided. No complaint of dizziness, headache, cough or shortness of breath. Appetite and sleep were good. Urination and bowel movement were normal. Physical examination revealed unremarkable findings. The patient returns for periodic outpatient follow-ups and her illness is under control.

The patient has been living with lung cancer for 5 years. Currently, the patient has a stable quality of life and has almost recovered.

Mouth Cancer

L11, male, 65 years old.

He was admitted with “pain of left-sided tongue for 3 months” on August 29, 2009.

The patient presented with unexplained pain on left side of the tongue in the last third of May, 2009. He took some medications by himself (detail unknown) but gained no improvement. Later, as the pain intensified, he went to a hospital and underwent a biopsy for tongue neoplasm, which disclosed well-differentiated squamous cell carcinoma (on dorsum of the tongue). Consultants suggested surgical resection of half of the tongue and part of the mandible and stated that speech and swallowing would be badly affected after surgery. Therefore, he turned to Clifford Hospital for medical attention.

Physical examination: There was an about 3cm×1.5cm neoplasm at the margin of left root of tongue, about 0.3 cm protruding from the surface, with surface ulceration and tenderness.

Assistant examination: Blood count, liver and renal function tests were basically normal. A CT scan of the neck and nasopharynx revealed pathological change of left tongue root, which suggested tongue cancer, together with the pathology report. Lingual tonsils enlarged. Multiple small lymph nodes were noted in level II, III of bilateral neck. Abnormal calcification was detected under the skin of the lateral part of the right parotid gland.

Diagnosis: Well-differentiated squamous cell carcinoma of the tongue.

Integrative treatment plan: The oncologist team reviewed the case and developed an integrative treatment plan including cryoablation surgery, radiotherapy, chemotherapy, local hyperthermia, chelation, medical ozone and TCM therapy. The patient underwent a cryoablation for tongue cancer under general anesthesia with tracheal intubation on September 4, 2009. TP (Paclitaxel, cisplatin) whole body chemotherapy started in October, 2009, in addition to local hyperthermia, chelation, major ozonated autohemotherapy, TCM and acupuncture therapy.

The patient’s tongue was dark in color with white coating. His pulse was wiry and rapid. According to the traditional Chinese medicine (TCM) syndrome differentiation, it was Qi deficiency and blood stasis. Therefore, TCM treatment was mainly to tonify the spleen and Qi, promote blood circulation and remove stasis. Prescription were as follows: Rhizoma Atractylodis Macrocephalae (Bai Zhu) 30g, Poria (Fu Ling) 30g, Radix Glycyrrhizae Preparata (Zhi Gan Cao) 6g, Rhizoma Alismatis (Ze Xie) 30g, Ramulus Cinnamomi (Gui Zhi)6g, Fructus Perillae (Zi Su Zi)15g, Spica Prunellae (Xia Ku Cao)15g, Semen Vaccariae (Wan Bu Liu Xing)30g, Herba Hedyotis Diffusae (Bai Hua She She Cao)30g, Herba Scutellariae Barbatae (Ban Zhi Lian)15g, Herba Agrimoniae (Xian He Cao)30g, Herba Lophatheri (Dan Zhu Ye)10g, Medulla Junci (Deng Xin Cao)10 sheaves, Radix Rehmanniae (Sheng Di Huang)15g, Herba Menthae Haplocalycis (Bo He)6g. The TMC was one dose daily for oral administration and should be decocted with water.

In acupuncture therapy, the following acupuncture points were selected: LI 11, LI 4, P 6, ST 36, SP 9, SP 6, KD 3, LR 3, KD 6 and Outer Three Passes (Waisanguan). Method: An “evenly reinforcing and reducing” method was adapted, with the needles remaining in the acupuncture points for 20 minutes. The therapy was applied once daily and 5 days weekly, followed by a 2-day rest.

Moxibustion therapy: Acupuncture points for moxibustion: CV 4, RN 6, RN 8, ST 36. Two of the above mentioned points were selected for moxa roll moxibustion and the therapy in each point lasted for 10 minutes. The moxibustion was employed once daily and for 5 days a week, followed by a 2-day rest.

Auricular therapy: Acupuncture points selected were as following: CO 13, CO 1, CO 10, CO 12, CO 18, AT 4, AH 6a, HX 6 7i, and TG2P. Method: auricular therapy alternated once a week between two ears. Cowherb Seeds were applied to the auricular points and the patient was instructed to press each acupoint 3 to 5 times per day, with each press lasting for 3 to 5 minutes. After 2 cycles of chemotherapy, the tumor shrank significantly.

Radiotherapy started on December 12, 2009, with a total dose of 50 Gy. Local hyperthermia and chelation therapy were included once every other day. TCM and acupuncture therapy remained unchanged.

After the radiotherapy, chemotherapy continued to the fourth cycle, followed by the whole-body moderate & low temperature hyperthermia and chelation therapy in the next day, as well as EBOO once the other day. During the chemotherapy, TCM and acupuncture still continued.

According to traditional Chinese medicine, blood and toxins stagnated in the patient's body. Thus TCM treatment was based on promoting blood circulation, removing stasis and toxins: Fructus Perillae (Zi Su Zi)15g, Concha Ostreae (Mu Li)30g, Spica Prunellae (Xia Ku Cao)30g, Semen Vaccariae (Wan Bu Liu Xing)30g, Herba Hedyotis Diffusae (Bai Hua She She Cao)30g, Herba Scutellariae Barbatae (Ban Zhi Lian)15g, Herba Houttuyniae (Yu Xing Cao)30g, Cortex Lycii (Di Gu Pi)30g, Rhizoma Belamcandae (Shen Gan)10g, Rhizoma Paridis (Chong Lou)10g. The TCM was one dose daily for oral administration and should be decocted with water. Acupuncture therapy continued as before.

After the treatment, the tumor disappeared. After discharge, the patient still kept treatment at Outpatient Department, including local hyperthermia, chelation, medical ozone, TCM and acupuncture therapies.

Since admission, the patient had received psychotherapy to boost the confidence against cancer. He also learned medical Qigong and exercises to improve self-healing.

Treatment outcome: The patient was admitted intermittently. He underwent chemotherapy at Inpatient Department and radiotherapy at Outpatient Department. In total, he received 4 whole body moderate & low temperature hyperthermia, 60 local hyperthermia, 55 chelation therapy and 20 EBOO. By these treatments, tumor of the tongue disappeared and the tongue returned to normal activity and clear speech. Tongue and oral ulcer once occurred, but was relieved after symptomatic treatment. Since then, the patient kept integrative treatment once a month at Outpatient Department and underwent follow-up examination every 3 months.

The patient has survived for 7 years and currently has a good quality of life.

Nasopharyngeal Cancer

L12, aged 39.

The patient was admitted on February 4, 2007, due to status post radiotherapy and chemotherapy of nasopharyngeal cancer for over 2 years. A lump was found below the left jaw in October, 2004 accompanied by enlargement of cervical lymph nodes and he was diagnosed with poorly differentiated nasopharyngeal squamous carcinoma with bone metastasis, stage IV. He had received radical radiotherapy and 6 cycles of chemotherapy.

Conditions on admission: He presented with headache, thirst, dry throat, swollen and painful gums, swollen and aching cheeks, hearing loss, tiredness and poor appetite.

Physical examination: Weight was 46kg. General conditions were bad and he looked emaciated. Superficial lymph nodes were not enlarged. Heart, lungs, liver and spleen were unremarkable. Cervical skin was stiff due to radiation injury. Left-sided hearing loss was noted. Tongue was red with thin coating. Pulse was weak and rapid. KPS was 70.

Assistant examinations: An ECT revealed nasopharyngeal cancer with metastasis to skull.

Diagnosis: Relapse of nasopharyngeal cancer with metastasis to bone after radiotherapy and chemotherapy

Integrative treatment plan: After admission, the patient was given intravenous nutritional supplement, acupuncture and traditional Chinese medicine in the frequency of once per day; medical ozone therapy and local hyperthermia every other day. Symptoms such as headache, poor spirit and appetite were relieved after one week treatment. Two courses of TP chemotherapy plan were administered. In each course of chemotherapy, one systemic moderate-low temperature hyperthermia was given and local hyperthermia every other day but stopped 3 days before and

after systemic one. Following 2 courses of chemotherapy, there were totally 35 sessions of radiotherapy and 21 sessions of local hyperthermia (every other day), and then TP chemotherapy plan + systemic hyperthermia + local hyperthermia were adopted again for 4 courses.

Chinese medicine and acupuncture therapy were given along with chemotherapy. Red tongue with thin coating and weak and rapid pulse acted as symptom of deficiency of qi and yin, Sheng Mai San was adopted for tonifying qi and yin, and detoxifying and dispersing mass.

The prescription as follows:

radix psuedostellariae (Tai Zi Shen) 15g	Lilyturf root (Mai Dong) 15g
Schisandra fruit (Wu Wei Zi) 12g	Prepared pinellia (Fa Ban Xia) 12g
Arisaema cum bile (Dan Nan Xing) 12g	Rhizoma pleionis (Shan Ci Gu) 15g
Agrimonia pilosa (Xian He Cao) 30g	Cortex Moutan (Dan Pi) 10g
Herba Selaginellae Doederleinii (Shi Shang Bai) 12g	
Fructus gardeniae (Zhi Zi) 10g	Fructus Xanthii (Cang Er Zi) 15g
Flos magnoliae (Xin Yi Hua) 10g	

One dose of the above herbs was decocted with water for oral administration once daily.

With principle of detoxifying and dispersing mass, acupuncture was applied to the acupoints (LI 4, LI 11, ST 36, DU4, DU 20, LI 20, GB 2, KI 3, BL 13, and Wai San Guan) with neutral supplementation and draining. The needle retained for 20 minutes, and 2-day interval after 5 sessions. Moxibustion was applied to 2 acupoints among ST 36, RN4, DU4, BL20, RN8, BL23 for 10 minutes respectively in the frequency of once per day and a 2-day interval after 5 session. Auriculotherapy alternated weekly between two ears. Auricular points included TG4, TG1,2i, TG3, AH6a, AT1.AT2, TG2p and CO14. Method: Cowherb Seeds were applied to auricular points and the patient was instructed to press them 3 to 5 times per day.

Treatment outcome: The patient received intermittent inpatient treatment for 6 months. At admission, general conditions were poor accompanied with poor appetite, headache and tired looking, therefore, treatment were mainly to improve symptoms and malnutrition. Medical ozone therapy and chelation therapy started at a low dose or basic dose and increased gradually until symptoms like headache and weakness were relieved. Radiotherapy and chemotherapy were given in combination with traditional Chinese medicine, chelation therapy, medical ozone therapy, systemic hyperthermia and local hyperthermia. Such a combination helped achieve anti-tumor efficacy and reduce side-effects of radiotherapy and chemotherapy. Two months of treatment led to disappearance of dry mouth and swollen gum, hearing improvement, 3kg of weight gain. KPS was 90.

He stayed on oral traditional Chinese medicine after discharge. He returned for 3 days of non-toxic integrative cancer treatments every 2 weeks, with the frequency changed to every month from the 3rd month of discharge. A follow-up CT scan 7 months after discharge revealed the lesion disappeared basically, while ECT indicated bone metastasis remained similar to the prior finding and no new lesion. The patient complied with periodic follow-ups, with stable conditions. There is no sign of recurrence or new metastasis in follow-up examinations.

The patient has lived for more than 10 years since diagnosis with cancer, and he has recovered.

Nasopharynx Cancer

Y3, male, 54 years old.

The patient noticed a firm, painless mass in left neck in May, 2013, without redness, swelling or fever. At that time he underwent a CT scan in Clifford Hospital, which was suggestive of "left-sided nasopharynx cancer with metastases to lymph nodes and bone". Subsequently he was transferred to Guangdong No.2 Provincial People's Hospital where he was given 35 sessions of radiotherapy (70 GY in total and 2 GY per session) and 6 cycles of chemotherapy with "Paclitaxel" and " Cisplatin" (specific dosages unknown). After the radiotherapy and

chemotherapy, the patient experienced dry mouth, foreign body sensation of the mouth, and suppuration in left auditory canal. He paid a few visits to our hospital for such symptoms and was diagnosed with radioactive otitis externa and radioactive otitis. He was provided with non-toxic integrative treatment and was discharged after improvement. He had a history of smoking and alcohol consumption.

Conditions on admission: The patient was alert and conscious, but looked tired. He experienced slight weakness and dry mouth, but denied dizziness, headache, fever, or chills. There was no chest tightness, shortness of breath, nausea or vomiting. Appetite, sleep, urination and bowel movement were normal. No significant weight loss was noted recently. Physical examination revealed normal findings.

Assistant examination: Head, chest and abdomen CT scan and bone ECT scan (May, 2013) were suggestive of "left nasopharynx cancer with metastases to lymph nodes and bone".

Diagnosis: Status post radiotherapy and chemotherapy for nasopharynx cancer

Integrative treatment plan:

Non-toxic integrative treatments: Chelation every other day; hyperthermia therapy every other day; Medical ozone treatment once per day; magneto-electric biofeedback therapy once per day.

TCM treatment: As the patient was a middle-aged man, his healthy Qi gradually declined due to aging, making the body vulnerable to external pathogens and toxins. Given the patient had been a chronic smoker, the external toxin and pathogen invaded his channels and collaterals, leading to lung collateral obstruction and further lung Qi blockage. Since the Qi passage was blocked, the external pathologic fire would reach the nose through Taiyin meridian. It could retain in nose and pharynx and finally form a tumor.

As pointed out in *Yi Xue Zhun Sheng Liu Yao* (《医学准绳六要》), "Like drinkers or those from wealthy family, they always prefer overly spicy, irritable, or roasted food, which makes the pathologic fire flame upward to and stuff in the nasal orifice. Consequently, turbid discharge pours out like the flowing spring water and gradually turns into a nosebleed. That is caused by long-term heat accumulation in Shang Jiao (including lungs and heart)." The patient's disease is located in nasopharynx, the breathing passage, which is closely related to the lungs. The lungs govern Qi, manage breathing and open at nose.

Because of long-term smoking, drinking and chemotherapy as well, the patient's pathologic heat retained in lung (i.e. lung Yin was deficient), causing the diffusion failure of lung Qi and steaming of fire and heat. It led to the scorching of fluid-humor and that's the reason he presented with dry mouth, red tongue, white-thin tongue coating, and thready and rapid pulse. Therefore, he was treated by nourishing Yin and clearing lung heat and fire, and reinforcing the earth to generate metal (the theory of Yin and Yang and five elements). TCM medicine was given by a famous TCM physician according to syndrome differentiation and dietary instruction by Dietetics.

Treatment outcome:

CT scan of nasopharynx and chest performed on August 30, 2014 showed post-chemotherapy (for nasopharynx cancer) changes:

1. Damage to clivus of occipital bone;
2. Thickened membranes of bilateral maxillary, ethmoidal, and sphenoid sinuses;
3. Fluid buildup in left mastoid cells.

The result was basically the same as that of June 1, 2014.

Bone ECT: Compared with the scan on September 2, 2014, no significant change was noted in previous locations of metastases. The follow-ups in the past 3 years showed no cancer recurrence and metastasis.

His follow-up check on July of 2016 revealed that he completely recovered from the cancer.

Now the patient's quality of life is scored 0, and he lives a normal life.

Paget's Disease of Penis

G3, aged 70.

The patient was admitted on February 23, 2014 due to status post operation of Paget's disease of penis for two and a half years. Penis base skin was rash without oozing or itch. Pathological analysis in Clifford Hospital reported Paget's disease of penis and then the patient received wide local resection of Paget's disease of penis and scrotal skin graft. The wound healed well. Postoperative pathological analysis reported Paget's disease of penis. But he did not undergo radiotherapy or chemotherapy after then. The patient returned for follow-ups in Clifford Hospital. History review was positive for cerebral infraction and left lower leg fracture.

Conditions on admission: The patient was alert and energetic. Appetite, urination and bowel movement were normal. He denied cough and shortness of breath. Skin of penis base was normal without rash, exudation or itch.

Physical examination: Well-healed surgical incision at the perineal region and graft site. Others were negative.

Assistant examinations: Pathology report revealed extramammary Paget's disease of penis base. Laboratory studies including complete blood count, urine test, stool test, liver function, kidney function, blood lipid, blood glucose and electrolyte were normal. Male tumor markers (6 items): CEA 5.58ng/ml, others were negative.

A color ultrasound scan of liver, gallbladder, pancreas and spleen was unremarkable.

A chest X-ray indicated increased lung markings and aortic arteriosclerosis, similar to the prior findings on March 26, 2013.

Pelvic MRI with contrast revealed postoperative changes related to wide local resection of lesion in Paget's disease of penis and scrotal skin graft without recurrence or metastasis, similar to the findings on March 26, 2013. Prostate hyperplasia was considered.

Diagnosis: Status post operation of Paget's disease of penis

Integrative treatment plan: Chelation (30g) for improving metabolism was given on every Tuesday, Thursday and Saturday; hyperthermia for improving circulation and immunity on every Tuesday, Thursday and Saturday; and intravenous medical ozone every day to improve immunity.

On TCM theory, the disease is named as Shenyan (pennis carcinoma). Yin deficiency of liver and kidney results in disturbance of ministerial fire, kidney's failure to nourish liver, and blood dryness at the liver channels. As liver channels surround external genitals and are impaired over time, Yin essence diminishes. Collaterals turn void and defenseless and cause damp toxins of liver downward, stagnation of pathogenic fire, and burning fluid into phlegm. Therefore, all these pathological factors build up in penis, resulting in carcinoma of penis.

According to differential diagnosis of TCM, it was everted flower-like Shenyan (carcinoma of penis), and the syndrome was downward of damp-heat. San Miao Wan was administered with therapeutic principle of clearing away heat and promoting dampness based on symptoms.

Treatment outcome: The patient continues non-toxic integrative cancer treatment in inpatient dept. since operation performed in 2011. No tumor recurrence or metastasis could be found in the follow-up examinations. The patient currently lives a normal life.

Pancreatic Cancer

L13, 83 years old.

The patient was admitted on September 4, 2007 due to status post operation of pancreatic cancer for one year and abdominal pain accompanied with poor appetite and emaciation for over 2 months. A CT scan revealed a mass of 5.7cm×3.6cm×4cm in the tail of pancreas in Toronto Hospital, Canada in September, 2006. He underwent partial pancreatectomy in a hospital in

Canada, during which multiple enlarged lymph nodes in the abdominal cavity could be found and gastric wall was involved. But he did not receive any treatment after surgery. A follow-up CT scan 6 months ago revealed abnormal growths around left renal artery and multiple intrahepatic metastases. The patient presented with recurrent dull abdominal pain accompanied with significant poor appetite and emaciation, and weight loss of 8kg since July, 2007. Therefore, he came to Clifford Hospital for treatment from Canada.

Physical examination: Body weight was 48kg. Surgical scar was at the upper abdomen. A protruding hard and ill-defined bulge in local upper abdomen was tender. Respiratory sounds bilaterally were clear, without dry or moist rales. Cardiac dullness was normal. HR was 60bpm. Heart rhythm was normal, without pathological murmurs at valves. KPS was 50.

Assistant examination:

Complete blood count: RBC $3.1\times 10^{12}/L$, Hb103g/L, WBC $4.7\times 10^9/L$, PLT $235\times 10^9/L$;

Biochemistry: ALT 125U/L, AST 87U/L, TBIL 32U/L, DBIL 15.5U/L, ALB 16.8g/L; ALP 312U/L, GGT 127U/L, Cr 8umol/L, Ua 313umol/L, BUN 3.6mmol/L, GLU 6.62mmol/L, TG 0.17mmol/L, GHO 1.65mmol/L, K⁺ 3.64mmol/L, Na⁺ 139mmol/L, Cl⁻ 99mmol/L, Ca²⁺ 2.21mmol/L;

Serum ammonia: 21umol/L;

Tumor markers: CEA 127.6ng/ml, AFP 9.09ng/ml, CA12-5(OV) 13.72U/ml, CA-199 47.14U/ml, PSA 3.1U/ml;

Immunological test (5 items) and micro-elements of Cu, Zn, Pb, Cd and Ni were normal.

Abdominal CT scan revealed a mass of 3cm \times 2cm in the tail of pancreas accompanied with abdominal wall, intrahepatic, abdominal and retroperitoneal lymph nodes enlargement. ECG and chest X-ray were negative.

Diagnosis: Status post operation of pancreatic cancer with recurrence and metastases to lymph nodes and liver.

Integrative treatment plan: The patient's admission symptoms mainly presented as poor appetite and emaciation. He also had pain but was in good spirits. For this, the symptoms were treated with supplement of pancreatin and herbal cuisine supplement of lipase and amino acid to improve nutrition. Meanwhile, anti-tumor treatment included general moderate hyperthermia and chelation therapy alternately with EBOO. Traditional Chinese medicine was used to soothe liver, regulate vital energy, resolve dampness and disperse stasis. The prescription included Radix Bupleuri (Chai Hu) 10g, Radix Paeoniae Alba (Bai Shao) 20g, Fructus Aurantii (Zhi Ke) 15g, Herba Pogostemonis (Guang Huo Xiang) 10g, Mangnolia officinalis (Hou Pu) 10g, Rhizoma Pinelliae Praeparata (Fa Ban Xia) 10g, Fructus Amomi Rotundus (Bai Dou Kou) 10g, Caulis Bambusae in Taeniam (Zhu Ru) 10g, Herba Eupatorii (Pei Lan) 10g, Radix Platycodi (Jie Geng) 6g, Semen Arecae (Bing Lang) 6g, Haematitum (Dai Zhe Shi) 20g, Dens Draconis (Long Chi) 30g, Rhizoma Corydalis (Yuan Hu) 10g, and Radix Glycyrrhizae Preparata (Zhi Gan Cao) 6g. One dose of the above herbs was decocted with water for oral administration once daily.

During treatment, the patient complained of stomach and abdominal pain, dry mouth, hiccups, weakness and constipation. Tongue was red with less fluid, and pulse was thready and weak. Herbal medicine was changed for liver-dredging and stasis-dispersing. The prescription included Radix Glehniae (Bei Sha Shen) 15g, Radix Ophiopogonis (Mai Dong) 15g, Radix Trichosanthis (Tian Hua Fen) 12g, Fructus Toosendan (Chuan Lian Zi) 10g, Rhizoma Anemarrhenae (Zhi Mu) 10g, Cortex Lycii (Di Gu Pi) 12g, Carapax Trionycis (Bie Jia) 12g, Colla Corii Asini (E Jiao) 12g, Fructus Polygoni Orientalis (Shui Hong Hua Zi) 12g, Semen Persicae (Tao Ren) 12g, Curcuma Zedoary (E Zhu) 10g, Radix Paeoniae Rubra (Chi Shao) 10g, Herba Hedyotidis Diffusae (Bai Hua She She Cao) 30g, Radix et Rhizoma Rhei Preparata (Zhi Da Huang) 6g, and Radix Glycyrrhizae (Gan Cao) 3g. One dose of the above herbs was decocted with water for oral administration twice daily.

And treatment plan of chelation therapy was changed to every other day with increased dosage. Traditional Chinese medicine named "Pei Yuan Decoction" was administered one dose orally every day. Proper exercise was recommended, preferably no sweating.

Treatment with acupuncture: Acupoints including ST 36, ST 37, SP 6, RN 12, ST 25, BL 20, BL 23, RN 4 were selected for acupuncture with equal tonifying and purging needling method, with the needle remained for 20minutes, once a day, and a 2-day interval after 5 needling sessions. Moxibustion was applied to the following points: RN 4, ST 36, BL 23 and BL 20. Methods: Each session was applied to 2 points for 10 minutes respectively in the frequency of once a day and a 2-day interval after 5 sessions. Auriculotherapy alternated once a week between two ears, applied to CO12, CO13, diaphragm, CO11, HX6,7, TG2p, AT4, AH6a.

Treatment outcome: After 45 days of non-toxic integrative cancer treatment. the patient had better spirits, relieved pain and normal appetite. His weight increased to 56kg. His quality of life improved to the extent that allowed him to do recreational activities, with a KPS of 90. At the second month of hospital stay, a follow-up CT scan of abdomen revealed: no recurrent lesion in the residual pancreatic head; intrahepatic hypo-attenuation lesions increased in number but decreased in size comparing to the prior study at admission. The patient continued outpatient treatments including chelation therapy twice weekly, ozone therapy and local hyperthermia on a weekly basis. A CT scan of the abdomen 5 months later revealed status postoperative change of pancreatic cancer with liver metastasis, and a decrease in the number and size of intrahepatic lesions. Complete blood count was normal. Liver function showed ALP of 135U/L, r-GT of 99U/L. Tumor markers showed CEA of 37.5ng/ml, CA-199 of 21.03U/ml. Other test results were negative. The patient lived normal life without discomfort and continued outpatient treatment per week.

The patient died of pancreatic cancer in September, 2009.

Prostate Cancer

T2, 78-year-old

A health checkup indicated elevated PSA level in April, 2009. A prostate biopsy done in a hospital of New Zealand revealed prostate cancer without metastasis, stage T1. He did not receive any treatment. In July, 2017, a PSA test in outpatient dept. of the Second Affiliated Hospital of Sun Yat-sen University showed T-PSA 9.210ug/L and F-PSA 1.490ug/L. Bilateral orchiectomy was performed and endocrine therapy was adopted after operation. Follow-ups showed a gradual increase in PSA level. History review was positive for hypertension and diabetes. The patient was admitted to Clifford Hospital on July 14, 2016 due to frequent urination for over one month.

Conditions on admission: He was alert and in good spirit. He stated frequent urination, but denied urgent urination, dysuria, and hematuria, fever, abdominal pain. Appetite and sleep were good, and urination and bowel movement were normal. The tongue was light dark with greasy coating. The pulse was deep and thin. Others were unremarkable.

Assistant examinations:

A pelvic MRI with contrast in May, 2013 revealed hyperplasia of prostate and multiple nodules at peripheral zones of prostate, suggestive of prostate cancer. Seminal vesicles were probably involved and the right side had mild effusion. Small lymph nodes were noted at the right mesorectum.

A CT scan of the abdomen and pelvis in July 2014 indicated post-operative change of prostate cancer, abnormal oval signal intensity in the right seminal vesicle with possibility of protein-containing cyst and hematocele.

Bone imaging showed possibly degenerative disease of lumbar spine.

Gastroendoscopy indicated chronic erosive gastritis, chronic enteritis and internal hemorrhoid.

Diagnoses:

1. Status post operation of prostate cancer;
2. Chronic gastritis;
3. Type 2 diabetes mellitus;

4. Grade 1 hypertension

Integrative treatment plan: Integrative treatment included deep hyperthermia of abdomen once every other day, EBOO and electro-magnetic biofeedback therapy once daily respectively.

On TCM theory, the senile and physically weak patient presented with hypofunction of spleen and stomach resulting in dampness accumulation and phlegm production. Meanwhile, obstruction of phlegm and stasis to bladder due to enduring illness induced bladder dysfunction, which was the cause of frequent urination. Tongue and pulse formed this evidence. At admission, the mainly symptom differentiation was obstruction of phlegm and stasis and treatment focused on activating blood, dispersing stasis, strengthening spleen and removing phlegm.

From July 14, 2014 to July 16, 2014, with a treatment principle of activating blood, dispersing stasis, strengthening spleen and removing phlegm, 3 doses of “Tao Hong Si Wu Tang” were administered. The detailed prescription included Semen Persicae (Tao Ren) 10g, Flos Carthami (Hong Hua) 10g, Radix Rehmanniae Preparata (Shu Di Huang) 15g, Radix Paeoniae Alba (Shao Yao) 10g, Radix Angelicae Sinensis (Dang Gui) 10g, Rhizoma Chuanxiong (Chuang Xiong) 10g, Rhizoma Pinelliae (Ban Xia) 10g, Mangnolia officinalis (Hou Pu) 10g, and Atractylodes Macrocephala (Bai Zhu) 10g. One dose of the listed herbs was decocted with water for oral administration once daily before meals.

Six doses of “Bu Zhong Yi Qi Tang” were administered in a principle of invigorating stomach-spleen and replenishing qi. The prescription included Radix Astragali (Huang Qi) 30g, Rhizoma Atractylodis Macrocephalae (Bai Zhu) 30g, Pericarpium Citri Reticulatae (Chen Pi) 10g, Rhizoma Cimicifugae (Sheng Ma) 6g, Radix Bupleuri (Chai Hu) 6g, Radix Codonopsis (Dang Shen) 15g, Radix Glycyrrhizae Preparata (Zhi Gan Cao) 6g, Radix Angelicae Sinensis (Dang Gui) 6g, Radix Ophiopogonis (Mai Dong) 10g, Fructus Schisandrae (Wu Wei Zi) 10g, Agrimonia pilosa (Xian He Cao) 30g, and Fructus Corni (Shan Yu Rou) 30g. One dose of the listed herbs was decocted with water for oral administration in warm temperature once daily after meals.

Treatment outcome: General conditions had improved significantly after 18 days inpatient treatment. Follow-up tumor markers test demonstrated CEA 4.11 ng/ml , AFP 3.34 ng/ml , CA15-3 12.00 U/ml , CA19-9 0.84U/ml , T-PSA 0.04ng/ml , F-PSA 0.01ug/ml , and F-PSA/T-PSA 0.25. No significant elevation of tumor markers could be found in follow-up tests done in outpatient dept.

The patient has been living for over 7 years since diagnosis with cancer, and he has recovered.

Y4, male, 80 years old.

The patient was admitted with status post prostate cancer surgery for over 6 years, status post repeated chemotherapy, lymphatic metastasis for 1.5 years, and bone metastasis found for 1 week on December 21, 2012. The patient received a checkup in New Zealand 1 week prior to admission, which revealed bone metastasis with significant pain. He did not respond well to analgesic therapy provided. He then presented to Clifford Hospital for continuous care. History review was positive for hypertension and surgery of right lower extremity varicosity.

Conditions on admission: The patient was alert and oriented and experienced swelling pain (score 5) of the waist which intensified and disturbed sleep during the night. His appetite and defecation were normal, but he suffered frequent urination. He denied painful or bloody urine, or recent weight loss. The tongue was light red without coating. The pulse was thready and uneven. Physical examination revealed unremarkable findings.

Assistant examinations:

1. Tumor markers: TPSA: 107.20ng/ml and Free-PSA: 35.33ng/ml. Remaining tumor markers were normal.

2. Color ultrasound of the heart: Left ventricular size in high normal range; luminal diameter of ascending aorta widened; slightly thickened interventricular septum; decreased diastolic function of left ventricle; these findings were supportive of hypertensive heart change. There was

evidence of mild regurgitation of aortic and mitral valves. It was free of abnormal segmental ventricular wall motion at rest. Normal systolic function in the left ventricle was noted.

3. Whole body bone imaging: Whole-body skeletons were clearly imaged. Significant radiotracer uptake was noted in bilateral kidneys, especially the right one. Bladder was not displayed. Posterior image revealed increased uptake in vertebrae L 3, 4 and 5 and sacrococcygeal vertebrae. There was slightly increased radionuclide uptake in upper end of right femur. There was no other radionuclide distribution anomaly. Increased bone metabolism was noted at locations mentioned above. It was suggestive of multiple bone metastases (suspected upper end of right femur).

4. Coronary CT angiography: There were evidences of multiple calcifications of left main coronary artery, left anterior descending artery, left circumflex artery and diagonal branch. There was a sign of soft plaque formation of upper segment of left anterior descending with moderate luminal stenosis. Myocardial bridge of middle segment of left anterior descending was noted. Aortosclerosis and multiple hepatic cysts were seen.

5. Lumbar MRI: Lumbar degeneration. L4/5 disc herniation. By correlating to past history, it was supportive of prostate cancer with multiple metastases to L3, 4 and 5 vertebrae. There was a significant dilation of right renal pelvis and ureter with fluid buildup. Thickening of bladder wall was noted.

6. Transrectal color ultrasound of the prostate: Status post prostatectomy: a nodule in residual prostate with rich blood flow and PSA test suggested. Bladder wall was coarse.

7. Gastroscopy: Multiple gastric polyps (already resected), erosive duodenitis and erosive gastritis.

Diagnoses: 1. Status post chemotherapy after prostate cancer surgery, with lymphatic and bone metastases. 2. Grade 1 hypertension (medium risk group). 3. Status post right lower extremity varicosity surgery. 4. Formation of bilateral lower limb thrombosis. 5. Multiple gastric polyps. 6. Erosive duodenitis. 7. Erosive gastritis. 8. Chronic colitis. 9. Intestinal polyp. 10. Internal hemorrhoid.

Integrative treatment plan: D3 and Zoledronic acid were administered for relieving pain and Sr89 was suspended. Besides such therapies, non-toxic integrative cancer treatments were provided, including Chinese medicine, acupuncture, chelation, hyperthermia, and medical ozone. TCM treatment: As the patient suffered deficiency of both blood and Qi and blood stasis, TCM treatment focused on boosting healthy Qi and tonifying kidney, and promoting blood and qi circulation for analgesia. Prescribed Chinese herbs included Rhizoma Sparganii (San Leng) 20 g, Curcuma Zedoary (E Zhu) 20 g, Fructus Aurantii Immaturus (Zhi Shi) 20 g, Rhizoma Atractylodis Macrocephalae (Bai Zhu) 20 g, Mangnolia officinalis (Hou Po) 20 g, Parched Hawthorn Fruit (Jiao Shan Zha) 20 g, Scorched Germonater Barley (Jiao Mai Ya) 20 g, stir-baked Massa Fermentata Medici-Nalis (Jiao Shen Qu) 20 g, Rhizoma Alpiniae Officinarum (Gao Liang Jiang) 20 g, Semen Raphani (Lai Fu Zi) 20 g, Fructus Tsaoko (Cao Guo) 20 g, Radix Aucklandiae (Mu Xiang) 20 g, Fructus Amomi (Sha Ren) 20 g, Ramulus Cinnamomi (Gui Zhi) 10 g, Poria (Fu Ling) 30 g, Grifola (Zhu Ling) 30 g, and Rhizoma Alismatis (Ze Xie) 30g. Chinese medicine foot bath was ordered for promoting blood circulation to remove meridian obstruction and stopping pain and promoting diuresis. Prescribed herbs included Radix Angelicae Sinensis (Dang Gui) 50 g, Radix Rehmanniae Preparata (Shu Di Huang) 50 g, Radix Paeoniae Alba (Bai Shao) 50 g, Rhizoma Chuanxiong (Chuan Xiong) 50 g, Poria (Fu Ling) 50 g, Rhizoma Atractylodis Macrocephalae (Bai Zhu) 50 g, Grifola (Zhu Ling) 50 g, and Radix Achyranthis Bidentatae(Niu Xi) 50 g. Acupuncture was administered in the principle of neutral supplementation and draining, with the needle retained for 20 minutes, once a day, and 2-day interval after 5 needling sessions. Each session of moxibustion was applied to 2 acupoints for 10 minutes respectively in the frequency of once a day and a 2-day interval after 5 sessions. Auricular acupoints for auriculotherapy included CO14, AH10, AT4, TF4, CO16, CO18, and AH6a. Method: Auriculotherapy alternated weekly between two ears. Cowherb Seeds were applied to auricular points and the patient was instructed to each acupoint 3 to 5 times per day, with each press lasting for 3 to 5 minutes. Shenqi Yiqi Injection and parenteral nutrition were administered in combination. Lumbar hyperthermia twice a week together

with chelation was given. Medical ozone therapy was used as well. The patient stayed as an inpatient for 1 month and was discharged with an improvement in his conditions. He returned for inpatient care in one week after discharge.

Treatment outcome: During hospital stay for 2 months, his lumbar pain, gastric bloating, and bilateral lower extremity edema subsided. He received one course of treatment before discharge. The patient complied with outpatient and inpatient follow-ups. Based on the 3-year follow-up, his quality of life was good.

In January 2016, the patient died of acute myocardial infarction in New Zealand.

Pulmonary fibrosis

C2, male, 53 years old.

Hong Kong resident, who had pulmonary fibrosis for about 5 years. He was predicted by a Hong Kong hospital with only 5 years of life left. When he came to our Hospital, it was his fifth year. After about 70 sessions of wholebody mild-high infrared hyperthermia in 2 years, his pulmonary function obviously improved. He could swim only 50 meters before, but now 1,000 meters, bicycle riding was only half an hour before, but now 3 hours. He had bad sleep before due to irritable cough, but now sleeping well. Now, patient is in good condition and leads a normal life and work.

Skin Cancer

L14, male, 45 years old.

He had received chemotherapy for 5 months after surgery due to left-sided scrotum skin cancer and was admitted to Clifford Hospital with “paroxysmal abdominal pain for 20 days” on December 22, 2007.

The patient experienced external scrotum itching in July, 2007. He scratched and accidentally broke the skin, causing repeated, unhealed ulcer. He went to Queen Mary Hospital and underwent an excision of local skin. Pathology analysis result was consistent with “eccrine carcinoma of the skin, Ki-67 (+)”. An abdominal MRI revealed metastasis to multiple lymph nodes in the abdominal cavity. The patient received chemotherapy with paclitaxel, cisplatin, methotrexate, and gemcitabine hydrochloride, etc (detailed regimen unknown) as well as tamoxifen.

An abdominal MRI in October, 2007 revealed multiple enlarged lymph nodes in bilateral groins, retroperitoneum and abdominal cavity. The patient experienced paroxysmal abdominal pain, accompanied by shortness of breath, weakness, sweating and mild edema in the right lower limb. Therefore he was admitted to Clifford Hospital for further treatment.

Physical examination: Multiple enlarged lymph nodes of about 2cm×3cm were palpated in bilateral groins. Part of them adhered with each other, with hard texture, limited mobility and mild tenderness. Mild edema was noted in the right lower limb. Karnofsky score was 80.

Assistant examination:

Abdominal CT after admission: Multiple enlarged lymph nodes were noted in bilateral groins, retroperitoneum and abdominal cavity, suggestive of skin cancer with lymphatic metastasis.

Biochemistry study: ALT 38U/L, AST 25U/L, TBIL 26U/L, DBIL 14.5U/L, ALB 38g/L; ALP 53U/L, GGT 321U/L, Cr 56umol/L, Ua 235umol/L, BUN 6.2mmol/L, GLU 4.31mmol/L.

Electrolytes and blood lipid tests were normal.

Tumor markers: CEA 6.1ng/ml, AFP 5.6ng/ml, CA-12 54U/ml, CA-15 33.8U/ml, CA19-9 13ml/L, TSGF 11.2U/ml.

Immunology (5 items): IgM (immune globulin) 0.7g/L, and others were normal.

Trace elements test was normal.

Diagnosis: Eccrine carcinoma of the scrotal skin, status post surgery and chemotherapy, stage III (metastasis to lymph nodes in the groins, retroperitoneum and abdominal cavity).

Integrative treatment plan: The patient was diagnosed with eccrine carcinoma of the scrotal skin, which is a rare case without established treatment plan. Metastasis to abdominal lymph nodes had been noted when the patient first visited Queen Mary Hospital. The primary lesion was removed, followed by treatment with multiple chemotherapy agents. As it was eccrine carcinoma, tamoxifen has also been provided for endocrinotherapy. Despite such therapies, the patient's condition remained uncontrollable. Because the patient was weak after many courses of chemotherapy, traditional Chinese medicine (TCM) and acupuncture were provided in Clifford Hospital.

The patient presented with weakness, shortness of breath, sweating, slight edema of the right lower limb, loose stool, light-red tongue, thin and white coating and slow-deep pulse, indicating deficiency of both Qi and blood. Tradition Chinese medicine was mainly to tonify Qi and blood, eliminate toxins and promote healing. Thus Shiquan Dabu Decoction was prescribed: Radix Ginseng (Ren Shen) 10g, Radix Rehmanniae Preparata (Shu Di) 12g, Rhizoma Atractylodis Macrocephalae (Bai Zhu) 15g, Poria (Fu Ling) 15g, Radix Angelicae Sinensis (Dang Gui) 10g, Radix Paeoniae Alba (Bai Shao) 15g, Rhizoma Ligustici Wallichii (Chuan Xiong) 10g, Radix Astragali (Huang Qi) 30g, Cortex Cinnamomi (Rou Gui) 5g, Radix Glycyrrhizae Preparata (Zhi Gan Cao) 10g, Rhizoma Zingiberis Recens (Sheng Jiang) 3 slices, and 8 Fructus Jujube (Da Zao). The TCM was administered one dose daily for oral administration and should be decocted with water.

Acupuncture therapy: The following acupoints were selected for the therapy: BL 13, LU 1, LU 9, ST 36, BL 20, BL 17, SP 9, ST 40, SP 10, BL 40, Spirit Bone (Linggu) and SP 3. The acupuncture adapted an "even reinforcing and reducing" method and the needles remained in the points for 20 minutes. The therapy was once daily for 5 days a week followed by a 2-day rest.

Moxibustion therapy: BL 20, BL 17, BL 13, CV 4 and ST 36 were selected for moxibustion therapy. Method: each session of moxibustion was applied to 2 acupoints for 10 minutes respectively in the frequency of once a day, and there was a 2-day interval after 5 sessions.

Auricular therapy: acupoints selected were as follows: AT 4, CO 15, HX 6 7i, AH 6a, CO 12, TF 4, SF1 Zi, TG2P and points that related to lesion region. The therapy was twice weekly and two ears were alternatively selected.

In addition, chelation therapy and intravenous medical ozone therapy were alternately applied, as well as right-sided groin local hyperthermia. One-week treatment alleviated pain in the patient's abdomen, shortness of breath and right lower limb edema. Whole-body moderate-high temperature hyperthermia therapy + intraperitoneal perfusion chemotherapy (with cisplatin and mitomycin) were applied totally 4 sessions. Before and after the treatment, routine pretreatment and symptomatic treatment were provided to prevent adverse reaction. During the interval of whole-body hyperthermia, local abdominal hyperthermia was also employed. In total, the patient had been hospitalized in Clifford Hospital for 50 days.

Treatment outcome: By the 50-day active therapy in Clifford Hospital, the patient's symptoms like abdominal pain, weakness, and sweating disappeared. Three lymph nodes of 1cm×2cm in size were palpated in bilateral groins, with medium texture and mobility but no tenderness. Karnofsky score was 90. Compared with previous findings, lymph nodes in the groins, retroperitoneum and abdominal cavity shrank significantly. Currently the patient complies a 5-day integrative treatment plan at Outpatient Department every 15 days. He is normal in appetite and sleep and has returned to his work in Hong Kong.

Stomach Cancer

D2, female, aged 56.

She was admitted to Clifford Hospital because of “one-year history of epigastric pain and melena, with one-week aggravation” on December 29, 2006.

In December 2005, the patient experienced unexplained epigastric pain and bloating pain, which were not radiating but intensified after eating or at night. She also complained of acid reflux, belching, heartburn and repeated melena but denied fever, nausea, vomiting or diarrhea. She took some Chinese medicine (unknown) but gained no improvement. One week before admission, the symptoms above were aggravated and then she presented to the Outpatient Department of Clifford Hospital for treatment. A gastroscopy and an abdominal CT scan revealed “stomach cancer, with multiple metastases to the right lobe of liver, pancreas, retroperitoneal lymph nodes and cancer thrombus of the main portal vein, left and right splenic veins, and superior mesenteric vein. Pathology result was consistent with “moderately differentiated gastric adenocarcinoma”. As the cancer was inoperable, she was admitted to Oncology Department in Clifford Hospital. The patient was general in spirits on admission, with poor appetite, poor sleep, normal urination, loose and tarry stools. She lost more than 10kg in the past 8 months.

Physical examination: The patient was emaciating, with a body weight of 37kg. She appeared moderately anemic and pale in whole body skin and mucus. Abdomen under xiphoid process was distended. An ill-defined mass of about 5cm×6cm×7cm was palpated. The mass was firm and hardly movable, with significant tenderness but no rebound tenderness. Slash sound was heard in the gastric cavity. Bowels sounds were active. Karnofsky score was 30.

Assistant examinations: An abdominal CT scan revealed soft tissue masses in the stomach body and antrum, accompanied by multiple metastases to the right lobe of liver, pancreas, and retroperitoneal lymph nodes, and cancer thrombus of the portal vein, left and right splenic veins, and superior mesenteric vein. Cavernous transformation of the portal vein and mild fluid buildup in the rectouterine pouch were noted. Pathology reported moderately differentiated gastric adenocarcinoma. Tumor markers (5 items): CEA: 1183.6ng/ml, AFP: 143.22ng/ml, CA199: 194.32U/ml.

Complete blood count: WBC $19.03 \times 10^9/L$, NEUT73.6%, RBC $3.19 \times 10^{12}/L$, HGB76g/L, HCT0.246.

Biochemistry study: ALT69U/L, AST78U/L, TP 65g/L, ALB31.3g/L, ALP157U/L, GGT231U/L, TBIL21.5umol/L, DBIt6.5umol/L, Cr 24umol/L, Ua144umol/L, BUN3.7mmol/L, GLU5.21mmol/L, TG1.11mmol/L, GHO3.42mmol/L, K⁺4.1mmol/L, Na⁺137mmol/L, Cl⁻97mmol/L, Ca²⁺1.78mmol/L.

Immunology test (5 items) and trace elements were basically normal.

Diagnosis: Stomach cancer (moderately differentiated adenocarcinoma, stage IV), accompanied by multiple lymphatic metastasis to the right lobe of liver, pancreas, and retroperitoneal lymph nodes, and cancer thrombus of the portal vein, left and right splenic veins, and superior mesenteric vein.

Integrative treatment plan: The patient was emaciating on admission. She was moderately anemic and physically weak. Therefore, blood transfusion was provided to reverse anemia; PTN to strengthen nutrition; acid inhibition and gastric mucosa protection to prevent bleeding. Traditional Chinese treatment: Huangqi Jianzhong Decoction + Lizhong Decoction was ordered and included the following herbs: Radix Astragali (Huang Qi) 20g, Rhizoma Zingiberis (Gan Jiang)10g, Poria (Fu Ling)12g, Radix Paeoniae Alba (Bai Shao)12g, Rhizoma Atractylodis Macrocephalae (Bai Zhu)12g, Rhizoma Pinelliae (Ban Xia)12g, Pericarpium Citri Reticulatae (Chen Pi)10g, Fructus Evodiae (Wu Zhu Yu)6g, Pericarpium Citri Reticulatae (Ju Pi)6g, Semen Coicis (Yi Yi Ren)30g, Radix Glycyrrhizae (Gan Cao)6g, Radix Notoginseng (Tian Qi)12g, Rhizoma Imperatae (Bai Mao Gen)12g, Fructus Oryzae Germinatus (Chao Gu Ya)12g & Fructus Hordei Germinatus (Chao Mai Ya)12g, Semen Cuscutae (Tu Si Zi)10g. The traditional Chinese medicine was taken one dose

daily and should be decocted with water for oral use. After 4-day treatment, a complete blood count showed HGB 93g/l and WBC $8.25 \times 10^9/l$. The patient denied significant abdominal pain and the digestive tract bleeding stopped. Stool was yellow and loose. She started the whole body moderate temperature hyperthermia combined with peritoneal perfusion with cisplatin + 5-FU. Granisetron was administered to prevent nausea before and after the treatment. Following the hyperthermia, chelation therapy was applied to reduce toxic side effects of chemotherapeutics and to promote chemotherapeutic sensitivity. As whole body hyperthermia tended to massive fluid loss, traditional Chinese medicine was mainly to tonify spleen, nourish Yin and supplement blood. Therefore Guipi Decoction and Danggui Buxue Decoction were prescribed: Poria (Fu Ling) 25g, Paricarpium Citri Reticulatae (Chen Pi) 15g, Radix Angelicae Sinensis (Dang Gui)10g, Radix Glycyrrhizae (Gan Cao)10g, Radix Glycyrrhizae Preparata (Zhi Gan Cao)10g, Radix Paeoniae Alba (Bai Shao)15g, Radix Ophiopogonis (Mai Dong)10g, Radix Codonopsis (Dang Shen)25g, Radix Salviae Miltiorrhizae (Dan Shen)10g, Rhizoma Atractylodis Macrocephalae (Bai Zhu)12g, Radix Rehmanniae (Sheng Di)25g, Rhizoma Dioscoreae (Shan Yao)25g, Radix Bupleuri (Chai Hu)10g, Radix Scutellariae (Huang Qin)10g. The herbs were prepared into water-bindered pills and the patient was instructed to take 10g each time and 3 times daily.

The patient presented with mild nausea after hyperthermia but there was no white blood cell decrease, diarrhea or abdominal pain. In acupuncture therapy, the following acupuncture points were selected: RN12, PC6, BL 21, LR 13, BL 20, SP 6, ST 36, BL 26, KD 3 and Outer Three Passes (Waisanguan). The acupuncture adapted a reinforcing method, and needles were inserted into the points and remained there for 20 minutes. This therapy was once daily, for 5 days a week, followed by a 2-day rest.

Moxibustion therapy: CV 4, RN 8, ST 36, RN 12, DU 14, BL 20 and BL 23 were selected for moxibustion therapy. Method: Two to three acupuncture points were selected each time for moxa roll moxibustion and the moxibustion for each point lasted for 10 minutes. The moxibustion therapy was applied once daily or once every other day.

Auricular therapy: Acupuncture points selected were as following: CO 4, CO 13, CO 12, AT 4, AH 6a, TF 4, AT 2 3 4i, CO 5, CO 18, TG2P and special tumor area. Method: auricular therapy alternated once a week between two ears. Cowherb Seeds were applied to the auricular points and the patient was instructed to press each acupoint 3 to 5 times per day, with each press lasting for 3 to 5 minutes. In addition, traditional Chinese medicine was offered during the whole treatment process.

The treatment plan was applied for 5 weeks, including whole body hyperthermia + peritoneal perfusion (3 sessions respectively), nutrition, chelation, medical ozone, acupuncture, and tradition Chinese medicine therapies. The patient's condition improved, with hemoglobin level controlled at about 95g/L and weight gain by 0.6kg weekly. There was no melena. Stomach function and appetite returned to normal. At that time, peritoneal perfusion drugs were adjusted as cisplatin+mitomycin. As such change resulted in a decreased white blood cell count (to $1.2 \times 10^9/l$), GM-CSF was administered as well as traditional Chinese medicine: Radix Astragali Preparata (Zhi Huang Qi)30g, Radix Angelicae Sinensis (Dang Gui)15g, Cortex Eucommiae (Du Zhong)15g, Cervus nippon Temminck (Lu Jiao Shuang)15g, Semen Persicae (Tao Ren)10g, Flos Carthami (Hong Hua)10g, Rhizoma Atractylodis Macrocephalae (Chao Bai Zhu)15g, Fructus Corni (Shan Yu Rou)15g, Colla Corii Asini (E Jiao) 15g, Plastrum Testudinis (Gui Ban) (decocted first)15g, Carapax Trionycis (Bie Jian) (decocted first)15g, Radix Codonopsis (Dang Shen)10g. At the same time, 3 slices of Rhizoma Zingiberis Recens (Sheng Jiang) and 5 Fructus Jujube (Da Zao) were introduced as the guiding medicine. The traditional Chinese medicine was taken one dose daily and should be decocted with water.

Chelation therapy and medical ozone therapy continued as before. Astragalus injection was added to inject into ST 36 during acupuncture. The patient presented with white blood cell decrease but that became stable 3 days after. She followed the treatment plan for more than one month. Whole body hyperthermia was applied once every 10 days and medical Qigong was also combined as part of the treatment.

Treatment outcome: The patient had been hospitalized for 81 days. After the integrative therapy, she improved significantly, with better spirits, normal appetite, sleep, urination and bowel movement. She was free of nausea, vomiting and abdominal pain. She gained 12kg and controlled the body weight around 56kg. Chinese medicine therapy continued and other therapies stopped. Contrast CT scan of the whole abdomen indicated significant shrinkage of the primary lesion, lymphatic metastatic lesion in the hepatic hilar area and thrombus of the portal vein, splenic veins and superior mesenteric vein. Tumor markers test (5 items) after treatment: CEA329.8ng/ml, AFP7.09ng/ml, CA12-5(OV) 34.99U/ml, CA19935.94U/ml, CA153 (BR) 56.45U/ml. (significant decrease compared to that on admission). Complete blood count: WBC $3.70 \times 10^9/l$, NEUT58.9%, RBC $1.61 \times 10^{12}/L$, HGB89g/l, HCT0.26. Blood count returned normal and anemia improved. Karnofsky score was 90.

The patient died of intestinal obstruction caused by stomach cancer relapse on June 2009. The patient lived with advanced stomach cancer for three and a half years.

Thyroid Cancer

Z4, 26 years old.

She was admitted on June 24, 2007 because of "status post total thyroidectomy secondary to medullary thyroid cancer for 18 months, multiple metastases to bilateral lungs for 9 months, and chest pain, cough and bloody sputum for 7 months".

In early 2006, the patient presented with a mass in left neck with hoarseness. Physical examination revealed a hard and fixed mass of 3cm×4cm in the left lobe of thyroid gland with multiple enlarged lymph nodes in left neck. She was diagnosed with stage III medullary thyroid cancer. After that she underwent a total thyroidectomy and lymph node dissection and received oral thyroxine tablets. In September, an examination for recurrent non-productive cough indicated multiple metastases to bilateral lungs, and she experienced significant emaciation, chest distress, shortness of breath, irritability, pain of head, neck and chest, cough productive of yellow and bloody sputum, hoarseness, breathing and swallowing discomfort, constipation and yellow urine since November. As above symptoms persisted and did not subside, the patient was then admitted for further treatment.

Physical examination on admission: Her general conditions were not good. She was emaciated and weighed 49kg and looked anemic. Superficial lymph nodes were impalpable and surgical incision healed. Heart rhythm was normal. Respiratory sounds were diminished. Liver and spleen were unremarkable. KPS was 40.

Assistant examinations:

Complete blood count: Hb 90g/L;

A chest CT scan showed multiple soft tissue masses in lungs with the largest one of 3.2cm×4.0cm, suggestive of pulmonary metastases. And a cervical CT scan showed status post thyroidectomy and multiple enlarged lymph nodes.

Diagnosis: Medullary thyroid cancer with metastasis to lungs.

Integrative treatment plan:

As the medullary thyroid cancer was in advanced stage and highly malignant with pulmonary metastases, there would be an extremely poor prognosis. After admission, the patient was immediately given western medicine treatments like intravenous nutrition, stoppage of cough and bleeding, phlegm elimination and anti-infection. Other integrative therapies included local hyperthermia, chelation therapy, major ozonated autohemotherapy, TCM (traditional Chinese medicine) and acupuncture. Symptoms like chest tightness, cough, expectoration and headache were gradually alleviated after 7 days of treatment. The patient gradually started therapies like EBOO, systemic medium-high hyperthermia, chelation therapy. TCM and acupuncture were adjusted based on syndrome differentiation.

According to TCM's theory, the patient's signs and symptoms at admission were attributed to pathogenic fire resulting from stagnation of liver Qi and treated in the principle of purging liver fire and detoxifying and dissipating binds.

Therefore, TCM decoction was prescribed and the detailed herbs included:

Radix bupleuri (Chai Hu) 10g
Dioscorea bulbifera (Huang Yao Zi) 10g
Radix paeoniae Alba (Bai Shao) 15g
Radix trichosanthis (Tian Hua Fen) 10g
Ligusticum wallichii (Chuan Xiong) 15g
Pericarpium trichosanthis (Gua Lou Pi) 10g
Fritillaria thunbergii miq (Zhe Bei Mu) 10g
Pericarpium citri reticulatae viride (Qing Pi) 15g
Arisaema cum bile (Dan Nan Xing) 15g
Pangolin scale (Chuan Shan Jia) 10g
Sargassum (Hai Zao) 15g
Salvia miltiorrhizae (Dan Shen) 15g
Prunella vulgaris (Xia Ku Cao) 15g
Solanum nigrum (Long Kui) 20g

The patient was given one dose daily for more than 1 week. And after treatment her symptoms were improved. Tongue was light red and pulse was weak and slow. The treatment subsequently was adjusted to fortify the spleen, replenish Qi, eliminate toxins, and dissipate masses.

The detailed herbs included:

Radices codonopsis (Dang Shen) 15g
Atractylodes macrocephala Koidz (Bai Zhu) 20g
Tangerine peel (Chen Pi) 10g
Poria cocos (Fu Lin) 10g
Hyacinth bean (Bian Dou) 15g
Fritillaria thunbergii miq (Zhe Bei Mu) 10g
Sargassum (Hai Zao) 15g
Dioscorea bulbifera (Huang Yao Zi) 10g
Solanum nigrum (Long Kui) 20g
Arisaema cum bile (Dan Nan Xing) 15g
Agrimoniae pilosa ledeb (Xian He Cao) 30g
Lily (Bai He) 15g

The decoction was taken once daily based on her signs and symptoms until she was discharged. Since then she continued traditional Chinese medicine for over 3 months.

Acupuncture therapy:

With neutral supplementation and draining method, each session of acupuncture was applied for 20 minutes in the frequency of once a day and there was a 2-day interval after 5 sessions.

Acupuncture points included:

Zusanli(ST36)
Yinlingquan (SP9)
Quchi (LI11)
Taiyuan (LU9)
Taichong (LR3)
Feishu (BL13)
Dazhui (DU14)

Fenglong (ST40)

Linggu

Dabai

Moxibustion therapy:

Each session of moxibustion was applied to 2 to 3 acupoints with moxa stick for 10 minutes respectively in the frequency of once every day or every other day.

Moxibustion points included:

Zusanli(ST36)

Guanyuan(RN4)

Dazhui(DU14)

Pishu(BL20)

Feishu(BL13)

Auricular therapy:

Auriculotherapy alternated once a week between two ears. Cowherb seeds were applied to the auricular points and the patient was instructed to press each acupoint 3 to 5 times per day, with each press lasting for 3 to 5 minutes.

The auricular points included:

Neibi(TG₄)

Waibi(TG_{1,2i})

Yanhou(TG₃)

Jiaogan(AH6_a)

E(AT₁)

Nie(AT₂)

Shenshangxian(CO₁₀)

Fei(CO₁₄)

Tumor specific region

Psychotherapy was provided to boost her confidence in fighting cancer. Afterwards, she started practicing medical Qi Gong and exercise to increase spontaneous healing powder.

Treatment outcome:

The patient had been hospitalized for 60 days, during which she was given totally 3 sessions of systemic medium-high hyperthermia, 20 sessions of local hyperthermia, 25 sessions of chelation therapy, and 16 sessions of EBOO. After non-toxic integrative cancer treatment, general conditions improved and she gained weight to 56kg and could take care of herself independently. Chest tightness or pain, cough or hemoptysis disappeared, even though there was occasional hoarseness. Besides, a follow-up CT scan revealed pulmonary metastatic lesions (maximal size of 1.2cm *1.2cm) became smaller than the finding in previous study. No new metastasis was noted.

Since then the patient has continued non-toxic integrative cancer treatment in Outpatient Department once per month and follow-up every three months. Currently, the patient has been living with thyroid cancer for more than 9 years with a completely normal quality of life.

Other cases

The statistics of 22 patients with benign prostatic hypertrophy (BPH) treated with local hyperthermia. They were treated between 10 and 20 times (average 13 times). The size of prostate diminished between 1 and 2.5cm (average 1.5cm). The symptom was obviously improved in 20 patients (20/22). The quantity of residue urine was reduced in 19 patients.

32 patients with primary dysmenorrheal were treated with infrared wholebody mild temperature hyperthermia with average treatments ranging from 3 to 6 times. Everyone has got a good effect.

16 female acne patients, ages from 18 to 25, after 3 sessions of wholebody mild - high temperature hyperthermia for every patient, 13 patients'acne disappeared, the other 3 patients'symptom obviously improved.

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Case reports

Dr. Saima Zahoor MD*, Dr. Unsa Mohsin MD*

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Case reports

Case – Head and Neck cancer.

Patient identification: MA, 50y, male. Referent physician Dr. M. Ali Memon

CT diagnosis: posteriorly mass is seen infiltrating masseter muscle. Posteromedially mass is also showing extension into the retro molar trigone with possible infiltration of the pterygoid muscle. However, no underlying bony erosion of alveolar process of mandible or maxilla is identified. There is evidence of multiple sub centimeter sized, as well as enlarged enhancing and necrotic lymph nodes seen in submental, right submandibular and at cervical level II on right side. Largest necrotic lymph node at cervical level II is measuring 2.0 x 2.3 cm. These are most likely malignant in nature.

- No significant cervical lymphadenopathy is seen on left side.
- There is no evidence of mass in the supra-glottic, glottic or infra-glottic region.
- The bilateral vocal cords, prelaryngeal spaces, valleculae and pyriform sinuses are normal.
- The pharynx and parapharyngeal spaces are normal.
- The laryngeal, arytenoid and cricoid cartilages are normal.
- Tongue and palatine tonsils show no gross pathology.
- Submandibular, parotid and thyroid glands show no lesion.
- Cervical vessels show normal course and caliber.
- Imaged sections through neurocranium and orbits show no gross pathology.
- Imaged sections through upper chest on mediastinal window show no gross pathology.

Large ill-defined enhancing soft tissue density mass is seen involving right buccal mucosa / right cheek with infiltration of the overlying subcutaneous tissues and skin with its ulceration. It is highly consistent with malignant neoplastic lesion.

Multiple sub centimeter sized, as well as enlarged enhancing and necrotic lymph nodes seen in submental, right submandibular and at cervical level II on right side. These are most likely malignant in nature.

Biopsy proved the malignancy.

Indications: K/C of neoplastic mass involving left cheek.

Before oncothermia treatment



Therapy: Oncothermia Monotherapy in first 3 sessions, then along with chemotherapy weekly in a low dose.

After treatment CT investigation: axial images were obtained before and after contrast. There is redemonstration of soft tissue density mass seen along the right buccal mucosa. It has markedly reduced in its dimension on comparison. It is again reaching up to the skin and involving the subcutaneous tissues in few sections. The lesion is extending up to the remolar trigone is also involving the masseter muscle. There is again extension into the bucco gingival recess. No definite cortical irregularity of mandible or maxilla is noted. Lesion now measures approximately 2.0 cm in maximum width. Previously it measured 4.5 cm in maximum width.

- Few lymph nodes are seen in submandibular region, these are all subcentimeter which have also reduced in size and number.
- There is no evidence of mass in the supra-glottic, glottis or infra-glottic region.
- The bilateral vocal cords, prelaryngeal spaces, valleculae and pyriform sinuses are normal.
- The oropharynx and parapharyngeal spaces are normal.
- The laryngeal, arytenoid and cricoid cartilages are normal.
- The thyroid gland shows no lesion.
- Nasopharynx and pterygoids appear normal.

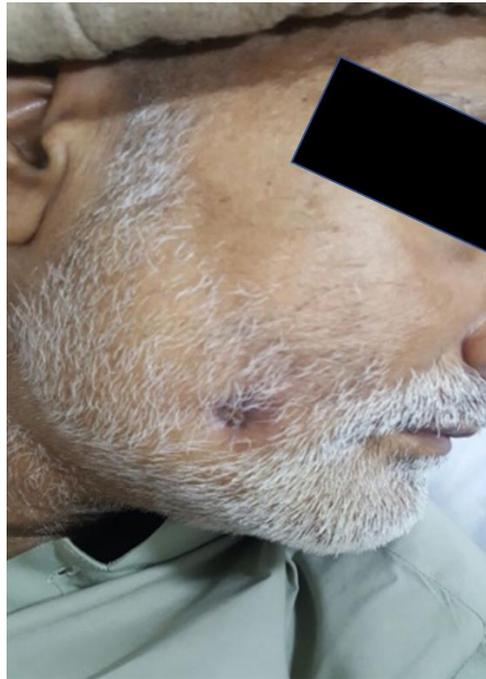
After 5 sessions of oncothermia treatment along with low dose chemotherapy



After 8 sessions of oncothermia treatment



After completion of 10 sessions of oncothermia treatment



Conclusion: Oncothermia partly with low-dose chemotherapy, partly in monotherapy application made remarkable regression of the tumor.

Case – Head and Neck cancer.

Patient identification: TQ, 61y, female. Referent physician Dr. Ahemed Usman

Diagnosis: Mammary carcinoma (left) and gastric (stomach) cancer

Comorbidities: hypertension, diabetes mellitus. When patient attended to our clinic, she had gangrenous foot (R) so amputation was already done above knee joint.

CT scan before oncothermia treatment (Oct.2016)

CT scan chest

- Lobulated soft tissue mass in left breast 3.5cm x 1.5cm, adjacent skin thickening, few enlarge lymph node identified in left axilla largest one measuring 1.1cm. B/L moderate plural effusion seen.
- No evidence of parenchymal consolidation or cavitary lesion identified.
- No nodular shadowing or interstitial prominence seen in either lung fields.
- No evidence of any mass lesion seen.
- No evidence of pneumothorax on either side.
- On mediastinal window settings, few sub centimeter lymph nodes noted.
- Trachea and mainstem bronchi appear patent.
- Visualized esophagus appears normal.
- Normal enhancing mediastinal vessels noted.
- No enhancing nodule noted in both lung fields.

CT abdomen

- Circumferential wall thickening of stomach at the antral fold up to pylorus it measures 1.3cm in maximum thickness along the lesser curvature. It is closely abutting the body of pancreas however no definite evidence of infiltration of pancreas noted on present examination.
- The lymph node inferior to stomach now measure 0.8 x 0.3cm. Another lymph node in gastrohepatic ligament measure 1.2 x 0.3cm.
- Gallbladder is not visualized (status post cholecystectomy).

Treatment: oncothermia was applied as monotherapy.

Results: CT scan after oncothermia monotherapy treatment

		Dow University of Health Sciences ڈاؤ یونیورسٹی آف ہیلتھ سائنسز، کراچی DOW INSTITUTE OF RADIOLOGY				
MR No:	001337876	Scan Date:	22 Feb, 2017			
Name :	[REDACTED]	Gender/Age:	Female /62 Year(s)			
Referred By: DR..		Imaging No:	170282466			
MRI (1.5 Tesla)	CT Scan (Multi Slice)	Echocardiography	Elastography	Ultrasound with Colour Doppler		
MRI Real open Magnet	Mammography	Fluoroscopy	Dexa Scan	X-Ray with CR & DR - VIF		

CT CHEST & ABDOMEN

Multiple axial sections of CT scan of chest abdomen and pelvis were carried out after non-ionic IV contrast enhancement. Coronal and Sagittal reformations were also acquired. Imaging was performed on multi-slice (16 slices) scanner and reporting was done at workstation.

Clinical Indication:

Known case of carcinoma breast and carcinoma stomach.
Status post radiotherapy 10 cycles ✓
Previous CT scan dated 1st October 2016 is compared

Findings:

CT CHEST:

Previously seen mass lesion in left breast has shown interval reduction in size, previously it was measured 3.5 x 1.5cm. It now measures 1.3 x 1.8cm. ✓

Previously noted few left axillary lymph node has also shown reduction in size, the largest lymph node was previously measured 1.4 x 1.6cm, it now measures 1.1 x 1.5cm. ✓

Previously seen moderate bilateral pleural effusion shows complete resolution in current scan. ✓

Small pleural based nodule measuring upto 3.4mm noted along posterior basal segment of left lower lobe. This is too small to characterize.

Pleural based nodule measuring 3mm noted in apical basal segment of left lower lobe. Another pleural based nodule noted in right middle lobe measuring 3.9mm. These nodules require follow up.

Mild centrilobular emphysematous changes noted bilaterally.
No evidence of enlarged mediastinal or hilar lymphadenopathy noted.

No evidence of parenchymal consolidation or cavitory lesion identified.
No evidence of pneumothorax on either side.
Trachea and main stem bronchi appear patent.
Visualized esophagus appears normal.
Normal enhancing mediastinal vessels noted.
Bony thoracic cage appear unremarkable.

CT ABDOMEN AND PELVIS:

There is redemonstration of circumferential wall thickening noted in the region of distal stomach/antrum, previously the wall thickness measured 1.3cm. It has shown interval reduction and now the posterior wall in this region measures 7.8mm in maximum dimension. It is closely abutting body of pancreas which appear atrophic. ✓

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Page 1 of 2

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Ojha Campus Contract No: UAN 111-113-847. 021-38771111,021-99232660 Ext No: 2302, 2293.



Dow University of Health Sciences
ڈاؤ یونیورسٹی آف ہیلتھ سائنسز، کراچی
DOW INSTITUTE OF RADIOLOGY



MR No: 001337876

Scan Date: 22 Feb, 2017

Name :

Gender/Age: Female /62 Year(s)

Referred By: DR..

Imaging No: 170282466

MRI (1.5 Tesla)	CT Scan (Multi Slice)	Echocardiography	Elastography	Ultrasound with Colour Doppler
MRI Real open Magnet	Mammography	Fluoroscopy	Dexa Scan	X-Ray with CR & DR - VIF

No evidence of any enlarged perigastric lymphadenopathy noted in current study. Few subcentimeter lymph nodes visualized.

There is interrupted calcific foci noted along the hepatic margin in segment VI.

Gall bladder is not visualized. Surgical staples noted at portahepatis. These findings are likely consistent with cholecystectomy.

Redemonstration of double IVC below the level of renal veins.

There is redemonstration of multiple calcified uterine fibroid.

Intra and extra hepatic biliary ducts are not dilated. Portal vein show normal opacification. No evidence of portal venous thrombosis.

Spleen appears normal. No evidence of focal mass seen.

Pancreas appears normal. No evidence of mass lesion noted.

Both adrenal glands and kidneys are enhancing normally. No evidence of focal mass, calculus or hydronephrosis noted.

Urinary bladder is smooth in outline, without evidence of cystitis, vesical calculus or intra luminal mass.

Visualized small and large bowel loops appear normal.

No evidence of lymphadenopathy noted.

No evidence of ascites or significant mesenteric stranding noted.

On appropriate bone window settings, degenerative changes seen in spine.

Impression:

Previously seen mass lesion in left breast and left axillary lymph node has shown interval reduction in size.

Previously seen moderate bilateral pleural effusion shows complete resolution in current scan.

Few tiny pleural based nodule noted in both lungs as described above, these nodules require follow up.

There is redemonstration of circumferential wall thickening noted in the region of distal stomach/antrum, it has shown interval reduction.

No evidence of any enlarged perigastric lymphadenopathy noted in current study.

Overall findings represent interval improvement since previous study

DR SOHAIL AHMED KHAN

M.B.B.S, M.C.P.S, F.C.P.S

ASSISTANT PROFESSOR

CONSULTANT RADIOLOGIST

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Ojha Campus Contract No: UAN 111-113-847. 021-38771111, 021-99232660 Ext No: 2302, 2293.

Conclusion:

According to the latest CT scan done after 12 Sessions of oncothermia (monotherapy) significant reduction in size at both sites (breast and stomach antrium noticed).

According to the patient her health status has been improved significantly. No history of vomiting or associated symptoms of CA stomach noticed breast, lung on examination was unnoticeable. Over all her health status is getting significantly better.

**Oncothermia-Booster (Targeted Radiofrequency) treatment –
in some non-oncological diseases as special physiotherapy**

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Oncothermia-Booster (Targeted Radiofrequency) Treatment -in Some Non- Oncological Diseases as Special Physiotherapy



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Abstract

Introduction: Oncothermia (OTM) is based on electromagnetic interactions with the living organism. Its nano-targeting approach [established a newer paradigm, which could be applied not only in case of malignancies but in any other diseases, when the non-selective conditions are existing. This technique by now is well proven from the simple laboratory level to the several different clinical applications. Oncothermia method ignites the natural processes to rescue them from the system, re-establishing the better communication harmony between the cells of organism. This method will lead us to the treatment of some non-malignant diseases too to try delaying their development or offering earlier recovery. Our aim was to use OTM on the common basis of equilibrium demand; and use the recognition of the deviations from the complex harmony of the organism or its part for selection to act properly.

Study protocol and Method: Oncothermia was successfully applied for non malignant conditions like Lyme disease, for non-specific low-back pain, for Peyronie disease, and for Dupuytren's contracture, too. We made more extended study, proving in details the applicability of the OTM in these diseases, especially in the situations when traditional Chinese Medicine (TCM) is also applicable (acupuncture, permanent needle techniques). Our special permanent acupuncture method was proven previously and well fits to the complementary applications.

Results & Discussion: The synergy of the ancient knowledge - application of heat energy - and the high-tech state-of-art of the medical knowledge could be established with our research. Recognition of the distortions in the healthy tissue have some common principles and possibilities in TCM and OTM: the left complexity of the living organization is recognized by both the methods. OTM application is a useful, harmless additional complementary treatment for management of selected diseases. Our topic is giving western trained physicians clinical applications of modern (Oncothermia-Booster) as a physiotherapeutic - equipment to accommodate accelerating interests in modern complex treatment of chronic low back pain and Dupuytren's contracture.

Conclusion: In recent study data verified the relevant end-points of the study: the safety, the quality of life (QoL), the shortened rest time, duration of painless state, cost/benefit ratio.

Keywords: Physiotherapy; Oncothermia; Dupuytren's contracture; Non-specific low back pain

Abbreviations: OTH: Oncothermy; LBP: Low Back Pain; TCM: Traditional Chinese Medicine; VAS: Visual Analog Scale; QoL: Quality of Life

Introduction

Oncothermia (OTM) is based on electromagnetic interactions with the living tissue [1]. Its nano-targeting approach [2,3] establishes a new paradigm, which could be applied not only in case of malignancies but also in other diseases, when the non-selective conditions [4] are valid. Oncothermia method ignites the natural processes to eliminate them from the system reestablishing the communication harmony between the cells. Our aim is to use OTM on the common basis of equilibrium demand; and use the recognition of the deviations from the

complex harmony of the organism or its part for selection to act properly. This method will lead us to the successful treatment of some non-malignant diseases, too. This technique is well-proven from the many kind of the laboratory level to the clinical applications [5].

Method and Procedure

We decided to apply Oncothermia in the following 2 group of non-malignant disease:

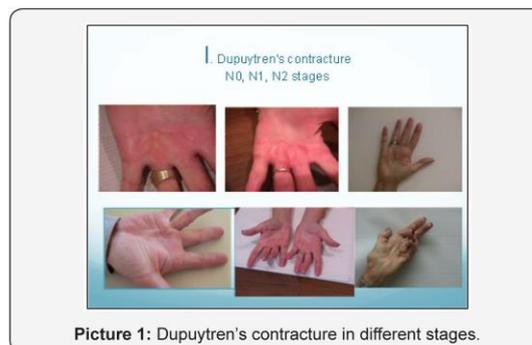
Dupuytren's contracture

(Also known as Morbus Dupuytren's, or Dupuytren's disease and slang terms "Viking disease" or "Celtic hand"), is a fixed flexion contracture of the thenar due to a palmar fibromatosis. the fingers tend to move towards the palm and cannot be fully extended (straightened). Most commonly affected the ring finger and little finger. The middle finger may be affected in some more advanced cases, but the index finger and the thumb are not affected as frequently. This disease sorted to the inherited proliferative connective tissue disorder that involves the hand's palmar fascia. It is called after Baron Guillaume Dupuytren, he was the first who described an solution of the operation to correct the affliction, it was published in the Lancet in 1831. The progress of Dupuytren's contracture is slowly. Often is accompanied by less or more aching and itching. In this condition, the palmar fascia of patients thickens and shortens so that the tendons connected to the fingers cannot move freely. Incidence of the disease increases after age 40; at this age, men are affected more often than women. The progressive situation can be improved by operation in stage No, N1 and other alternative therapies can be tried, like Quercetin, Bromelain, DMSO, MSM, Acetylcarnitin HCl, PABA, Nattokinase, Vitamin E (1940) Copper, Vitamin C, Massage. The palmar fascia becomes hyperplasic and contracts by time to time.

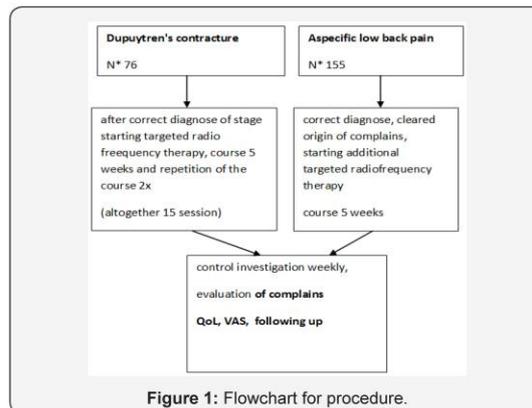
Non-specific low back pain

(LBP), also known as lower back pain or lumbago, is a common disorder involving the muscles and bones of the back, but sometimes the lumbar nerve is affected. Low back pain may be classified by duration as acute (pain lasting less than 6 weeks), sub-chronic (6 to 12 weeks), or chronic (more than 12 weeks). The condition may be further classified mechanical, non-mechanical, or referred pain. In most episodes of this condition, a specific underlying cause is not identified or even looked for, with the pain believed to be due to mechanical problems such as muscle or joint strain. If the pain does not go away with conservative treatment further testing may be needed to look for a more serious underlying problem. In most cases, imaging tools -X-ray computed tomography- are not useful and carry their own risks. Some low back pain is caused by less or more damaged intervertebral discs, and the "Lasegue test" is useful to identify this cause. In those with chronic pain, the pain processing system may malfunction, causing large amounts of pain in response to non-serious events. Despite this, the use of imaging in low back pain has increased. The treatment of acute non-specific low back pain is typically with conservative measures at reumatological outpatient surgery or General Practice (GP) consultation: using of some well-proved pain medications and the continuation of normal activity as the pain allows without bed rest. Chronic non-specific lower back pain needs more management for relieving permanent pain. The Booster, which is the unique instrument, was developed first for oncology, but can nevertheless also be successfully used in other medical fields in addition to oncology, in the follows: in fields such as rheumatology, sports medicine, neurology and neurosurgery, dermatology and analgesic therapy. We know that Oncothermia was successfully applied previously

for Lyme-disease [6], for low-back pain [7], for Peyronie disease [8], and for Dupuytren's contracture [9], too. The number of patients was small one in the last mentioned study; therefore we made more extended study, proving in details the applicability of the OTM in these diseases, especially in the situations when traditional Chinese Medicine (TCM) is also applicable. Our special acupuncture method [10] well fits to the complementary applications. We enlarged number of selected patients suffering from Dupuytren's contracture in different stages of disease to investigate whether progression without side-effect could be stopped with elevation of QoL of patients and non-specific low back pain lasting more than 4 weeks where we used focused radiofrequency heat therapy as special physiotherapy.



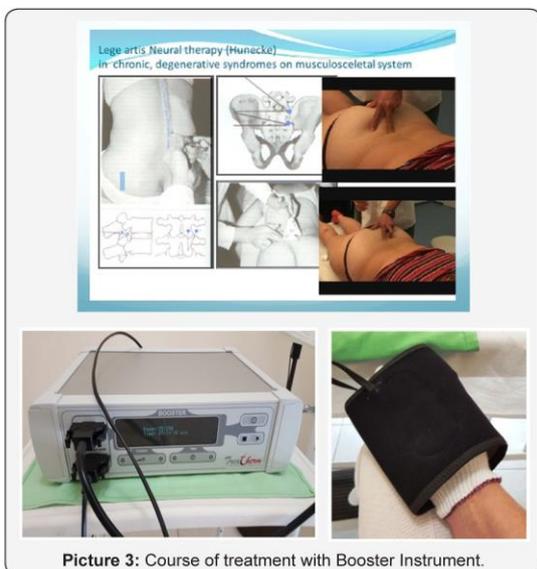
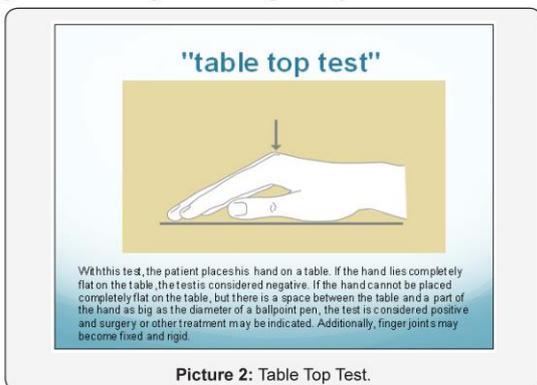
The study for selected diseases was performed according to Helsinki Declaration and local ethical approval. Patient selection was made by rheumatologist outpatient's clinic. The period of study was 2012-2015. We selected 76 patients suffering from Dupuytren's contracture in different stages. (Picture 1, The selected patients were suffering from N0, N1, N2 stages received 2 times/week special booster-physiotherapy with Instrument (Booster, Oncotherm GmbH, Germany), 30W, 25 minutes, 1 course is 4 weeks (8 session), after ½ years it was repeated 3 times. The primer outcome measurement was "top of plate test", see picture 2, painless extension of palm. Second outcome measurements were QoL, VAS of patients.



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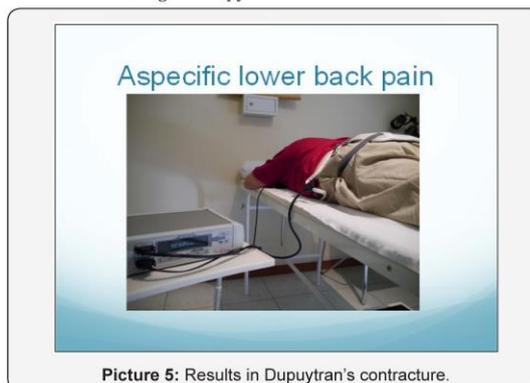
Also, we selected 155 patients suffering from non-specific low back pain, including verified ischialgy, discopathy, disc herniation and degenerative disease. Excluding criteria were ruptured disc herniation, caudal syndrome, malignancy- (bone metastasis from lung, breast, prostate, thyroid, among others), infectious (osteomyelitis; abscess). (Figure 1: flowchart).

The selected patients received 2-times/week special Booster-physiotherapy (with instrument Booster Oncotherm GmbH, Germany), 30W, duration was 25 minutes, 1 course is 4 weeks (8 sessions), and after ½ years it was repeated 3 times. Additionally, all patients received mesotherapy (neuraltherapy by local anesthetic Procain 0, 5%, 2-3ml/session and acupuncture (permanent monofilamentum insertion 1 time / month according to TCM protocol and protocol of Neural therapy). See Pictures 3 & 4. Questionnaire on pain and QoL was filled in all sessions during physical examination. Visual Analog Scale (VAS), "Top of plate test" was registered during the all period of treatments.



Results

We recognized in N0 and N 1st stage of Dupuytren's cases significant delay of progression, moderately in 2nd, no changes in progressive stages after 2 years follow-up. According to delayed progression in VAS can be seen result (Picture 5). The following additional therapies used to apply for Dupuytren's cases Quercetin, Bromelain, DMSO, MSM, Acetylcarnitin HCl, PABA, Nattokinase, Vitamin E (1940) Copper, Vitamin C, usual continuous massage therapy.

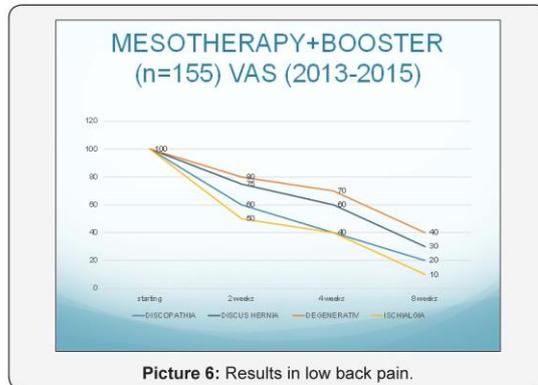


Discussion

The second investigated group was non-specific low back pain. Better results were achieved in cases originated from ischialgy, chronic degenerative lumbar disc cases, low back pain caused by post-operative edema. The rest time out of work was less. The low back patients needed fewer intakes of analgesic pills (Picture 6). According to our experience the "targeted radiofrequency-physiotherapy as Booster" application is free of side effects (but skill, practice is necessary), harmless, well tolerable by patients, easy to apply by skilled administration. It is advised to consider that complementary treatment of selected diseases is valuable for introducing into daily rheumatologic

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practice. Also we recognized the less intake of medicaments in cases during sessions of low back pain, which is important to avoid unnecessary side effects of medicaments (NSAID).



Picture 6: Results in low back pain.

Conclusion

The targeted radiofrequency therapy performed by Booster Instrument, is used as a supplement to physiotherapy, general used drug treatments. It is not advised to be a stand-alone treatment device, but should be used in a supporting role with drug treatments to enhance their effects. The purpose of usage of the Booster is to increase the blood flow in the treatment area. Selection at cellular level does not occur, only a heating of the deep layers of tissue in the region where the electrode is positioned. The deep-heating effect is a result of Joule loss and leads to vascular dilatation in the treatment area, that in turn, improves higher and better blood perfusion and thus the drugs and more oxygen are transported to the treated area. The temperature in this area is 37-39 °C (moderate, classic Hyperthermia). This is the optimum temperature for the effect of booster. Further improvements are the follows: increased fibroblast activity and increased capillary growth, increased nutrient concentration and metabolic activity, synergetic increase in the field-dependent effects. It leads to the optimization of membrane stimulation and activation of signal channels etc.). More recognized effects are: increased reactions to heat and field exposure (mainly the development of heat shock proteins, HSP), increased venous and lymphatic flow, which finally causes changes in the physical properties of the tissue.

Recognition of the distortions in the healthy tissue has some common principles and possibilities in TCM and OTM: the loss of

complexity of the living system is recognized by both methods. The synergy of the ancient well-proved knowledge and the high-tech state-of-art of the medical knowledge (newer application of targeted radiofrequency) could be established with this research. The positive result of this study was the recognition to apply the radiofrequency heat therapy for non-malignant, developing connective tissue diseases with positive result.

The limitation of this study is lack of double-blind control and lack of "sham" application. We need further researches in the future to clarify the exact undergoing process in selected disease group, but results show improvement and better QoL on regarded diseases, therefore it is advisable to use this physiotherapeutic method in daily practice of mentioned disease after careful selection [11,12].

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Connections between Warburg's and Szentgyorgyi's approach about the causes of cancer

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Connections between Warburg's and Szentgyorgyi's Approach about the Causes of Cancer

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Abstract

Numerous theories and hypotheses are published about the causes of cancer and its hallmarks. Two remarkable principles were established and debated for a long time. The first is the Warburg-effect, which based on mitochondrial dysfunction, connected to the intensive metabolic activity of the malignancy. The other is the Szentgyorgyi's effect which describes the malignancy by changing of the cellular state ($\alpha \leftrightarrow \beta$) explained by evolutionary biology and supported by definitely improved dielectric properties of the malignant tissue from their normal counterpart while these theories have stable explanations, developed many controversies. Both are partial of completely revised time-by-time, showing new insights with new evidence as additions to these old ideas. Our objective is to demonstrate connections between these theories and start new considerations in the actual debates.

Keywords: Warburg-effect; Szentgyorgyi-effect; Fermentation; Irreversibility; Cancer

Introduction

Various theories and hypotheses are existing about the cause and origin of cancer from ancient medicine to a long line of new explanations. The advanced search for an answer was started more than a century ago with virus concept [1,2]; the genetic clues were later favoured [3,4], and the mutation concepts became popular [5-7]. Recently, the immune-dependences [8], and connections with wound-repair have been intensively researched [9-13]. Despite the enormous efforts, the cause of cancer remains open [14], with groups trying to "fish" for the clue [15]. Despite even special quantum-physical explanation [16], the recent studies do not give a final solution [17,18]. The final explanation is missing, but the hallmarks are well defined [19,20]. More studies turn

to the environmental, diet and habit origins of malignant diseases [21-23].

Most widely, cancer is believed to be an abnormal tissue triggered by a gene mutation. However, the proto-oncogene and the oncogene appear not only in cancerous cases [24], but with pregnancy [25], with embryogenesis [26,27], with the healing of wounds [28] and with the synthesis of growth factors [29]. Oncogenes show a great variety of anti-apoptotic functions with the cells taking part in the wound-healing [30]. To summarize, some oncogenic features appear in normal, non-malignant cases, such as in growth and repair processes. More cancer risk factors are associated with wound-like conditions or chronic stresses and poisoning. For instance, smoking cause's chronic bronchitis and the risk factor can be found with lung cancer, hepatitis and so on [31-34]. Nobel laureate Albert Szentgyorgyi clearly described these environmental points [35]: It is unimportant that the monkey goes through the jungle; the important fact is that the jungle goes through the monkey, in the form of nutrition, water, and oxygen.

The appearance of the oncogene activity and the anti-apoptotic functions is one of the most striking similarities between cancerous and certain standard processes, for example, growth, and repair. Since apoptosis is strongly connected with the mitochondrion, just like the oxidative ATP production, it can be suspected that functions of mitochondria also degrade temporarily with the growth and repair processes. The mode of the ATP production is also the starting point of the century-old Warburg theory [36].

Warburg started his work with the energetics of malignant growth. The cancerous tissue needs more energy than its healthy counterpart, because of the permanent fission and necessary amount of ATP for all steps to create daughter cells. The difference between the energetics of the healthy and malignant cells is that in malignancy, massive anaerobic (fermentative) ATP production takes place in the cytosol, while the aerobic process dominates in healthy cells. The cytosol could produce two ATPs from a glucose molecule in very simple steps, while the mitochondria produce 34 ATPs by the complicated and time-consuming citrate cycle process. The

transport processes are also crucial: the function of the glucose, sodium, pyruvate and lactate, as well as the hydrogen ion transporters, have to serve the actual energy-production processes in time. These transports are also simpler in the case of anaerobic compared to aerobic energizing procedures. Note that this type of fermentative ATP production was characteristic at the beginning of the development of life on Earth. The early environment in our Globe lacked oxygen but was presumably rich in geochemically-produced molecules; producing ATP may have similarities to present-day forms of fermentation.

Method

Warburg's effect

Warburg explained definite metabolic differences between the processes of malignant and healthy cells by the anaerobic glycolysis Warburg. The anaerobic glycolysis is a more intensive and simpler process to produce ATPs than the complicated Krebs-cycle via the mitochondria [37]. Warburg stated the primary cause of cancer is a kind of mitochondrial dysfunction. He meant that the glycolytic fermentation of production of ATP energy molecules in the cells plays a decisional part. The discovery of the accelerated glycolysis to produce the ATP molecules was honored by Nobel-prize for Warburg.

The theory was soon induced debate. The question is immediate: is the shortage of the ATP due to the underperforming mitochondria, so the cause of the cancer is mitochondrial dysfunction or only a huge demand of ATP? The unusually high request for ATP is much more than the actively functioning mitochondria could provide for limited time applications via anaerobic glycolysis. It is similar to the massive sports activities when the aerobic process has a shortage of energy supply, so anaerobic glycolysis is used temporarily when the extreme load persists. This last supposes the permanent activity of mitochondria, and the fermentative ATP production is the only addition to that. Is it the case in the malignant cell as well?

Not everybody was convinced by cancer being caused by damaged mitochondria [38,39]. It was found that cancer cells are also able to oxidize glucose comparable to those of healthy cells [40]. The argument reversed Warburg's claim: cancer cells have reduced mitochondrial activity due to the demand of increased glycolytic flux, [41,42]. The relationship between the opinions is similar to the apparent controversy of the chicken-and-egg "paradox" [43]; whether mitochondrial dysfunction decides the anaerobic glycolysis or reverse is valid: this fermentative way suppresses mitochondrial functions. Both models are supported by relevant data. The "enigma" of the primacy of one of the processes is unsolved [44]. The fate of pyruvate after the intake of glucose is the important process and not the glucose utilization alone. The activity of pyruvate kinase M2 is decisional. The reduced activity of this process prefers the anaerobic phosphorylation, while the high activity goes towards aerobic way [45]. The mitochondrial citric-cycle

hindered by anaerobic glycolysis, it redirects pyruvate to ineffective but chemically pure and indeed quick ATP production. Warburg theory describes the lactate production as dominant, regardless of the available oxygen. Normal, healthy proliferative tissues have such processes too when the mitochondria are functional at full capacity for oxidative phosphorylation, but the increased demand is fulfilled by an addition of simple glycolysis, (Figure 1) [45]. The reprogramming process of the metabolic activity can be measured on mitochondrial DNA somatic mutation [46].

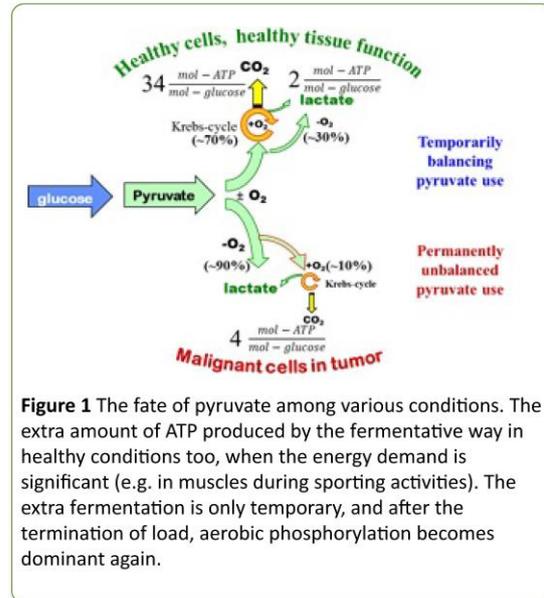


Figure 1 The fate of pyruvate among various conditions. The extra amount of ATP produced by the fermentative way in healthy conditions too, when the energy demand is significant (e.g. in muscles during sporting activities). The extra fermentation is only temporary, and after the termination of load, aerobic phosphorylation becomes dominant again.

The primary cause of cancer is anaerobic glycolysis stated by Warburg, and the mutation of the genome is a consequence of fermentative metabolism. His theory emphasizes the mitochondrial dysfunction in the cause of cancer, supposing that the malignant transformation produced by hypoxia.

The similarities of oncogenes' activity and the anti-apoptotic functions in cancer and various healthy processes (like growth and reparation) are one of the most challenging facts in the present research. Due to the apoptotic processes as well as the oxidative ATP production, which are suppressed in numerous growth and reparative processes, the function of mitochondria degrades (at least temporarily). The observed degradation of mitochondria is the reason for the renaissance of Warburg's theory, despite its controversial observations. The mitochondrial connection of metabolism of tumours is intensively investigated [47,48]. Warburg's idea has since been revised [49,50] having a renaissance nowadays [51], and "returns in a New Theory of Cancer" [52], and new hypotheses are born on this basis [53,54].

Questions arise about the hereditary of dysfunctionality: is it stored in every mitochondrion, or the environmental conditions causing their dysfunction? The inherited dysfunction assumes the problem with the mitochondrion,

while in the environmental cause with the cytosol and its compartments (mainly the cytoskeleton and ER) of the host cell.

If a cancerous cell separates then, other cancerous cells will be created. Does it mean that dysfunctionality is hereditary? Or are the environmental conditions hereditary?

The existence of mitochondria is common in most of the eukaryotes [55]. Some mitochondria, as well as its location, vary by cell type. The bean-like structure of mitochondria is not autonomic, this forms dynamic network in most cells, arranging a complex 3D branching with the cellular cytoskeleton. Mitochondria are distributed along microtubules, and their distribution is also correlated with the endoplasmic reticulum [56]. The complex formation with cytoskeleton regulates mitochondrial shape, and consequently, it can affect the function too [57]. Different structures of the mitochondrial network may manage a variety of physical, chemical and signalling processes governing advantages or disadvantages in the cellular function [58]. A single mitochondrion is often found in unicellular organisms mostly single mitochondrion serves the ATP production, but in the cells of multicellular systems, numerous mitochondria help the cellular functions. A huge number of mitochondria exist in human liver cells (approx. 1000-2000), filling up 20% of the entire cell volume and cooperatively working to serve the hepatocellular ATP demand [59]. Even the otherwise similar cells may vary substantially of their mitochondrial content, together with their size and membrane potential, [60]. The variation arises from uneven partitioning at cell division, producing extrinsic differences in energy demand and supplied cellular processes [61]. Interestingly, nestled mitochondria can be found between myofibrils of the muscle [56].

Mitochondria respond to fundamental stresses, including hypoxia, by changing their sub-cellular localization. The definite hypoxic conditions ignite mitochondrial fragmentation with spatial dynamics, and form perinuclear clustering [62,63]. Mitochondria relocate around the nuclei (Figure 2) [64].

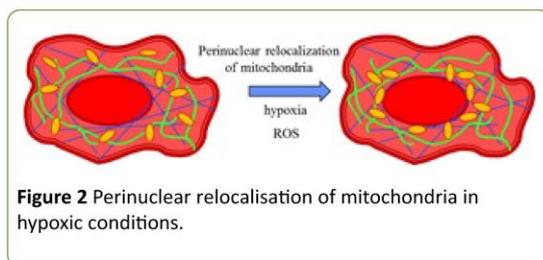


Figure 2 Perinuclear relocalisation of mitochondria in hypoxic conditions.

The hypoxia-induced nuclear relocation of mitochondria is associated with increased nuclear reactive oxygen species (ROS) by the mitochondrial gene mutations, which can suppress the electron flux and so increases the mitochondrial ROS production [65]. This process targets gene (VEGF) expression, suggesting that mitochondrial clustering may play a role in allowing the ROS signal more directly to the nucleus.

In the phase of growing and reparation, the growth and repair genes (GR genes: the oncogenes and the proto-

oncogenes...etc.) activate to create cells of the healthy network, which will become tissues [25,66,67]. When, for example, there is a wound and then healing starts: a platelet closes the injured capillaries. T-cells, macrophages, and NK-cells migrate to the injured tissue to remove the debris and the injured cells. The T-cells, the monocytes and the macrophages present growth- and repair factors [68-70]. The GR genes activate the neighboring cells (bystander effect), which also give out GR factors. The GR factors require stem cells from the adjacent tissue and from the bone marrow to the edge of the wound [71]. The healing is perfect when the GR genes turn off or when the tumor suppressors turn on [72] and homeostasis is re-established. In tumorous cases, this process never finishes; the wound healing remains permanent [73].

Szentgyorgyi's effect

Warburg recognized the excessive lactate generation of cancer cells. This phenomenon is the simple unicellular development. In this context, it looks like the evolutionary return to simpler life, and so cancer could be regarded as "dismantling of multicellularity" [74]. This was the starting point of Szentgyorgyi is an aetiological approach: the disappearance of cellular collectivity [35]. He studied the decisional role of the pyruvate metabolic pathways in processes producing ATP. From this point of view, he distinguished two different states of the cells. When the fermentative processes are dominant in a cell, he denoted it with the alpha (α)-state. Development of the life started when the aggressive electron acceptor, the free oxygen, was not present, [75]. This is a simple, primitive form of life could exist at the beginning of evolution and the existing unicellular objects characterized this period. The character of this state is only replication, simple operating the living features; developing of a complex network and process division was not possible in this reproduction-oriented state. These cells are competing for their individual demands; acting autonomously, no cooperative communication is developed between the cells in α -state.

The presence of free oxygen in the evolution process changed the game of life. Cooperation of the individual cells was promoted, a new state, the beta (β)-state of life was developed. The presence of oxygen produced by the higher value of electric charges, made possible to form unsaturated proteins, which allowed more complex interactions. The diversity of life had been started. The cells in β -state are cooperatively connected, dividing the various tasks to optimize the intake of nutrients, the adaptability of the environment and the reproduction processes. The only multiplication in α -state became a complex diversity for optimal adjustment to life, optimizing the energy consumption of the life-processes. In this is a phase of evolution, avoid the poisoning direct oxygen exposure mitochondria was integrated into the cell. Mitochondria became the "power plant" of the cell, making oxidative ATP production with a complicated cycle but in a massive number of these energizing molecules.

Szentgyorgyi [35] described the life evolution on a cellular level with the interplay of α - and β -stages. The life of

complexly organized living organisms based on their cells in β -state. The cell-division of this organism integrity became controlled. Due to the cooperative intercellular forces are slack in fission, there are inherent autonomic actions motivate the cellular division. Its control is mandatory to keep the system functional during the production daughter cells when a part of the structure should be dissolved and rearranged. The cellular status in the division is α -state, which locally terminates the cooperative complexity.

The α -state is the minimal conditional status of life when the cell completely concentrates on its fate. The complexity of life could easily be transformed into this basic state when the network is broken; the system becomes unstable, parallel with the forming of independent stable cells in α -state [76]. The cells in β -state are cooperative, energizing themselves with oxidative metabolism provided by their mitochondria. Their division should be strictly controlled by the networking cells and dynamic processes.

Normal cellular division (transforming locally the β -state to α -state) could be regular and irregular, depending on the reason which forcing it. Replacing the elder cells with young daughter cells, maintaining the cellular homeostasis is a regular process renewing the system working optimal, changing the weak-points of the network. When the cellular division is forced, constrained (e.g. reparations, wound-healing, even the embryonic development, etc.), the network tries to re-establish the homeostatic situation, regulating the processes with negative feedback control. Than α -state of cells form again, cells in β -state try (at least partly) devoted to producing the missing cells from the network, giving up their collective behavior. The remaining part of the collective network stabilizes the cooperative state and fixes the newborn cells from their α -state to β -state (Figure 3). The stability is broken by fission of the individual cell and again it turns into the α -state.

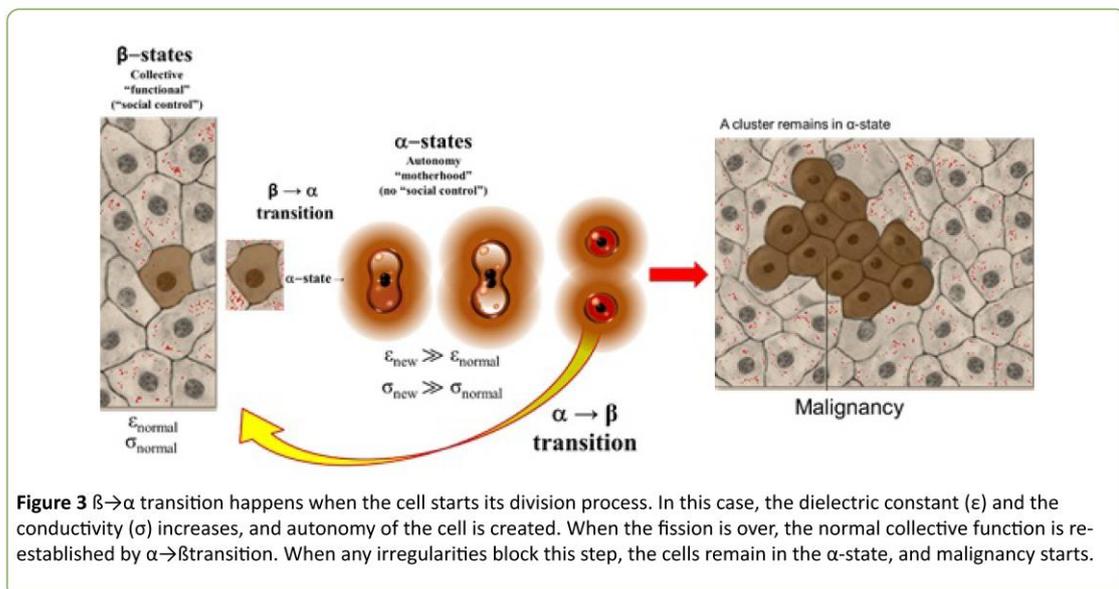


Figure 3 $\beta \rightarrow \alpha$ transition happens when the cell starts its division process. In this case, the dielectric constant (ϵ) and the conductivity (σ) increases, and autonomy of the cell is created. When the fission is over, the normal collective function is re-established by $\alpha \rightarrow \beta$ transition. When any irregularities block this step, the cells remain in the α -state, and malignancy starts.

Discussion

The local circulatory disturbance causes permanent oxygen deficiency, which activates the anaerobic ATP production of the involved cells. This low-efficacy production should be intensive enough to energize the higher demand of the neoplasm. This increased transport intensity requests larger active surface area at the plasma membrane. Enlarging the active glycolytic transport could happen by broken cell-junctions, increasing the effective glycolytic surface of the membrane by free surfaces. This process blocks the natural collective behaviour of the cells. The high metabolism of the forming cancerous cluster forces the neighbouring cells intensify their metabolic demand, (bystander effect) due to the redirected glucose transport from the healthy to the neoplasms. The anaerobe environment starts to be permanent and enlarging dynamically. The lost junctional connections of

the cells create compulsory proliferation like Szentgyorgyi described it with the α -state. This is a typical precancerous state of the cluster of the involved cells.

In general, the higher energy-transport to an organ by sports activity or by other temporary high load of the actual function does not mean uncontrollable higher energy consumption of the cells involved. The limit is the actual energy distribution of the healthy transport network. The secondary network (cellular connections) is responsible for the collective organization of the cells in the organ. Consequently, the blockage of this secondary network blocks the collective behaviour too. The cancerous cells have mostly autonomic character, and the consequence of this is their proliferative behaviour.

The increase of the transport network is simple due to the growing mass of the organ. The neo-angiogenesis formally

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satisfies the demand of the growth, which could be explained by allometric evolution [77].

Due to the permanent hypoxic conditions, the blood tries to buffer the situation (electrolyte homeostasis), its pH grows and could deliver more oxygen than before. However, this extra oxygen probably supports the cells at the peripheries of the neoplasm, supplying the accelerated metabolism of the area. The enhanced metabolic activity is a direct mechanism of the growth of a neoplasm. The process will be soon anaerobic, which according to the Occam-razor [78], could dominate the metabolism by its simplicity compared to the more complicated Krebs-cycle.

Transport properties

The control of the balance of β - and α -states acts probably via the electromagnetic route [79]. The process to start division and complete it by networking to the neighbors has extreme energy needs. The transport of electrons in the internal signal pathway of protons in most of the transports. The electron is transferable in a chemical way; however, a fast hydrogen transmitter with low dissipation is necessary. This process is allowed by the structured water in the living state [80], which is semi-crystalline [81].

Mitochondria are shielded against the direct oxygen flux by the host cell. Its proper function supposes than an effective proton transporter which transports the hydrogen from the mitochondria to a more oxygen-rich part of the cell. The effective proton transport is driven by the active proton pumps energized by ATP (produced by mitochondria) as well. The proton alone does not exist in aqua-solution, it associates with a water molecule and could be transported only by a slow diffusion to the proton pumps. Having quick, effective proton transporter with small energy dissipation is necessary, which is simply the ordered water [78], which could transport the proton with high speed.

The monomer water molecule has a simple tetrahedron structure, which is slightly asymmetric by the two proton occupied positions and two lone pairs. However, the simple water has a rather complex structure in the bulk conditions [82,83]. The stochastic proton migration in hydrogen bonds makes the bulky water collective, [81]. The solid water (ice) has hydrogen-bridge connections over the entire volume [84]. The entire bridge bonded ice turns to water by the first kind of phase transition, but only a fraction of the bridges broke, about every seventh, which was approximated from the evaporation and melting heat ratio ($W_e \approx 2256$ kJ/kg and $W_m \approx 334$ kJ/kg). Remarkably, a high number of hydrogen bridges exist even at the boiling point of water [85]. In fact, the water is always a mixture of two phases [86,87]: disordered, highly dynamic, mainly monomer and ordered, clustered ones (the clusters could even have various structures, including an entirely closed clathrate with icosahedral symmetry [88]. The statistical, stochastic transformations of the phases make the water complex. The simple bifurcative phenomenon (the proton-chare is oscillating between the two possible positions) of the hydrogen bridges. The charge transfer of such oscillating bonds could be very different depending on the dwelling in the

different states (the oscillation in general chemical bonding could be multi-state, not necessarily bifurcation only). The generalized solution of the bifurcative phenomena in living materials was worked out earlier, [77]. The ordered water was supposed to account for as much as 50% of the total amount of water in the living bodies [89], but the systematic investigations showed more of it [90,91].

Rearranging the water structure requires energy [92]. The energy intake took for the change of the structure, like the way, when water boils, the energy is massively supplied into the system, but the temperature is unchanged, fixed in 100°C. This drastic change (phase transition) in the structure of water modifies its physical properties (e.g. its dielectric constant) without changing its composition. It is a microscopic reordering in the water.

The hydrogen ion can be transported by hydrogen bridges. This high-speed and low dissipation of the transport propagation is based on Grotthuss-mechanism [93,94], where the proton can tunnel (jump) from one water cluster to another bridged by hydrogen bonds. The lifetime of H_3O^+ (hydronium ion) is rather small ($\sim 3 \cdot 10^{-12}$ s) so the speed of proton transport by Grotthuss-mechanism is approximately ten times higher than that by diffusion.

The Grotthuss-mechanism is, in fact, the propagation of ionizing of a water molecule. The dissociation and recombination steps are altered in "traveling". The recombination-dissipation is a quantum-mechanical process; in principle, it is free of dissipation [95]. However, it has temperature dependence, and the vector potential is also able to modify the quantum states of the water [96,97], which could modify the chain processes.

As a consequence of malignant changes, the metabolism gradually favours the fermentation method (host cell performs the task instead of the blocked mitochondria). The metabolism is completed in the aqua-based electrolyte, and so its input and end-products are ions. In one side the molecules are involved in the oxidative cycle, like $6CO_2 + 6H_2O \leftrightarrow 12H^+ + 6CO_3^{2-}$, while fermentation happens like $2CH_3CHOHCOOH \leftrightarrow 2CH_3CHOHCOO^- + 2H^+$. Equal proton production ensures the inert electric state of the solution, which fulfilled by more intensive fermentation and at the end the negative ions differ, the rapid growth of complex lactate-ion concentration increases its osmotic pressure. The unchanged pressure during the reaction increases the dissolvent monomer water, solving the ionic products in non-ordered water. Various malignancies show the change of water clusters to disordered monomers [98-100]. Consequently, the concentration of ordered water in cancerous tissues is smaller than in their healthy counterpart. This process weakens the networking signal between the species and between the cells. The hydrogen ions have reduced activity due to the weaker ionic transmitter. The intracellular pH decreases together with the weakened proton gradient in mitochondria, suppressing the efficacy of ATP production. The membrane potential of mitochondria grows trying to compensate the lowered proton-gradient. The higher potential of mitochondrial membrane lowers its permeability, decreases the mitochondrial permeability transition (MPT).

The process decreases the apoptotic availability where MPT has a crucial role, [101,102] Indeed, cancerous cells have high mitochondrial membrane potential and low K-channel expression [103]. The developed resistance to apoptosis supports the ATP production by the fermentative way to supply enough energy to the cell. Production of extra HSP chaperone stress proteins induced by the increased free ion concentration in the cytoplasm. This process also needs an extra amount of ATP. The growing HSP protection is anti-apoptotic, and on this way, a complete block of apoptosis could be developed.

The processes are interconnected because the increase of the fissionability lowers the membrane potential, which again decreases the order of the water structure. The developing disorder raises the dielectric permeability (ϵ_r) of the water [35]. The higher ϵ_r effectively decreases the cell-cell adhesion, creating a positive feedback loop causing the cell-division and the uncontrolled proliferation [35]. It was detected as one of the signs of the tumor by NMR. The observation is also proof for Szentgyorgyi's bioelectric considerations [104,105] of cancer development.

The primary effect of the malignant deviations connected to the changed metabolic pathways. The balance of the phosphorylation and fermentative metabolism determines the balance of the cellular collectively and cellular autonomy. The cooperative or non-cooperative conditions balanced by the energy exchange and signal transport between the cell and its actual environment. The variation of the metabolic pathway changes the intracellular transport too. Increased amount of heat is liberated by intensive energy flux of the fermentative metabolism, which builds up a temperature gradient between the extra- and intracellular electrolytes. The growing temperature could reach a critical threshold of the heat flow, turning the heat-flow from conductive to convective [106], which is the phenomenon of the Bernard instability [107]. The ionic flows through the cellular membrane promoted by the convective heat flow, which increases the intake of glucose. This again supports the fermentative metabolism and changes the intracellular circulations [108,109]. The mitochondrial oxidative metabolism is down-regulated by these complex processes.

The energy loss in optimal biochemical ATP production is large. The glucose liberates 2881 kJ/mol in the phosphorylation (aerobic) process, but the produced ATP is only 1159 kJ/mol; the efficacy of the process is $\approx 40\%$. The "missing" value (1722 kJ/mol) wasted by the non-used chemical species and by the heat, which makes a body temperature independent from its environment.

From an energetic point of view, high-intensity mass-production of ATP is necessary to fulfill the strong energy demand of the permanent proliferation of malignant cells. The higher metabolic rate could be routinely measured by positron emission tomography (PET) [110]. The reaction rate of the simple fermentative reaction could be 100 times quicker (approximated from the positron annihilation data) [111] than the oxidative way. However, the oxidative way has an at least 18 times higher efficacy due to the ATP amount at the end.

The result is funny: the simple, primitive fermentative process produces at the end six times more ATP during a given period than its high efficacy, but there was too complicated an oxidative counterpart, which is why the extreme situations constrain the anaerobe metabolism. The balance is broken at out of normal homeostasis situation. The glucose demand in fermentation at a given time is higher by two orders of magnitude than in oxidative phosphorylation. The high glucose demand needs intensive glucose transport, as well as the end-product (lactate) also has to be transported away. The low efficacy of fermentation produces more heat in the lesion, and the locally higher temperature promotes the diffusion processes, as well as inducing higher blood perfusion and easier permeability of the vessel walls.

The massive and speedy demand for energy (in fact glucose), should be supported by the transport availabilities. The intracellular transport has numerous restrictions of ATP energy-transfer [112] also; the diffusion has very complex heterogeneity in the cytosol, as described by Levy's flight [113]. The anomalous diffusion in the cytosol needs support from the cytoskeleton, [114,115] which in the case of proliferative conditions partly of completely collapsed [116]. Consequently, the demand for the massive energy supply from mitochondria has numerous limitations, and in fact favours the simple and extra speedy anaerobic glycolysis, which is directly produced in the place where it is used, in the cytosol. A further challenge for the transport is the collapse of the water-hydrogen-bridge network by the lowered membrane potential of malignant cells. The missing Grotthuss mechanism, in this case, limits the diffusivity of protons, and the disordered electrolyte limits the diffusion of any ions [117].

The picture, however, is not as simple as it looks. Many malignant tumors have massive aerobic, oxidative phosphorylation in mitochondria, together with more or less anaerobic ATP production as well. This apparent controversy may be explained by differences in tumor size, hypoxia, and the sequence of oncogenes activated [118]. This picture has a similarity to sport medicine, when the prompt energy supply to the muscles in the sprint-sports are solved by the anaerobic fermentation [119]. However, when the extra need is over, the normal aerobic function is re-established. In tumors, however, the load and the consequent need for ATP is never terminated; instead, it exponentially grows in time.

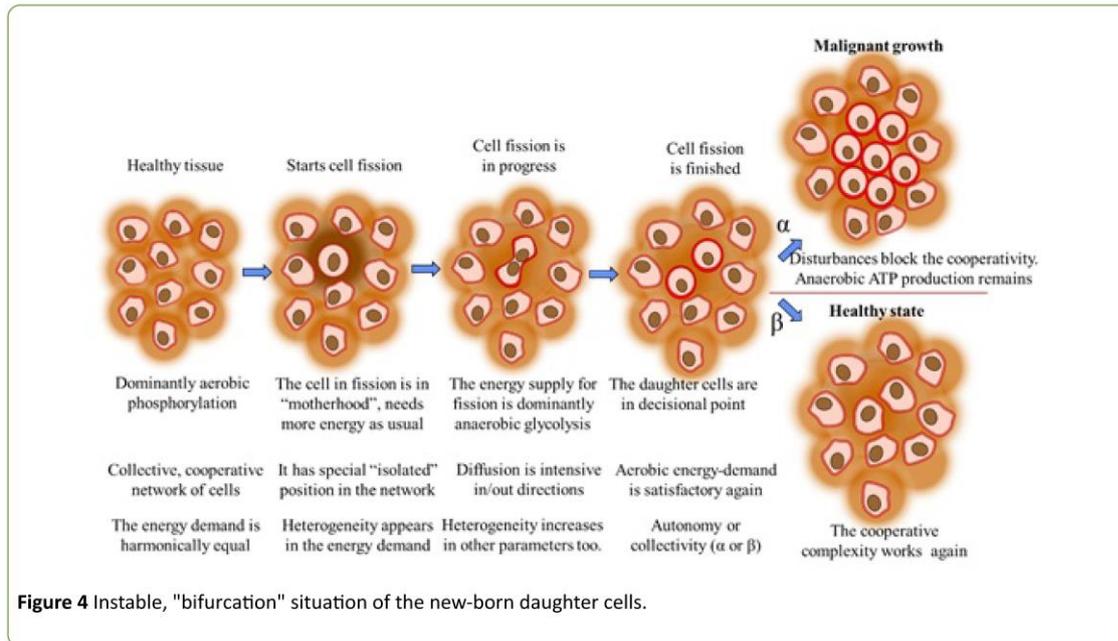
Generalisation

The simple comparison could be made between Szentgyorgyi's α - and β -states and Warburg's metabolic pathways approach. The electron transport and change of electronic properties of the tissues supposed by Szentgyorgyi in malignant transformation [35,120,121], and the mitochondrial dysfunction proposed by Warburg [36,37], have a common origin. The oxygen-deficiency and in consequence the actual energy flow are in the center of both considerations. Szentgyorgyi's theory α -states well corresponds with the dominance of the fermentative metabolism in Warburg's theory, while the normal phosphorylation of mitochondria shows common with β -

states. The α -state prefers intensive anaerobic ATP production, while β -state works with perfect mitochondrial function.

Cells in any stage work in both the possible glucose utilization, only the dominance of activities defines their state. The balance of the ATP production could be described by the cell status of cooperativity ($\alpha \leftrightarrow \beta$); or by the metabolic process (anaerobic \leftrightarrow aerobic). Both formulae define what is the acting the part of metabolic energizing (host-cell \leftrightarrow mitochondrion). The meaning of both theories expresses the

actual energetic state of the cell. The energy flux and cooperability are tightly interrelated, the growing energy-flux weakens the cellular cooperativity, makes the arrangement more individual, autonomic. Oppositely, the low energy flux creates cooperative cells which are forming complex, sophisticated networks, and they are highly effective in their energy production and their adaptation to changing environmental conditions (Figure 4).



The concentration of the components determines the amount of dissolvent in the aqueous electrolytes of living objects, promoted by the order-disorder transitions of the cytoplasm as well as depend on the osmotic water flow through the cell membrane. The outside stimuli inside enrichment of a component could produce a misbalance of ionic concentrations, which could be a constraint or a normal aging process too.

The decisional order-disorder transformation of water changes the diffusion of the hydrogen ions, which mirrored in the dielectric constant of the medium [77]. The disorder increases the dielectric constant of the aqueous solution, increasing the ability of electrical isolation. On this way, the promoted charge-division and the suppressed polymerization activity creates positive feedback to the fermentation processes. The actual balance of ATP production is broken, the fermentation became important; the cell turns to α -state. Usually, it is not a malignant transition, which happens with any regular cell fission too. Fermentative ATP production characterizes the "motherhood" of the cell in the division, energizing the "delivery" of the daughter cells. The "individualism" of the mother-cell is due to its extremely increased energy demand during the fission process. However,

after the creation of the daughter cells, the previous healthy order should be re-established. The motherhood is in the "infancy" of the evolution, having autonomy instead of common networking. Their "infancy" at the start is standard like the "babyhood" is normal after deliveries. However, it is not normal when it is too long. The "babyhood" must be transferred back to collective order after finishing the fission. When the daughter cells do not find the way back to the cooperability, the cells are "frozen" in the uncontrolled proliferative α -state. The frozen state is a defect of the complex controlling mechanism [35], which correlates with the single "renegade cell" concept [106], Weinberg describes cancer as a long process to produce "a renegade cell" as an ancestor of the billion-cell group called cancer. Epidemiological research showed the complexity of the developing of cancer. It is demonstrated on a statistical basis that at least five different coincident mutations are involved in the development of malignancy [67].

One of the driving forces to re-establish the β -state after the division of the cell is the reduced demand of energy-flux. During the cell-fission, tremendous energy should supply the process, which spends to produce many proteins and other cellular elements (lipids, enzymes, etc.). The conditions of α -

state fit for this demand. When the fission finishes, the energy consumption lowers but remains doubled compared to the single original mother cell. The dissolvent capacity is enough supplying the new cells. The overall loss of the cellular energy demand acts like cooling phase transition from liquid to solid, (disorder-order transition). Similar phase change happens in this case as when the division was started, the only difference is the opposite direction of the process. The proton bifurcation in hydrogen-bridges reorganizes the order without opposing driving force; even the neighboring environment supports this arranging process.

The new-born cells are more negatively charged than the host cells. This negative state vanishes by the gathering of the elder cells in the collective network. After the cellular division, the daughter cells separated. The larger overall membrane surfaces of the separated volumes (double cells) limit the intracellular dynamics and restructure it for the final cytoskeletal form. The increased surface area down-regulates the heat-flow through the cellular membrane and turns the energy-exchange back from convective to the conductive [66]. The intensive diffusion of the large-molecule like glucose is not supported ever more in the rearranged conductive situation, so the slow but massive mitochondrial ATP production became regular, the normal homeostatic conditions will dominate again.

The repair mechanism could be blocked or limited. An obvious reason could be the permanent irritation by a mechanical, chemical or physical (e.g. ionization) factor. However, in the case of any damage, some cells produce such a functional state which repairs the actual dysfunction. The growth- or repairing-phase special genes are activated to produce such cells, which repair the damaged tissue [69,68]. Growth and reparative factors are released [71,72]. Proto-oncogenes became active in the area [122], collecting stem cells to the wound [73], which are repaired by their differentiation [123]. After the process, all of the activation genes are down-regulated, or tumor suppressors are activated [124], and the normal homeostasis became re-established. In the cancerous state, the repair conditions are not blocked after finishing the reparation process itself. Permanent reparation demands depletion of the available stem cells [125,126], and will be more emphasized the third way to repair: the proto-oncogenes are activated, and malignant transformation could happen to induce clinical cancer [127]. The malignant transformation of the wound makes secretion of proto-oncogenes [128-130], and intensive capture and stimulation of the stem cells from other places [131,132], the cancer cells produce repair [133,134], molecules increasing the stem-cell concentration in the cancer tissue [135].

When an island is formed from the cells in the α -state in healthy tissue, then current starts between the island and the tissue inducing cell migration and proliferation. This current is called the injury current [136]. The process is essential in wound healing [137], and the current is gradually limited by the healing wound. In the case of a cluster of cells in the α -state, it has positive feedback, increased by time, the grouping of the new-born cells, having no possibility to neutralize

themselves to the potential level of the normal surroundings. This process never heals this "wound," even the opposite, it grows. This process has extra high energy demand, so the massive ATP production of the fermentative way is preferred and became irreversible in this stage.

The boundary of the cancerous tissue embedded in its healthy neighborhood is not sharp and not well defined. The smeared border of the cancerous tissue is also the boundary of the different biological, chemical and electric processes, and is the interface of special transports (Figure 5). The glucose influx and lactate efflux are due to fermentation, which causes low pH in the volume; while the injury current is due to charge inhomogeneity. The high intensity of low efficacy fermentation creates a higher temperature in the tumor than its neighborhood, inducing heat-flow from the tumor.

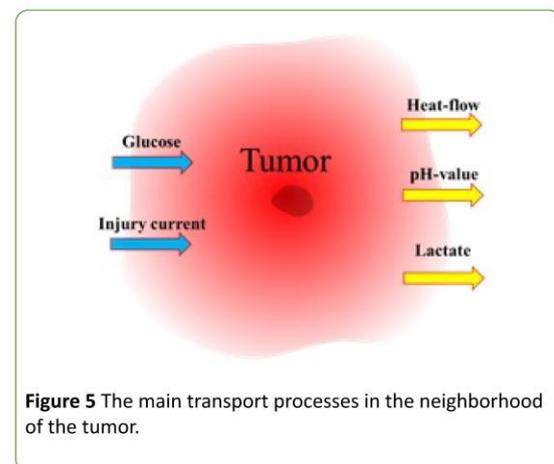


Figure 5 The main transport processes in the neighborhood of the tumor.

Despite the huge variety of tumors and healthy tissues, the allometric scaling (biasing) [138] could be discussed in a universal frame, [139], even on the subcellular energy consumption as well as even the mitochondria and the respiratory complexes [138]. Naturally, these differences are not based on independent properties, their connections and interactions are important governors over the process of the expansion of tumor volume, their complexity controls the dynamism and actual state of the malignancy. The interplay of the conditions of ATP production and the polarization ability of the cells are well connected with each other and with the pattern forming of the developing structures [140,141]. The method of ATP production influences the ionic concentration and pH in the extracellular electrolyte, which naturally affects the polarization properties of the media and interacts with the decreased membrane potential of malignant cells while the conductivity of the volume will also be modified. The diverging scaling is connected to the high metabolic rate where the scaling exponent approaches the unity which induces high vascularisation and intensive cellular proliferation at the frontiers of the different tissues. Due to the more negative average charge of the malignant tissue, a definite fluctuation of the electric field strength is also developed on the boundaries of the tumor.

The scaling exponents could follow changes in the metabolic processes, [142]. The lowest average scaling exponent shows the surface-volume ratio of $\frac{1}{3}$. The dominantly anaerobic metabolism of benthic invertebrates (n=215) have exponent $p_{\text{mean}}=0.63$ (near to $\frac{1}{3}$), [143]. However the animals (n=496) having dominantly mitochondrial ATP production have and exponent $p_{\text{mean}}=0.74$, (near to $\frac{1}{2}$), [140]. Moreover, the scaling of the metabolic activity is different in mitochondrial or non-mitochondrial metabolism. The normal mitochondrial metabolism performs the Krebs cycle, and its scaling exponent is well distributed around $p=\frac{1}{2}$, [77,137], while the scaling exponent of fermentative respiration is near to $\frac{1}{3}$ [144]. Remarkably, the healthy mammalian cells and the mitochondria that are 5 orders of magnitude lighter, as the respiratory complexes (having further 5 orders of magnitude less mass than mitochondria) are fit well on the allometric scaling with $\frac{1}{3}$, [145].

A further interesting relation between energy flux and cooperatively is that, *in vitro*, the specific metabolic rate in the cultured cells (overall metabolic rate normalized on the actual mass) is constant [146] no scaling could be introduced. *In vitro* the practically infinite nutrients from the media electrolyte keep the cells autonomic; they are in α -state.

Conclusion

Warburg's effect fits well with Szentgyorgyi's theory. The dominance of anaerobic glycolysis in malignant cells characteristic for the autonomous α -state, while the proper mitochondrial function is connected to the collective β -states. Central consideration of both principles is the extra energy demand, which appears by quick and simple nonmitochondrial ATP production and in consequences the autonomy of the cells using this process. The phenomenon is like the increased ATP supply of the heavy load of muscles in some sports; however, that fermentative step is reversible, the ATP production will be mitochondrial when the energy-demand turns back to normal. This increased ATP production is not reversible in malignancy; the proliferative cells remain in autonomy (α -state). In this case, the lack of negative feedback (lowering the energy consumption) is missing. The huge variety of disturbances either genetic or environmental origin blocks the reversibility, the demand for extra energy growths by continued proliferation of cells.

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Why modulated electrohyperthermia (mEHT) destroys the rouleaux formation of erythrocytes?

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Why modulated electrohyperthermia (mEHT) destroys the rouleaux formation of erythrocytes?

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ABSTRACT

Our aim in this paper is to describe systemic observations of blood samples before and after modulated electrohyperthermia (mEHT) treatment, to clarify its systemic effect on blood. The method is also feasible to control the efficacy of the mEHT treatment process.

Keywords

oncothermia, rouleaux formation, erythrocytes, electric field, electrophoretic force, disaggregation, mice, human

INTRODUCTION

Observations and explanations of the rouleaux phenomenon have induced much debate since its discovery. Erythrocytes often form rouleaux-patterns (RP) caused by surface adhesion between them. This is a way to decrease the surface energy (Dirichlet-principle, [1]) connected to their surface area. The aggregation of erythrocytes is a prominent feature in humans as well as other species. The rheological parameters of blood are mainly the apparent viscosity at low shear rates and the red blood cell (RBC) sedimentation rate. The aggregation also correlates with oxygen consumption [2].

In vitro studies have shown that aggregation of blood increases as shear rate decreases. Aggregation also depends on hematocrit, the concentration of macromolecules in the plasma or suspending medium [3] and on the presence of high molecular weight polymers, such as plasma proteins or dextrans, which aggregate to form RP and rouleaux networks [4]. However, the circumstances in which aggregations occur are not well understood. Correlations of aggregation parameters with C-reactive proteins and fibrinogen were found in unstable angina, acute myocardial infarctions and bacterial infections [5].

RP has an important role in the hydrodynamics of blood. The viscosity of the suspension grows with the average size of the dispersed solids at a constant volume and concentration of dispersion. As a consequence RP could have a control role in blood-flow, as their presence limits blood-flow in the large vessels due to their viscosity, while smaller sizes could increase the flow in the capillaries.

The reason why a RP is formed in large vessels is that blood is not a simple (Newtonian) liquid but a Bingham-type [6], with a threshold value (shear stress, share rate) that starts the flow. In mathematical form it is

$$\tau = \tau_f + \eta D \quad (1)$$

where τ is the stress in the liquid, τ_f is the flow-stress and η and D are the viscosity and the shear rate respectively. The stress of the flow in the axis of the tube is zero and increases linearly to its maximum at the inner surface of the vessel. The tendency of bias towards aggregation increases with decreasing blood-flow in the venous network; the blood-flow tends to Bingham-liquids [7] by increasing deviation from the classical Newtonian liquids [8], (see figure 1). Blood rheology has a crucial role in RP formation, [9].

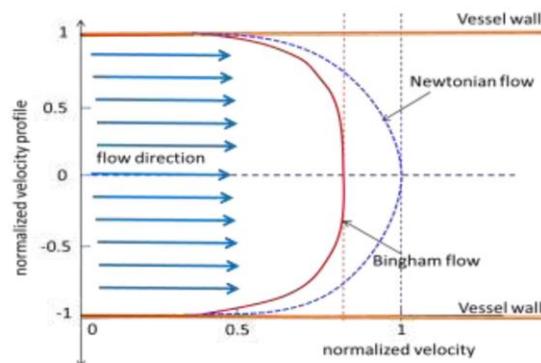


Figure 1. The blood-flow velocity profiles. Newton's flow and Bingham's flow (cork profile), depending on the various concentrations of erythrocyte aggregates and surfactants of filaments [10].

Geometrical criteria decide the RP and network of the aggregation [11]. The aggregates may branch, forming trees, and when RP grow large they may contain rings or loops and form network-like structures [12]. The shape of the erythrocytes in the RP is the function of their diameter [13] together with adhesion and area differences (see Figure 2) [14].

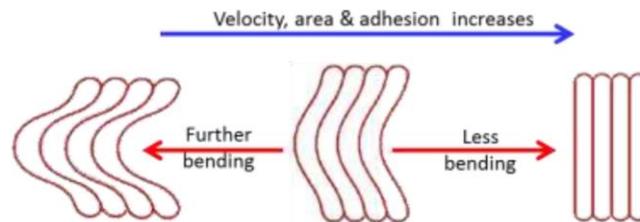


Figure 2. Bending of erythrocytes in the RP formations depending on various environmental and internal parameters.

The low shear rates in tumor vessels may facilitate RP formation [10]. However, despite the large shear rates present in microcapillaries, fibrinogen or synthetic polymer dextran content leads to enhanced RP formation, even at low concentrations of haematocrits [15].

Thrombocytes influence the aggregation of erythrocytes, which is enhanced by higher platelet concentrations [16]. The activation of platelets leads to clot formation, which is a double-edged sword; it is lifesaving in the wound healing process but on the other hand clot formation causes the majority of deaths in thrombus induced strokes [17]. RP formation correlates with inflammation states as well [18] and in this way it may also correlate with cancerous states, which we show below. The study of the electrical properties of red blood cells and their RP formation can contribute to immunohematology practice [19].

METHODS

The treatment was performed using modulated electrohyperthermia (mEHT, trade name oncothermia) with a special laboratory device for small animals (EHY110, Oncotherm GmbH, Germany). The method was an impedance based capacitive coupled, amplitude modulated radiofrequency treatment [20]. The carrier frequency was 13.56 MHz, the modulation was a time-fractal pattern [21]. mEHT selectively targets the rafts on the membranes of malignant cells [22]. The nano-selection is based on certain deviations in the metabolic-processes of cellular connections and in the organising patterns of malignant cells compared to their healthy counterparts. The cell-killing mechanism is connected to the intensive, but very local, nano-range energy absorption, which is selectively delivered by electrodynamic conditions.

Blood samples of nude mice were studied before and after the oncothermia treatment. The mice (Balb/C nu/nu) were xenografted with the human HT-29 colorectal carcinoma cell-line in both femoral regions symmetrically in the heterotopic subcutaneous. The electrode was flexible and the applied power spectrum and temperature plot are shown in Figure 3.

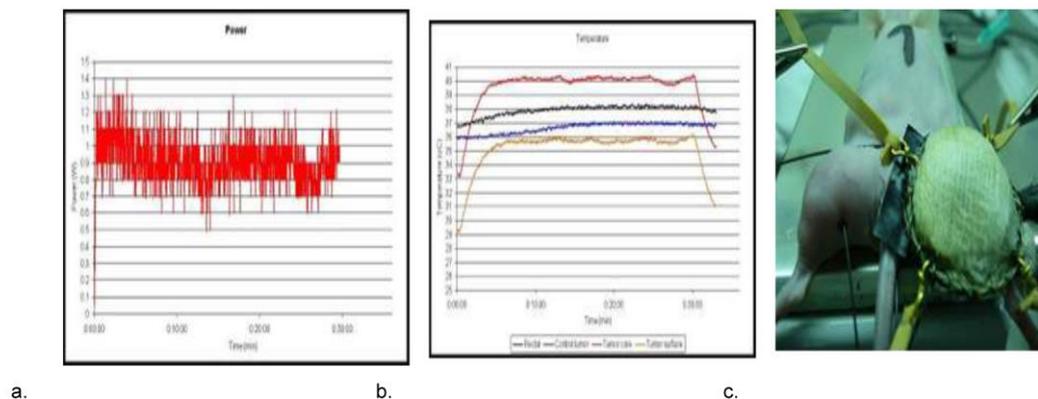


Figure 3. Typical experimental details from left to right: power control, temperature pattern and electrode arrangement

The mice (ten animals) are shown for reference in Figure 4. The treatment consisted of a single shot for 30 minutes, reaching and keeping 40°C constantly in the tumor, while the other tumor (always the left one) was not treated but instead used as a reference (modelling a non-treated distant metastasis in the animal.) Blood samples from the mice were carefully collected from the tails (venipuncture in the tail vein) of the mice under anesthesia.



Figure 4. The set of mice involved in this study

Blood samples from human volunteers were also collected. The human donors had suffered various malignant diseases. The human samples were peripheral, obtained from capillaries in the finger-pad. Samples of venous blood from humans were also collected for comparison. The blood collection was done immediately before and immediately after mEHT treatment, as well as being systemically performed during subsequent treatments in humans. The samples were freshly measured by dark-field microscopy (the slide-holder table was not heated). The pictures were archived using high resolution photo or video techniques.

RESULTS

Before the treatment, RP formations in blood samples were observed in 40% of the investigated animals (see Figure 5.) and in the majority of the human individuals. In all cases where the RP formation was found, the mEHT treatment changed the RP network and a large proportion of the samples were free of erythrocyte aggregates. This phenomenon was independent of the treatment localisation and also from the venous or arterial origin of the blood sample.

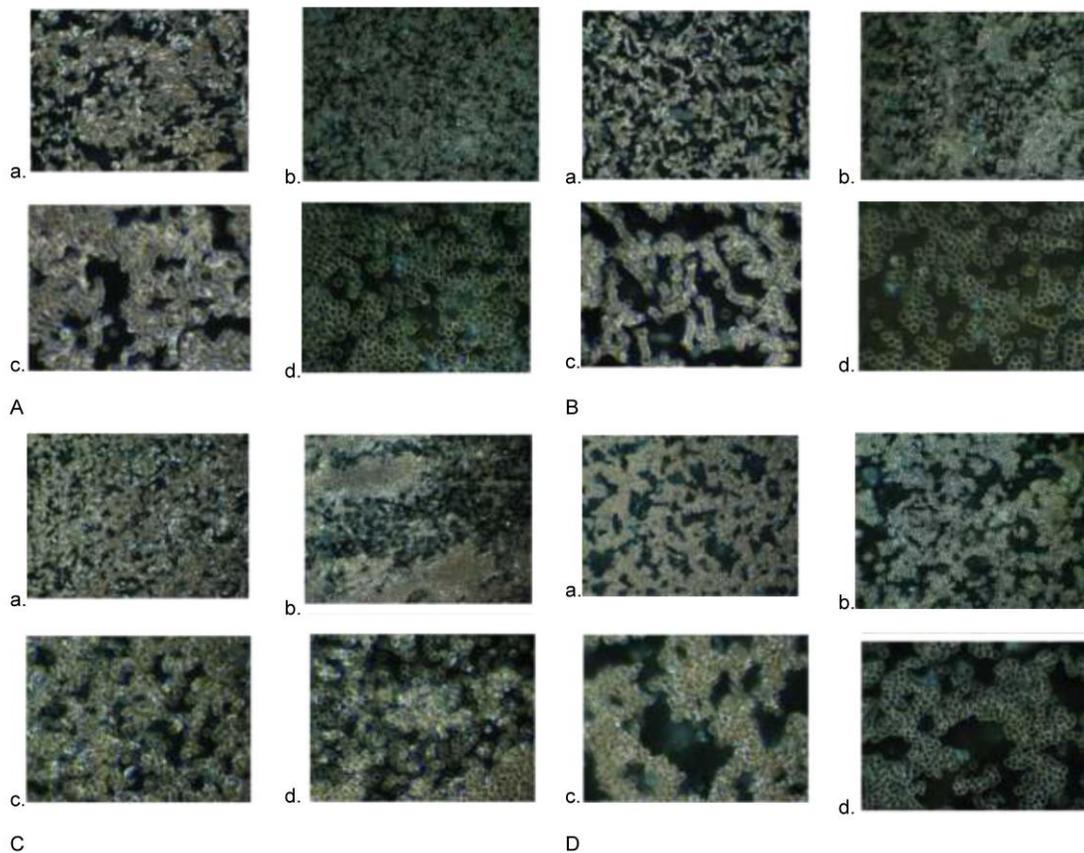


Figure 5. Mice identifications: A=2, B=3, C=6, D=7. Disaggregation of the RP in a HT29 xenograft before (a. & b.) and after (c. & d.) treatment, 100x (a & c.) and 400x (b. & d.) magnifications

One mouse (mouse no.4.) was inoculated with a PC3 human prostate tumor (from bone metastasis) cell-line; it also showed disaggregation, (see Figure 6).

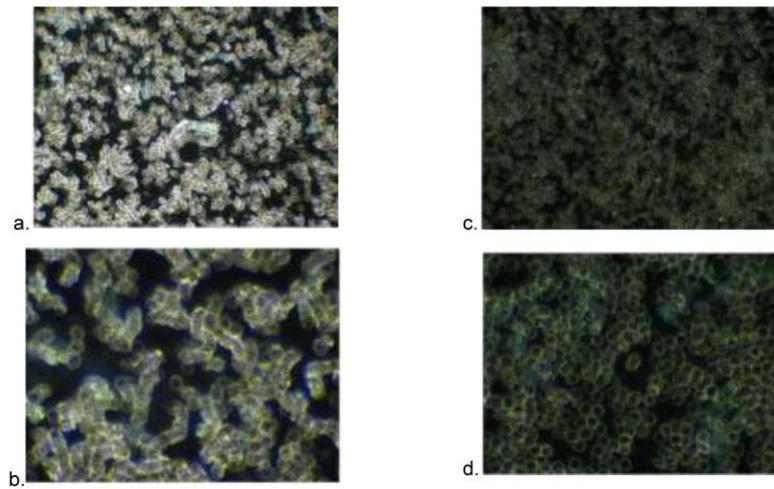
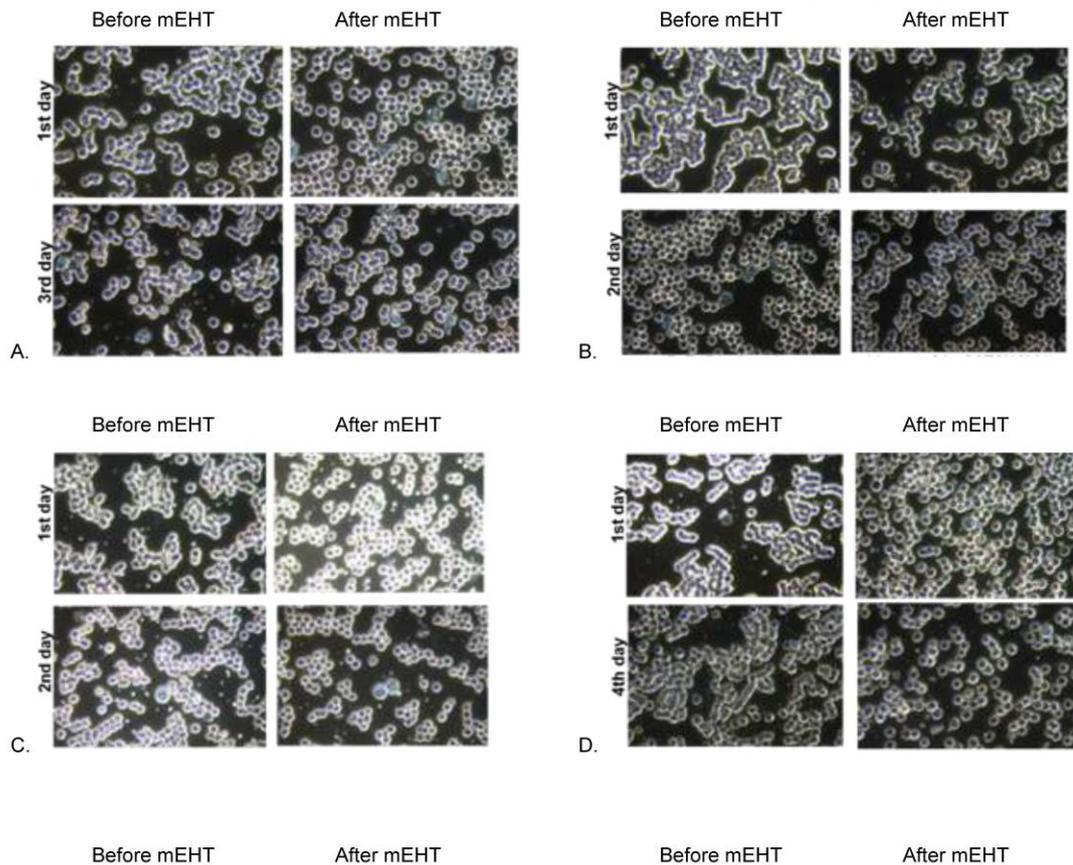


Figure 6. Disaggregation of the RP in a PC3 xenograft before (a. & b.) and after (c. & d.) treatment, 100x (a & c.) and 400x (b. & d.) magnifications

We observed the systematic distortion of RP formations in various human cancer cases, (see Figure. 7).



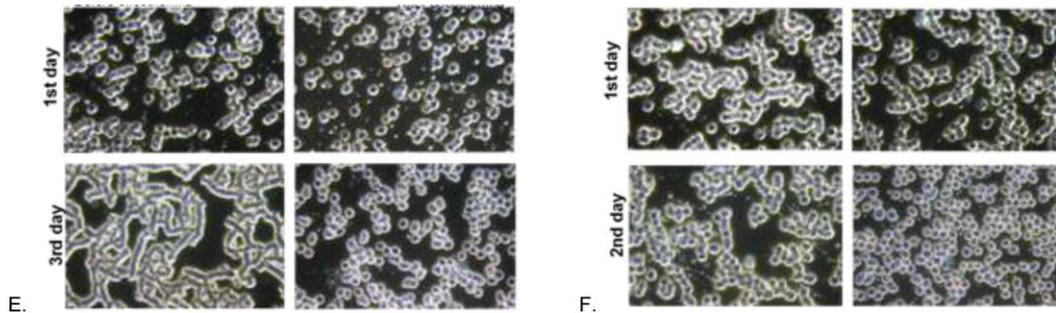


Figure 7. Blood samples of patients with various advanced cancer lesions. A=46 y old female, advanced metastatic uterus carcinoma; B=54 y old female, locally advanced breast cancer; C=20 y old female, advanced metastatic ovarian cancer; D=61 y old female, advanced metastatic breast cancer; E=70 y old female, advanced non-Hodgkin lymphoma; F=49 y old female, advanced metastatic breast cancer.

DISCUSSION

The movement of an object caused by a spatially non-uniform electric field is the phenomena of dielectrophoresis (DEP), operating by the well-known dielectrophoretic forces created outside the electric field (it differs from the interaction of non-uniform electric fields with dielectric objects, which are suspended and free to move in a conductive medium.) In inhomogeneous alternating electric fields, the time averaged force $\langle F \rangle$ that acts on a homogeneous dielectric particle can be expressed by the real part of the average of the product of the induced dipole moment and the gradient of the complex conjugate of the external field [23]. Based on this model calculation, the dielectrophoretic force from the external radiofrequency current grows by the number of erythrocytes in the RP line, (see Figure 8).

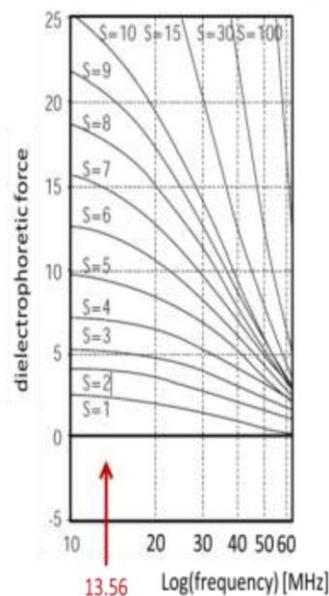


Figure 8. S=number of the erythrocytes in the RP (Modified after [23])

Keeping the RP stable, the adherent internal forces in the RP compensate for the external forces, which are measured by the use of atomic force microscopy based on single cell force spectroscopy (SCFS) [24].

The distortion of the erythrocyte aggregates could be well explained by the action of the dielectrophoretic forces when they exceed the internal adhesion. The RP are dielectric particles in an aqueous electrolyte. The inhomogeneous field polarises them together with their host matrix, the electrolyte. The polarisation creates different charges at the ends of the RP-chain, as well as in the electrolyte (see Figure 9).

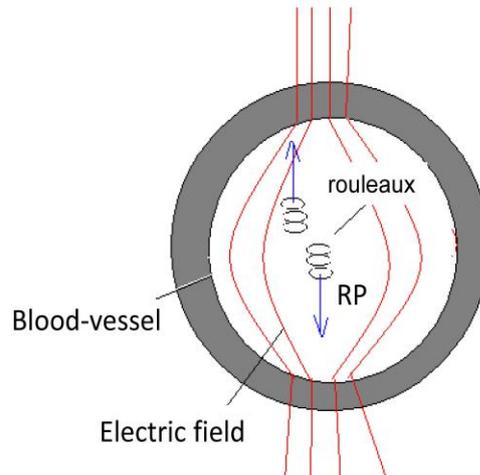


Figure 9. Effect of the outside electric field inside the blood vessel

The movement of the RP depends on the charge values at its ends and in the host electrolyte. The force depends on the dielectric properties of the RP, which is also sharply frequency dependent [25]. The relative dielectric permittivity in low frequencies (10 kHz region) could be as high as 10,000 in stationary flow; however, in turbulent cases it is only half of this value. In high frequencies this value drops to around 100 and does not affect the stationary and turbulent flow. The conductivity behaves in the opposite manner, small (~3 mS/cm) at low frequencies (~10 kHz) and in higher RF (such as 13.56 MHz, which was used in our study) it increases to 8 mS/cm. The good conductivity allows longer RF current flow along the vessel tubing. The inhomogeneous field polarises it together with its host matrix, the electrolyte. The polarisation creates different charges at the ends of the RP, as well as in the electrolyte, (see Figure 10). The movement of the RP depends on the charge values at its ends and in the host electrolyte.

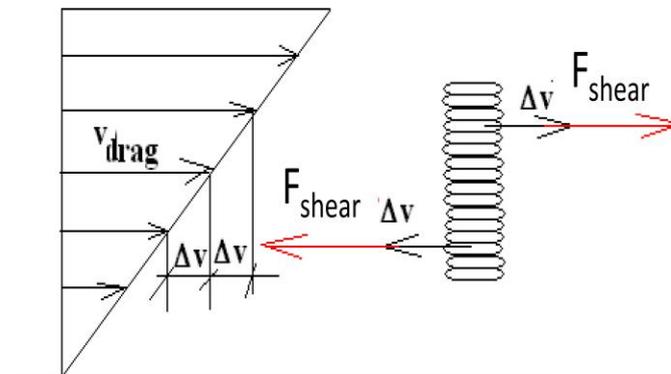


Figure 10. The shear forces, by dielectrophoretic effect, twist the RP

Dielectrophoretic force has some specialties in the 13.56 MHz region:

1. maximal polarisation exists in the axis of the RP,
2. the dielectrophoretic force grows with the length of the RP,
3. the RP fixes its direction from low field-strength to high,
4. the maximal polarising direction in short RP is radial.

The effect of mEHT is based on the rules above. The long RP directs itself to the field-direction (rule 1.) and moves from the cork-flow to the shear flow region (rule 3.). This tendency is based on the length of the RP (rule 2.). In the region of shear-flow (Newton's flow) the middle of the RP moves with speed v_{drag} . Consequently, its ends have opposite drag-forces and so the shear destroys the long RP, (see Figure 11). The small parts of the destroyed RP turn perpendicularly, with their axis to the outside field, so they have no further distortions (rule 4.).

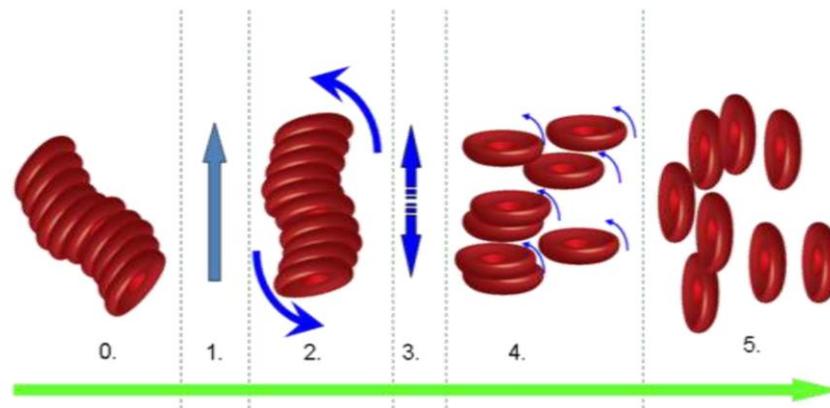


Figure 11. The RP is effectively destroyed by the gradient of EF. 0. →Original RP, 1. →EF, 2. →EF turns the RP, 3. →dielectrophoretic force breaks the adhesive connections, 4. →dielectrophoretic forces turn the erythrocytes, 5. → the aggregates of the RP are dissolved

CONCLUSIONS

In blood specimens where RP formations of erythrocytes are observed, mEHT may dissolve the aggregates. Measurement of the oncothermia effect on the RP phenomena could lead us to a simple control for treatment efficacy, but the present data cannot provide definite conclusions and further investigations are in progress.

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Author' biography with Photo



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Personalised Dosing of Hyperthermia

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Personalised Dosing of Hyperthermia

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Abstract

Objective: Our objective is to show the superiority of the membrane selection and connected energy dose fixed via personal sensing.

Method: Hyperthermia in oncology involves heating malignant cells and causing thermal damage in an attempt to destroy them. This could be immediate (necrotic) cell-distortion and ignite natural cell elimination, like apoptosis or autophagy.

Two concepts determine the dose of hyperthermia: (1) isothermal tumour heating, homogeneous tumour temperature, which is used for necrosis based cumulative equivalent minutes (CEM), and (2) inhomogeneous heating of the tumour following the heterogeneity of the lesion itself. The personalized dosing used by oncothermia is heterogenic, it selects the membrane rafts of malignant cells that sense temperature on a cellular level targeting the nano-clusters of transmembrane proteins. The method uses the standard specific energy dosing controlled by personal sensing of the treated patient maintaining homeostatic control through gradual step-up heating process.

Results: The nano excitation is thermal (fits to Arrhenius plot), and acts directly on the membrane of malignant cells. The homeostatic physiology reactions do not suppress the effective hyperthermia action with this heating. The stress reactions could be more regulated, the vasoconstriction and vasodilatation effects roughly compensate each other. This allows a clear measurability of the dose of the treatment: instead of the temperature based cumulative equivalent minutes (CEM) it uses absorbed energy controlled by the RF-circuit. Due to the small mass of targets the applied power is low, the energy-sink surface cooling is fixed to homeostasis ensuring the accuracy of the energy-dose and improving the safety of the hyperthermia method.

Conclusion: The nanoselection of malignant cells via oncothermia allows us to return to the dosing "gold standard," which is also applied in radiotherapy. This energy-based dose is personalised with accurate step-up heating taking the wash-out time and the personal sensing of the patient into account.

Keywords: Hyperthermia; Oncothermia; Dose; Personalisation; Heat sensing; Step-up heating; Homeostasis; Fight-or-flight reaction

Introduction

Hyperthermia as an oncologic therapy has a long history. Although the treatment has a long history; hyperthermia has only recently become accepted as a valid option. Sceptical opinions in connection with hyperthermia dominate the clinical practice, and the sometimes "miraculous" results of hyperthermia raises the scepticism even higher; the "miracles" are naturally out of the realm of our current scientific approaches.

The goal of hyperthermia in oncology is, of course, to eliminate malignant cells. The tool has the thermal effect, which could be provided by various kinds of energy absorptions [1]. It is considered a complementary therapy. Its clinical applications mostly concentrate on various chemo- and radiotherapies allowing the physiological feedback to support these therapies through heat flow and intensified blood flow. This, in turn, affects drug delivery and oxygenation in chemo- and radiotherapies [2].

We know from everyday practice that the difference between poison and medicine is merely the dose. Dose is an important factor for efficacy, safety and reproducibility, too [3]. In the case of medication or radiation oncology, we know dose units as quantitatively measurable values in mg/m² or J/kg in chemo- or radiotherapies, respectively. The main challenge in the clinical use of hyperthermia is the lack of a definite dose concept; consequently, the repeatability of a given therapy gives way to serious doubts.

In hyperthermia, temperature is overemphasized as a dose; since it is not a quantitative parameter. Rather, it is a quality that creates equilibrium spread in the system. In chemotherapy, cytotoxic remedies could have very serious side effects, and the role of their safety has been emphasized. Chemotherapy doses are determined by safety (toxicity) limits, independently of the individual person or the size of the tumorous target. The result (efficacy) is measured a definite time later, when it is measurable or symptoms of toxicity (by personal variability) appear. Then, the chemo dose is modified or a complete change of medication is applied. The actual dose varies then, considering the actual patient and the specific situation.

When the medication demonstrates no side effects (or the side effects are controlled) in the individual, then the dose, according to the safety role, has no upper limit. When the dose is limited but it is too high for the patient due to the biovariable poisoning limit, then the actual applied dose is lowered according to the needs of the particular patient.

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The dose concept, which is applied in ionising radiation (Gy), causes problems in non-ionising cases: the provided energy naturally spreads despite the careful focusing of the beam. Applying a certainly local, invasive heating (ablation), the time of heating is short; the provided specific energy could characterise the process. However, in the case of non-invasive local applications, the physiological feedback (thermal homeostasis) becomes active and spreads the heat during the relatively long treatment time. After this longer time, the thermal homeostatic control becomes active and vasodilates the arteries to maintain homeostasis. The characteristic reaction time of the blood flow (wash-out time) is approx. five to seven minutes in humans [4], which is the threshold of using the absorbed energy as a controlling dose. Over this limit, thermal homeostasis is active; the actual heat exchange of the target with its environment determines the actual heating process (Figure 1). The intensive blood flow could increase tumour growth, as well as the risk of metastases, suppressing the possible curative effect.

However, like everything in the complex networks of negatively feedback controls, the high blood flow can have the opposite effect, too – the high blood flow delivers more chemo-drugs and sensitises the individual to radiotherapy, as well. When forcing higher temperatures on the tumour, there is another effect on the blood supply, which was pointed out first by Song [5,6] and later by others [7-10]. This suppressed blood flow, and consequently the limited heat spreading, create another situation [11-19]. A calculation showed the absolute blood flow changes, defining the threshold *in silico* [20], where the blood flow of surrounding muscles overtakes the tumours (Figure 2). These considerations opened a new approach to hyperthermia, pointing out the importance of physiological feedback mechanisms that do not naturally exist *in vitro* and could vary by species *in vivo*, and by individual in clinical applications. The blood vessels of the tumour sustain vasoconstriction over a temperature threshold. This threshold depends on many actual factors, but ranges between 39 and 42°C.

Vasoconstriction functions as a heat trap [21] for the tumour and helps its local heating by increasing the temperature rapidly in the tumour compared to the non-tumorous regions. This is an “apparent” success. It looks like a quick and effective heating, but in fact, the complementary therapies are blocked (Figure 3).

Together with this blockage, the periphery (which is the most vivid part of the tumour) has intensive blood flow and rapidly increases the risk of invasion and dissemination. This could be the reason why local control is sometimes miraculously successful, while the overall survival [22,23] and toxicity [24] levels tend towards the opposite.

Method

When the goal is the reproducibility of the treatment, all of the above parameters have to be controlled. The main parameter to check and regulate is the vasoconstriction threshold, which could essentially modify the complete protocol of the therapy.

The solution must be complex, like the situation itself: we have to heat up the malignant cells to an extreme level without igniting robust blood flow as feedback to compensate for the thermal misbalance. This issue is addressed when selecting and heating the malignant cells. Their mass is much less compared to the complete tumour itself, so the heating energy is also relatively small. The heat naturally spreads over time, but it causes only mild hyperthermia in the tumour at the time when the malignant cells are heated more intensively (Figure 4). It is highly probable that the mass temperature of the tumour does not exceed the vasoconstriction threshold. Consequently, the complementary clinical

applications are stable during the therapy. This method is referred to as oncothermia, and information on this particular method has been published elsewhere [25,26].

By its very definition, hyperthermia is a thermal process. The Arrhenius plot could be regarded as proof of the thermal character when the reaction rate exponentially depends on the inverse temperature. This probability distribution is the basis of simple chemical kinetics and determines the Arrhenius equation [27,28]:

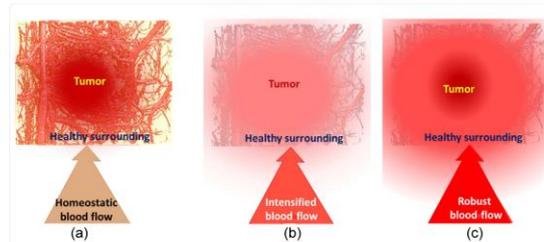


Figure 1: The heat induced blood flow in various conditions. (a) At the start of heating, short-term observation; (b) longer observation time, the temperature spreads, the blood flow intensifies; (c) intensive heating remarkably increases the tumour temperature, but the consequence is a robust blood flow trying to compensate for the increased temperature. a. At the start of heating, b. Moving from mild heating, c. Set to extreme heating.

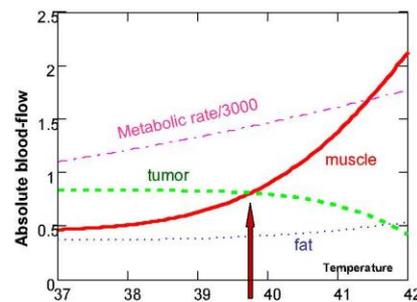


Figure 2: The blood flow rapidly grows according to the local temperature of the muscle tissue (The relative change has been reviewed [2]). The *in-silico* calculation of the absolute blood flow shows the turning point from vasodilation to vasoconstriction, [17]. An arrow notes the threshold (The metabolic rate is shown for reference).

	Below threshold		Above threshold	
	healthy	tumor	healthy	tumor
Blood-flow	↑	↑	↑	↓
Radio-efficacy;(pO₂)	↑	↑	↑	↓
Chemo-efficacy (drug-penetration)	↑	↑	↑	↓
Possible cell-dissemination (!)	–	↑	–	↑

Figure 3: The threshold of vasoconstriction (which is very much individual) determines the harmony of hyperthermia with complementary therapies. Under the threshold, the complementary therapies work together in synergy, while over the threshold, the synergy is terminated.

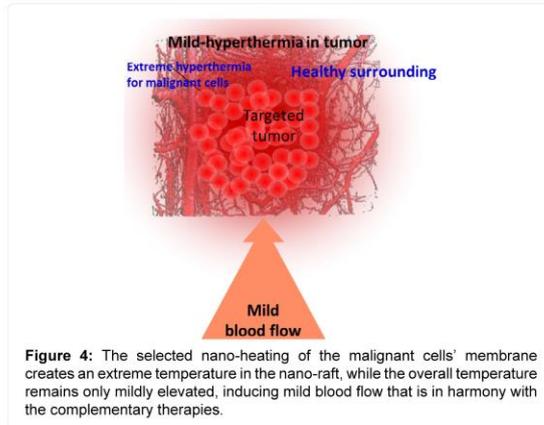


Figure 4: The selected nano-heating of the malignant cells' membrane creates an extreme temperature in the nano-raft, while the overall temperature remains only mildly elevated, inducing mild blood flow that is in harmony with the complementary therapies.

$$D = Ae^{-\frac{E_a}{RT}} \quad (1)$$

Where E_a is the activation energy of the given reaction [R is the universal gas constant, $R \approx 8.3 \text{ J/K/mol}$], T is the absolute temperature], A is the pre-exponential (normalising) factor, and D is the rate constant of the given reaction in T temperature.

This simple relationship is the consequence of the ratio of activation energy (E_a) to thermal energy (RT), showing the reaction when the thermal energy is large enough to exceed the barrier by E_a . Through the gradually increasing thermal energy, a reaction (going over the barrier E_a) becomes more likely, expressing the exponential probability of the Arrhenius law. The logarithm of the reaction rate vs. the inverse temperature shows a linear dependence in the case of thermal effects, and the value of the slope characterizes the activation energy (Figure 5). When the slope changes, a kink appears showing a phase transition-like character when the new phase has new activation energy (new bonding).

However, characteristic non-Arrhenius behaviours could be observed in complex systems [29]. These are multi-step reaction mechanisms or radical changes in the reactions, producing chemical reactions or restructuring the system during the process (e.g. phase transition occurs). The living objects regularly consume the energy in multi-step processes and could be described by the multiple kinks on the actual steps on the Arrhenius plot. The metabolic rate and body temperature are definitely connected having Arrhenius-like behaviour with 0.6–0.8 eV activation energy and a mass dependent pre-exponential factor [30].

Results

The key issue with medical acceptance is the therapy's protocol, which directly shows the demand for a definition of the dose [31]. The dosing of hyperthermia, however, remains a challenge.

In case of dosing there are three parameters to be considered:

1. The value that is prescribed in the complete individual protocol for the particular patient (repeatability).
2. The value that could be controlled during the treatment process to ensure the proper therapy (process control).

3. The value that is under the tolerance limit of the actual patient when the prescribed dose is administered (safety).

A strong indication from clinical practice is patient tolerance (safety), as this governs the overall therapy. The majority of the treated patients cannot have the prescribed dose due to issues with tolerance [32], and the protocol of the actual treatment is based on the patient's tolerance [33], the heat increase has to be stopped when the patient experiences remarkable discomfort. Other studies have excluded low-tolerance patients (not-heatable) from the study [34].

Presently, in most researches, hyperthermia uses temperature as the basis of the dose, as well as to determine the safety limit. Unfortunately, the temperature-dose does not satisfy an important requirement of the dosing: the extensive behaviour. Temperature does not depend on any size parameters. To overcome this problem and consider the time dependence of hyperthermia, time and temperature were used in parallel, resulting in doses that consider the length of time that a particular temperature was maintained. This simply creates a unit (temperature multiplied by time, [Ks]) that has no physical relevance.

Using the surprisingly accurate in vitro fits of the Arrhenius plot for the experimental results [35,36], CEM43°C_{T₉₀} was introduced [37], measuring the cumulative equivalent minutes at 43°C where the temperature exceeds the 43°C at 90% of the locations during treatment (referred to as the thermal isoeffect dose at 90% of the area) [38]. Unfortunately, it is such a complicated construction with a very complex way of measuring that it is not viable in practice. This problem is demonstrated in the case of whole body hyperthermia, where it is very

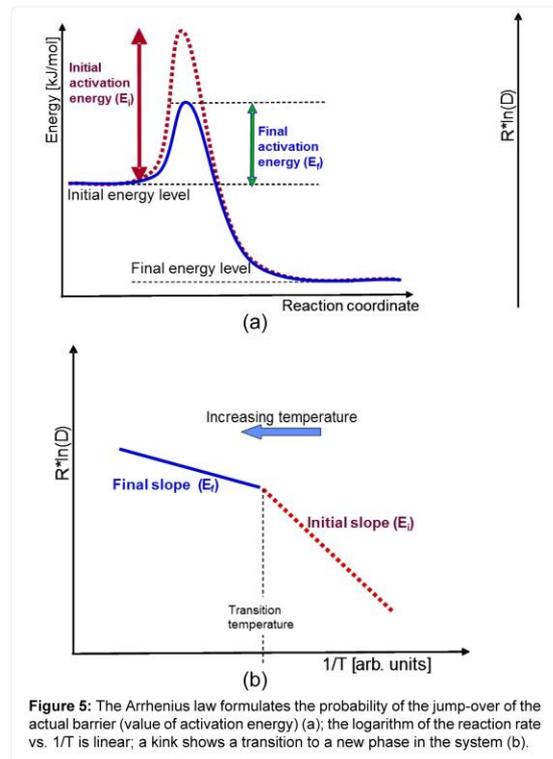


Figure 5: The Arrhenius law formulates the probability of the jump-over of the actual barrier (value of activation energy) (a); the logarithm of the reaction rate vs. $1/T$ is linear; a kink shows a transition to a new phase in the system (b).

easy to measure this dose (basically, the body and the tumour inside are at a homogenous temperature), but the results are very different from the same dose provided by the local-regional treatments. It is even more interesting that the lower CEM43°Ct90 dose applied with local-regional treatment provides better results compared to the increased dose in the whole body treatment. Therefore, we can claim that this dose unit does not satisfy the basic requirements for the dose concept in general [39-42].

The problem is simple compared to the complexity of the human body and in consequence the complexity of its treatments [43]. The real physiological feedback mechanisms drastically modify the *in vitro* or phantom-measured dose definition. However, measuring the actual physiologic parameters is very complicated, if it is possible at all. Choosing the actual malignant target in the living body is a complex task which needs complex approach too [44,45]. A general indication of the actual situation could be measured via the impedance during the electromagnetic heating processes [46-48]. In addition, the Arrhenius activation energy could be measured using the impedance [49]. Nevertheless, the impedance depends on multiple actual physiologic changes and personal variants, which are thus far not reproducible for use in dosing hyperthermia.

There are two concepts in the heating dynamism: step-down and step-up heating processes. Step-down heating means starting at a high power [50]. The applied high power could be used for short-duration, over long-duration, tolerance of the patient, and it gets down-regulated when the patient complains. The principle behind step-down heating is based on the speciality of the Arrhenius plot for heating the tumour.

The step-down heating intends the phase transition, which is measured using the slope of the Arrhenius plot. When heating the tumour, the activation energy suddenly changes at around 42°C, and remains at this significantly lower value, even when cooling down to the temperature of the kink, where the activation energy was high previously. This is a characteristic of the irreversible phase transition and helps to destroy the cancer cells using lower energy (step-down). This idea is well-proven *in vitro*, but casts numerous doubts *in vivo*. It seems that over the phase transition, the cells are necrotising, so further heating at low temperatures is superfluous. Another modification is that the necrotic tissue has no fresh blood perfusion, so a rapid increase in temperature at this local spot is likely. It is apparent, however, that it is unnecessary from the cell destruction point of view.

The kink temperature appears to be accurately reproducible among the identical conditions; however, this could change depending on the actual circumstances.

- The kink of the Arrhenius graph depends on the applied chemotherapy [51,52]. This is important because hyperthermia is complementary in a large number of cases.
- The kink of the Arrhenius graph depends on the prehistory and dynamics of the treatment [53-57].
- The Arrhenius graph gives different time doses for the different points of the target (because of its non-homogeneous structure); this promotes chemical reactions and lowers the activation energy [58].

The physiological feedback and the vasodilatation/vasocontraction threshold also make a difference in step-down heating. The Arrhenius kink, which has to be overheated, corresponds well to the believed cellular phase transition observed at around 42.5°C [59], and the sudden intense heating at the beginning could lead the system over

the vasocontraction threshold. In this case, the applied complementary therapies could be considerably suppressed. Consequently, the complementary application of the step-down heating with chemotherapy needs careful consideration. Blocking the blood flow before the chemo had reached its maximum intake in the tumour suppresses the chemo-efficacy, thus reducing the advantage of the complementary application.

Through the induced vasocontraction, the cooling effect of the bloodstream is drastically decreased. In consequence of this low blood supply, much less energy is required to maintain this temperature compared to the situation when the blood significantly cooled the area. The tumour's blood flow depends on its weight using negative logarithmic function [60], which further promotes a quick rise of the tumour's temperature. The process is directly connected to the temperature expectations and the actual immediate real time changes in the tumour status. Its real advantage is the relatively low energy supply after overcoming the relatively high activation energy. Step-down heating is a good option for temperature oriented hyperthermia approaches.

Step-up heating uses a different philosophy. While step-down heating focuses on the tumour and its elimination via necrosis, step-up heating concentrates on the patient's homeostasis in an attempt to be in harmony with the complexity of the body, helping the natural actions' during the treatment. The viewpoint of step-down heating is good local control with immediate cell-killing (necrosis); the step-up heating considers the integrative patient oriented actions that are in synchrony with the homeostatic equilibrium, causing minimal discomfort to the patient. With this gentle approach, step-up heating focuses on quality of life and survival time instead of local control. This methodology fits well with the new trend towards the personalisation of oncological treatments [61].

Discussion

The natural physiological processes form a dynamic equilibrium, dominated by homeostatic logistics of transports in the complex bio-systems. The physiological logistic distribution function is formally identical with the typical general logistics and it is the Weibull distribution [62]:

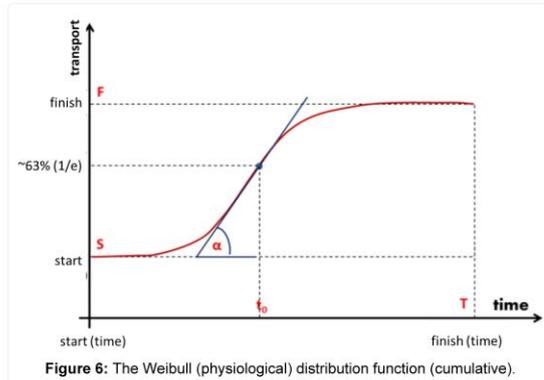
$$f(x) = e^{-(x/t_0)^a} \quad (2)$$

Where t_0 is the unit time when the value of the function is $1/e \approx 0.63$ and the a -power in the distribution defines the shape of the curve (Figure 6). The derivative in the inflexion point equals $(a/t_0) \cdot [\approx 0.63^a \cdot a$, when $t_0 = 1$]. The popular interpretation of the parameters is: t_0 is the stretching in x -direction (time-transformation) and a is the stretching in y (incline of the curve).

The a -exponents, which are strictly connected to the α -slope, were measured in various bio-transport processes. Cope [63,64] functionally studied the so-called Avrami-exponents (a parameter I Weibull distribution), showing the universality of this logistic function.

The Weibull distribution function approaches multiple clinical applications and is well-established, both theoretically and practically [65-68]. It is used for survival studies in gerontology [69,70] and in oncology [71]. The Weibull distribution could be approached using a normal (Gaussian) distribution over $a > 2$. Step-up heating follows the Weibull function for the best homeostatic support.

A further advantage of the step-up heating process is the selective manipulation of the development of heat-shock proteins (HSPs).



A portion of the HSPs rapidly appears during heating [72]. Both the malignant and healthy cells develop HSPs, but their amount is significantly different, [73]. The stressed malignant cells develop fewer than 50% more HSPs compared to their normal high value, while in healthy cells, the stress is “new”, and thus they develop approx. eight times as many HSPs compared to the level prior to the stress. At the end of the process the amount of HSPs is approximately equal in both cell types [67]. This has a great selection advantage – the step-up process could produce better heat tolerance compared to the malignant cells, but the development of this difference needs time, which the step-up heating process allows. The radiative (phase-array) hyperthermia treatments started with step-down heating [32], which later was changed to a step-up process [30].

The stress for the patient from the treatment process itself is also an important factor in sensing the tolerance and adjusting the actual dose. Stress is a personalised response, but it is consensual, so in principle it is ideal for a dosing frame. Treatment stress induces the sympathetic nervous system to kick-out the complex living object from its actual homeostatic state activation using the parasympathetic network for negative feedback corrections [74]. This effect is more complex than physiology itself; this is psycho-physiology [75], modifications of the fight or flight decision–response process depend on the actual psychology status of the individual [76,77] (Figure 7).

The fight or flight response activates and reorients the energy in the living system to concentrate on a possible emergency situation. It makes important physiologic rearrangements by increasing the blood supply of the prime organs through vasodilatation, it pumps up their metabolic flux, and makes a parallel decrease in the metabolic rate in other parts of the system, mainly via vasoconstriction. In the oncothermia application, an important consequence is the decrease of blood flow in the skin. In case of transient stress, the feedback seeks the system’s homeostasis again, and during this period the cutaneous volume has high blood perfusion and sweating could occur. This is the consequence of radiation of the extra heat produced by increased metabolism of the prime organs.

The stress-caused vasoconstriction and vasodilatation, as a consequence of heating in cutis, could partly be compensated by the fight or flight reaction, more easily addressing the homeostatic control (Figure 8).

The oncothermia dose is adjusted to support the homeostatic complex equilibrium, solving the problem deviation from the normal

complex feedback regulations [78]. The controlled micro-heating [79] makes it possible to introduce the dose as the absorbed power like in standard radiotherapy [80-82].

The heating is selective in the nanoscopic range of the oncothermia process, which is ideal for gradual step-up heating without overheating the tumour mass or creating macroscopic hotspots. The oncothermia step-up heating is specialized according to the patient’s sensing. The patient senses the process, and thus guides the personalised homeostatic heating up dosing. It is more patient-friendly causing as little discomfort as possible because the patient’s homeostatic control is active. The central task is to provide the proper dose. The actual protocol for the treated patient has to be optimized to the given

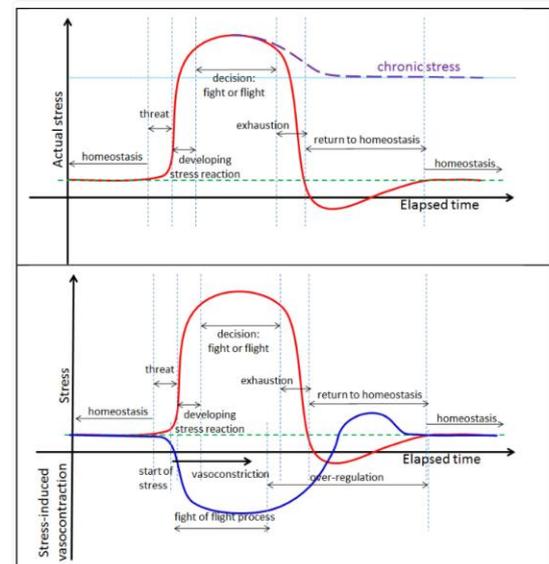


Figure 7: Fight or flight process of a stress reaction. (a) The transient process returns to homeostasis (smooth line) but the stress could become chronic (dashed line), as well. (b) The stress-induced vasoconstriction does not precisely follow the fight or flight process, but rather, it indicates the physiological reaction.

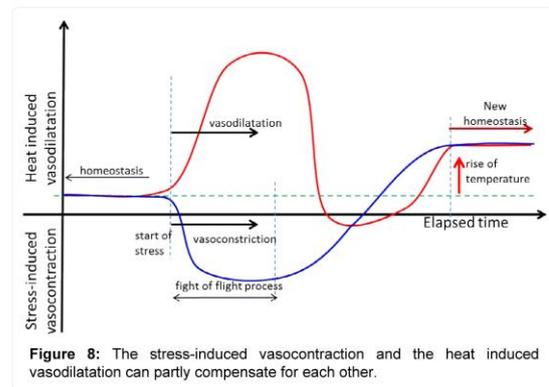


Figure 8: The stress-induced vasoconstriction and the heat induced vasodilatation can partly compensate for each other.

conditions, and needs to be curatively effective together with a high standard for safety limiting the applied dose. This concept is completely different from the conventional hyperthermia goals, because instead of trying to produce isothermal volumes (equal temperature in the tumour) it uses heterogenic heating, following the heterogeneity of the tissue itself. This far-from-equilibrium heating keeps the driving force between the heated membrane rafts and its environment, pumping the heat from these nano-clusters to the cell interior.

Oncothermia is governed in a much personalised way – the patient immediately (during the treatment and sometimes afterwards) senses and notes the toxicity. The heat pain immediately limits the oncothermia dose. When the intended dose is too much, it has to be corrected via personal signalling. On the other hand, when the protocol pre-sets too small of an energy dose, then higher energy has to be applied until the patient indicates the personalised limit. Overheating is practically impossible because the surface of the skin has the highest thermal load and the heat sensing is also there. This personalised dose regulation is the main factor of the safety and together with this for the efficacy, too.

In proper step-up heating, no continuous increase of the temperature is applied. The main governing process is homeostasis, so the heating is fit to that equilibrium. A steady-state gradual heating is necessary. The physiological response time has to be considered. This characteristic time refers to when the homeostatic equilibrium is re-established in the new conditions after a definite disturbance. The average wash-out time in humans is approx. five to seven minutes. Considering the transient “break” of six min, the step-up heating is shown below (Figure 9).

The personal sensing homeostatic step-up heating solves a set of problems, but at the same time, many physiologic controls could be neglected; the overall temperature remains completely under the vasoconstriction threshold despite the extreme heating of the selected malignant cells. The prescribed control is actually substituted by the personal sensing, which is regarded as the best homeostatic control for the patient.

The question naturally arises regarding the reliability of subjective sensing. According to the personal homeostasis, which is the individual set of feedback mechanisms and physiological conditions of the actual patient, personal sensing is the best available method for monitoring the heating process when all parameters of thermal homeostasis are

actually involved. Personal sensing is typically used to drive many of the protocols active in today’s medical treatments. When the patient is not able to tolerate the prescribed dose, it is lowered trying to fit it to the personal tolerance level. There is no reliable personalised dosing without controlling the guidance of the personal sensing.

The conditions for using personal sensing in the heating process requires a full ability to sense heat in the treated area (not modified by analgesic application), in addition to constant personal communication contact with the patient, in addition to the ability to provide immediate intervention when indicated.

Sensing heat and pain is a complex issue dominantly connected to the nociceptors [83]. Moreover, there are specific ion channels in the cell membrane of numerous cell types in animals. Their function is to sense chemical substances and heat, mostly belonging to the transient receptor potential channels (TRP channels) family [84]. These work like “nano-thermometers” of the cells [85]. In the case of the channel for sensing heat via TRP, the rise in temperature increases the energy of the thermal movement which can tear off this closing molecule, thus opening the channel. In the case of chemical sensors, like for example the VR1 ion channel for sensing capsaicin, the closing molecule is torn off in the chemical reaction. The characteristic of these ion channels is that they are cation channels, so they are permeable to positive ions, mainly Ca^{2+} . Capsaicin [86] and ethanol [87] could trigger the heat sensing TRP channels.

Note, with the decrease in pH, and thus increases in the hydrogen ion concentration, pain sensing can be triggered more easily. In other words, for example, in the case of inflammation, when the non-aerobic glucose ATP reaction is dominant, the pH decreases and so the threshold for sensing pain decreases as well [88].

In addition to the cellular sensor, the major controlling organ of the temperature forming thermal homeostatic equilibrium is the skin [89-91]. There are systemic [92] and local [93] controlling progressions. In both, controlling the blood has a central role as heat exchange media, in addition to controlling the flow for delivering thyroid hormones and controlling the metabolic activity. The systemic control could have sympathetic nerve activity, and in cold conditions acts via shivering (activity of skeletal muscle). The vasodilatation-vasoconstriction balance and the sweating and pilomotor reflexes are involved both in local and in systemic reactions. The systemic sensing is based on relative temperature between the body and the environment, while the local sensing focuses on the temperature difference between the tissues.

In observing the effect of the applied RF-frequency on heat-pain sensing, the RF-current is able to sense the heterogeneity of the tissues where it flows through. The current has two components: the ohmic and the capacitive parts. The ohmic current flows mainly in the ionic solution of the extracellular space, where the ionic displacements create the current. The capacitive current excites the dipoles, and the orientation change in them creates the capacitive current, thus this part of the current dominantly flows in the membranes. While the quantity of the complete consequent current is unchanged, the current components might vary from tissue to tissue.

The optimal frequency is around 10 MHz [94-96], which we approach using the standard for medical use: 13.56 MHz [97]. In consequence of the complex RF current, when using half of the optimal frequency, the RF current will flow dominantly in the extracellular matrix, while in cases of doubling the optimum it will not be selective at all (Figure 10).

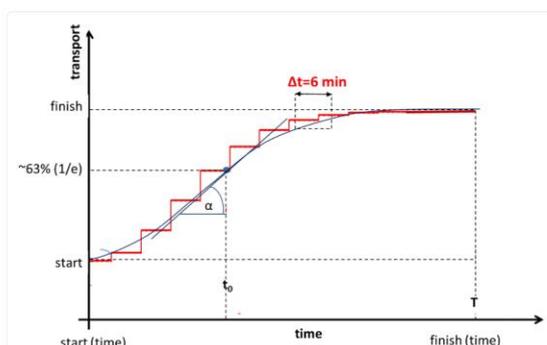


Figure 9: The step-up heating follows the Weibull curve and maintains the steps until homeostatic equilibrium (here, six min is shown). The provided cumulative energy could vary with the time intervals of the steps.

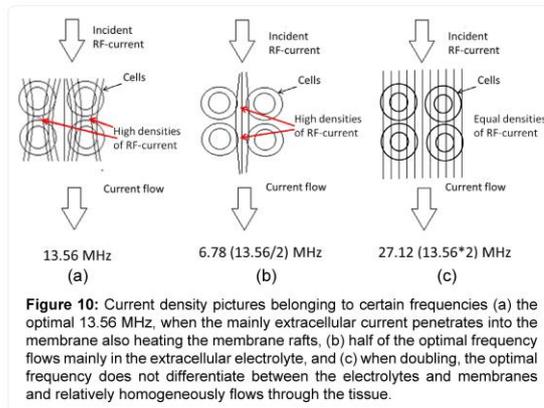


Figure 10: Current density pictures belonging to certain frequencies (a) the optimal 13.56 MHz, when the mainly extracellular current penetrates into the membrane also heating the membrane rafts, (b) half of the optimal frequency flows mainly in the extracellular electrolyte, and (c) when doubling, the optimal frequency does not differentiate between the electrolytes and membranes and relatively homogeneously flows through the tissue.

On the optimal 13.56 MHz frequency, the cell membrane and the heat sensing ion channels are locally heated, leading to functional sensing heat and pain. The heating is local in the cell membrane and the heat- and pain sensing is also locally connected to this.

Conclusion

The nanoselection of malignant cells via oncothermia allows us to return to the dosing “gold standard,” which is also applied in radiotherapy. This energy-based dose is personalised with accurate step-up heating taking into account the wash-out time and the personal sensing of the patient. The emerging new immune-oncologic connections of nanoselection [98-100], will probably change the personalization taking the immune-status of the patients into account additionally to the actual physiological parameters.

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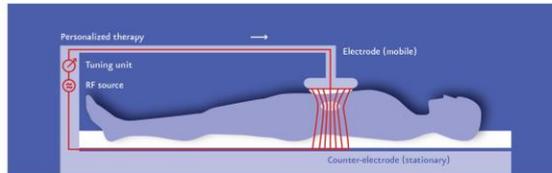
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Information

Oncothermia-Method & Oncotherm-Devices



Oncothermia is based on the classical method of Hyperthermia, one of the oldest cancer treatment methods. Unlike conventional Hyperthermia, Oncothermia does more than simply warm up deep layers of tissue. It combines such warming with a modulated electric field, with a carrier frequency of 13,56 MHz, that is generated by two active electrodes.

EHY-2030

EHY-2030 is our latest development in the treatment of loco-regional tumors. The newly designed device includes the Smart Electrode System (SES), the plug-in Patient Management System (PMS-100) and a user-friendly touch screen display with full system control. The new RF generator with increased power has been developed with a new intelligent controlled step motor tuning system for the reachable fastest impedance matching.

EHY-3010

EHY-3010 is designed for the simultaneous multi-local treatment of advanced, metastatic disseminated, malignant and solid tumors. Within the range of Oncothermia systems, it is the pioneering breakthrough in the field of multi-local tumor therapy. Instead of a bolus electrode, this system uses textile electrodes, which are even more flexible to adjust to the treatment area.

EHY-2000plus

EHY-2000plus is a widely accepted system for locoregional deep Hyperthermia applications. This model has been used for treatment worldwide for more than 20 years. Popular, versatile device, applicable for all kinds of solid tumors. It has been improved by taking into account the experiences of our doctors and experts, and the requirements of patients and the people treating them. The EHY-2000plus is an easy to use and reliable device.

EHY-1020

EHY-1020 is our professional device for treating prostate diseases. Both malignant and benign tumors (BPH) can be treated using this system: a catheter with built-in electronics and counter electrode. The EHY-1020 system is compact and easy to use. The method has been successfully used by our customers for many years. The results of the treatment are excellent and nevertheless many unpleasant side effects that are known from other forms of treatment can be avoided.

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