

The 6th International Symposium on Radiation Education

Main Theme: Radiation Education and Radiation in Medical Science

大會手冊



AUG. 7-8, 2021
CHANG YUNG-FA FOUNDATION INTERNATIONAL CONVENTION CENTER,
TAIPEI TAWAN



MR services. Helium-free.

The Philips Ingenia Ambition offers cutting-edge MR imaging techniques to help you excel clinically every day. Based on its new, revolutionary fully sealed BlueSeal magnet, the solution lets you experience more productive¹ helium-free MR operations. Get superb image quality even for challenging patients, and perform your MRI exams up to 50% faster with Compressed SENSE acceleration for all anatomies in both 2D- and 3D scanning². Fast overall exam-time is achieved by simplifying patient handling at the bore with the touchless guided patient setup. There's always a way to make life better.





Discover out latest innovations at www.philips.com/thenextmrwave

Compared to the Ingenia 1.5T ZBO magnet.
 Compared to Philips scans without Compressed SENSE.





DRX-Revolution 移動式無線數位X光機



DRX-Ascend System 無線數位X光機



DRX-Evolution 天井式無線數位X光機

費斯科技股份有限公司 Faith Biomed Limited

17x17

14x17

Carestream

10478 台北市中山區民生東路3段57號12樓之3 電話:(02)2515-2808 / 傳真:(02)2515-4813 E-mail: Faith@faith-biomed.com http://faith-biomed.com



DRX-Transportable 傳統移動式X光機升級DR解決方案





ISRE 2021 in Taipei

TABLE OF CONTENTS

Welcome Message	1
Organizing Committees	2
General Information	4
ISRE Sponsors & Supporters	7
Daily Program-Day 1, Saturday, Aug 07, 2021	8
Daily Program-Day 2, Sunday, Aug 08, 2021	10
Plenary Speakers	11
Keynote Speakers	26
Poster Sessions	74
Proceedings of the ISRE 2021	77

Welcome Message

Massage from the Conference President:

Good day, ladies and gentlemen! Thanks to Director Feng-Huei Lin, from Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, for his preparations and application for funding. Therefore, this International Symposium can be realized as scheduled.

The International Symposium on Radiation Education was initiated and guided by Professor Arima from Japan since 20 years ago. Until now, there have been six symposiums, including the first, third and fifth held in Japan, the second held in Hungary, and the fourth and sixth held in Taiwan. The results are fruitful for all symposiums.

Radiation has been found for more than a century, and it is now widely used in various fields, such as selective breeding, nuclear power, and even the development of atomic bombs. Some ways of using radiation threaten the living environment of human beings. However, besides researchers or workers engaged in this aspect, many people do not have complete comprehension toward radiation. This may lead to dangerous results.

The education of radiation in various countries has been strengthened, but there is still room for improvement. In Taiwan, radiation detection special units are not yet been set up in many cities. Therefore, it is not easy for citizen to obtain simple related equipment. Many countries have request citizen living within the regulated area should participate in nuclear disaster drill. On the other hand, citizen who do not need to participated in the drill should develop correct understanding of radiation. We hope this International Symposium can arise more respect of governments and people to radiation education and correct applications.

Finally, I would like to thank you for the participation, and support from Japan. I wish the successful Symposium.

2020 6th International Symposium on Radiation Education President

Chin-Wang Huang

Huang Ohn Work

Aug 05, 2021.

Organizing Committees

Conference President			
Chin-Wang Huang	Department of Chemistry, Chung Yuan Christian University, Taiwan		
Conference Co-President			
Tsair-Wang Chung	Chung Yuan Christian University, Taiwan		
Feng-Huei Lin	Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Taiwan		
Vice-President			
Ko-Li Chang	Fooyin University, Taiwan		
Chun-Hsu Yao	Biomaterials Translational Research Center, China Medical University, Taiwan		
Secretary-General			
Yu-Tzu Huang	Department of Chemical and Engineering, Chung Yuan Christian University, Taiwan		
Yueh-Sheng Chen	Biomaterials Translational Research Center, China Medical University, Taiwan		
Tung-Jung Chiang	Environment, Safety, & Health, National Health Research Institutes, Taiwan		
Deputy Secretary-general			
Ching-Hui Chen	Department of Radiology, Chang Gung Memorial Hospital Kaohsiung Medical Center, Taiwan		
San-Ho Hung	Fooyin University Hospital, Taiwan		
Ho-Chih Hao	Department of Medical Imaging, Taipei City Hospital, Taiwan		
Wen-Chih Su	Medical Image Division, Far Eastern Memorial Hospital, Taiwan		
Ming-Fang Lin	Department of Radiology Taipei Municipal Wan fang Hospital, Taiwan		
Cherng-Jyh Ke	Biomaterials Translational Research Center,		

	China Medical University, Taiwan		
Secretariant			
Chih-ying Chi	Biomaterials Translational Research Center, China Medical University, Taiwan		
Jyun-Han Wu			
Chen-Wei Hsiung	Institute of Biomedical Engineering and Nanomedicine Environment, Safety, & Health, National Health Research Institutes, Taiwan		
Chun-Mu Cheng			
Wei-Ling Lee			
Chia-Chi Chen			
You-Jie Chen			
Yung-Hsiang Shih			
Cheng-Feng Wu			
Ting-Chi Chang			

General Information

Registration Opening Hours

Aug 07, 2021. 08:20-08:50 (11F)

Aug 08, 2021. 08:20-08:50 (11F)

Poster Presentation

Location: 11 F (1101 Conference room)

Presentation time: Aug 07th (10:20-10:50; 15:00-15:30),2021.

Lunch

Aug 07, 2021. 12:10-13:10 (11F)

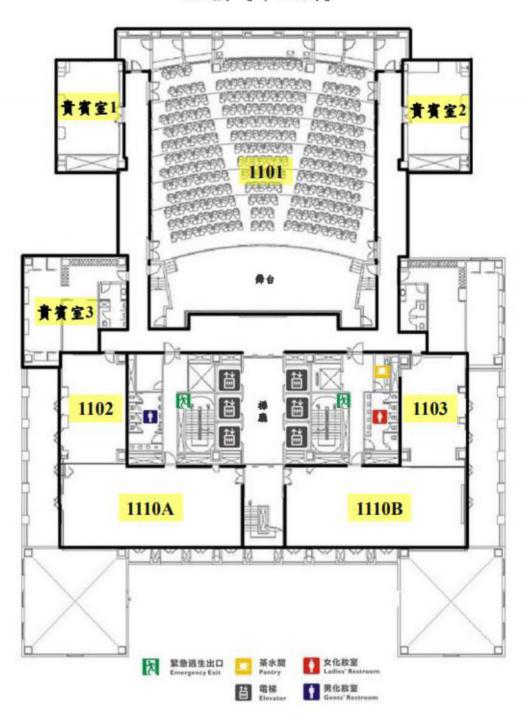
Aug 08, 2021. 12:20-13:20 (11F)

Map



Floor Plan- 11F

張榮發基金會國際會議中心 11樓〈平面圖〉



Gala Dinner & Interaction (Aug.07)

COSMOS Hotel, Taipei.



Parking:

The hotel has a two-level underground parking garage.

Address

No. 43, Section 1, Zhongxiao West Road, Zhongzheng District, Taipei City 100

Phone: +886-2-23617856 Fax: +886-2-23118921

Email: cosmos@cosmos-hotel.com.tw

ISRE Sponsors & Supporters























Daily Program-Day 1, Saturday, Aug 07, 2021

Program

Venue: 1101 Conference Room, CHANG YUNG-FA FOUNDATION International

Convention Center, Taipei.

Date: Saturday, August 7-8, 2021

Time August 7 (Sat)	Activity		
08:20- 08:50	Registration		
08:50- 09:20	Welcome & Opening Ceremony Chin-Wang HUANG, Ph.D., President, Organizing Committee, Taiwan. Feng-Huei LIN, Ph.D., Co-President, Director, Institute of Biomedical Engineering and Nanomedicine of NHRI, Taiwan. In Memory of Prof. Kunihiko HASEGAWA		
	Plenary Speakers I		
09:20- 09:50	Moderator: Li-Wei KUO, Ph.D. Associate Investigator, Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Taiwan.		
09:50- 10:20	Tiffany Ting-Fang SHIH, M.D. New Trend of Imaging Biomarkers in Precision Medicine Prof. Feng-Huei LIN Fe-doped CaS as Theranostic Biodegradable Magnetic Nanoparticle for Hyperthermia and MRI Imaging Enhancer		
10:20- 10:50	Refreshment (Poster Section & Competition)		
Section 1	Magnetic Resonance Imaging		
	Moderator: Feng-Huei LIN, Ph.D. Distinguished Investigator and Director, Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Taiwan.		
10:50- 11:10	Prof. Feza KORKUSUZ Musculoskeletal Imaging Advancements in Magnetic Resonance and Shear Wave Elastography		
11:10- 11:30	Prof. Li-Wei KUO Advanced Diffusion MRI in Neurological and Neurodegenerative Diseases		
11:30- 11:50	Prof. Maxim A. SOLOVCHUK MRI Guided Focused Ultrasound Treatment of Cancer: Treatment Planning and Monitoring		
11:50- 12:10	Prof. Vuk USKOKOVIC Hyperthermia with Composite Magnetic Nanoparticles as a Cancer Treatment Modality		

12:10- 13:10	Lunch Brook (Bostor Section & Competition)		
12.10- 13.10	Lunch Break (Poster Section & Competition)		
Section 2	Therapy and Diagnosis I		
	Moderator: Maxim A. SOLOVCHUK, Ph.D.		
	Associate Investigator, Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Taiwan.		
	Nanomedeline, National Fredian Research Institutes, Falwari.		
13:10- 13:30	Prof. Olga A. KOVAL		
	Novel Therapeutic Approaches Based on Cold Atmospheric Argon and		
	Helium Plasma Irradiation of Biotarget		
13:30- 13:50	Prof. Antonina V. LEVSHAKOVA		
	CT Perfusion in Differential Diagnosis and Evaluation of the Effectiveness		
13:50- 14:10	of Treatment of Malignant Tumors Prof. Michele IAFISCO		
13.30- 14.10	On the Use of Calcium Phosphate Nanoparticles as Agent for Magnetic		
	and Nuclear <i>In-vivo</i> Imaging		
	Plenary Speakers II		
	Moderator: Kuo-Wei WANG, Ph.D. President, Taiwan Society of Radiological Technologist,		
	Department of General Affairs, Landseed International Hospital, Taoyuan, Taiwan.		
14:10- 14:40	Prof. Hiroshi KUDO		
	Science in Radiation Education: The New Chemical Element Nihonium		
	and an Old One Nipponium		
14:40- 15:10	Prof. Kevin Chia-Wen WU		
	Pd-Loaded Metal-Organic Frameworks (Pd@VNU-2) for Radiation/		
	Photothermal Combined Cancer Therapy		
15:10- 15:40	Refreshment (Poster Section & Competition)		
Section 3	Radiation Education		
occion o	Moderator: Kevin Chia-Wen WU, Ph.D.		
	Director-Division of Strategic Planning, Office of Research and Development,		
	Dept. of Chem. Eng., National Taiwan University, Taiwan.		
15:40- 16:00	Drof Duujohi TANAKA		
15.40- 16.00	Prof. Ryuichi TANAKA Recent Progress of Radiation Education Support for School Teachers		
	Focusing on the Activities of Radiation Education Forum		
16:00- 16:20	Prof. Yoshimune OGATA		
	Practice of Radiation Education for Nurses		
16:20- 16:40	Prof. Masafumi AKIYOSHI		
	Radiation Safety Management for Crookes Tubes in Education Field		
16:40- 17:00	Prof. Wei-Hsung WANG		
47,00 47,00	Health Physics Education and Certification in the United States		
17:00- 17:20	Transportation CHANG YUNG-FA FOUNDATION Center - Hotel		
18:30- 21:30	Gala Dinner & Interaction		

Daily Program-Day 2, Sunday, Aug 08, 2021

Venue: 1101 Conference Room, CHANG YUNG-FA FOUNDATION International

Convention Center, Taipei.

Date: Saturday, August 7-8, 2021

Time August 8 (Sun)	Activity		
08:20- 09:00	Registration		
	Plenary Speakers III		
	Moderator: Yu-Tzu HUANG, Ph.D. Dept. of Chem. Eng., Chung Yuan Christian University, Taiwan.		
09:00- 09:30	Prof. Kazuko OHNO How Can Radiologists Mitigate the Public's Fear of Ionizing Radiation and Radioactive Materials? —The Usefulness of an E- learning System		
Section 4	Radiation in Environment / Education		
09:30- 09:50	Prof. Selichi SHIBATA Measurement of Fast-neutron Product of ⁶³ Ni for Reassessment of Neutron Dosimetry of the Hiroshima Atomic Bomb		
09:50- 10:10	Prof. Yukio YOSHIZAWA The Importance of Measuring Radon Concentrations as a Cause of		
10:10- 10:30	Lung Cancer Prof. Soichi HAYASHI Description of Radiation in the New Curriculum Guidelines - How Radiation is Treated in Japanese Language and Social Studies Textbooks in Primary and Junior High Schools		
10:30- 11:00	Refreshment (Poster Section & Competition)		
Section 5	Therapy and Diagnosis II		
	Moderator: Po-Chou Chen, Ph.D. Dept. of Biomedical Engineering, I-Shou University, Taiwan.		
11:00- 11:20	Prof. Chun-Yi WU Development of Theranostic Boron-containing Gold Nanoparticles for Boron Neutron Capture Therapy		
11:20- 11:40	Prof. Ömer UĞUR Radionuclide Therapy for Benign and Malignant Skeletal System Disorders		
11:40- 12:20	Poster Awards & Closing Ceremony		
12:20- 13:20	Lunch Break		

Plenary Speakers

Tiffany Ting-Fang SHIH

Professor, Department of Radiology and Medical Imaging, National Taiwan University Medical College and Hospital, Taiwan

Tel: +886-2-2312-3456 Fax: +886-2-2322-4552 E-Mail: ttfshih@ntu.edu.tw



Education

1977-1984 National Taiwan University College of Medicine.

Research and Professional Positions Held in Chronological Sequence

Training	
1983- 1984	Rotating Intern in National Taiwan University Hospital.
1984- 1985	Resident, Department of Internal Medicine, National Taiwan University Hospital.
1985- 1987	Resident, Department of Radiology, National Taiwan University Hospital.
1987- 1988	Chief Resident, Department of Radiology, National Taiwan University Hospital.
1989- 1990	Clinical Instructor, Department of Radiological Science, UCLA Medical Center.

Professional Experience

1988- present	Attending Staff, Department of Medical Imaging, National Taiwan
	University Hospital.
2004- present	Professor, Department of Radiology, National Taiwan University
•	College of Medicine.
2015- present	Tenured Professor, Department of Radiology, National Taiwan
**************************************	University College of Medicine.
0000	, ,
2020- present	Head, Division of Musculoskeletal Radiology, Department of
	Medical Imaging, National Taiwan University Hospital.
1993- 1996	Lecturer, National Taiwan University College of Medicine.
1995- 2008	Head, Division of Musculoskeletal Radiology, Department of
	Medical Imaging, National Taiwan University Hospital.
1006 2004	· · · · · · · · · · · · · · · · · · ·
1996- 2004	Associate Professor, National Taiwan University College of
	Medicine.

2002- 2008	Vice Chair, Department of Radiology and Medical Imaging,
	National Taiwan University College of Medicine and Hospital.
2008- 2014	Chair, Department of Radiology and Medical Imaging, National Taiwan
	University College of Medicine and Hospital.
2016- 2017	Deputy Chief Strategy Officer, Taipei City Hospital
2017- 2017	Chief Strategy Officer, Taipei City Hospital
2001- 2017	Chairman, Department of Medical Imaging, Taipei City Hospital

Publications

Chen BB, Lu YS, Yu Chih Wei, Lin CH, Chen TWW, Wei SY, Cheng AL, **Shih TTF***. Imaging biomarkers from multiparametric magnetic resonance imaging are associated with survival outcomes in patients with brain metastases from breast cancer. European Radiology, 2018; 28(11): 4860-4870.

Yu CW, Chen XJ, Lin YH, Tseng YH, Lu CC, Chen BB, Wei SY, Lee JM, **Shih TTF***. Prognostic value of 18F-FDG PET/MR imaging biomarkers in oesophageal squamous cell carcinoma. European Journal of Radiology, 2019 Sep, doi.org/10.1016/j.ejrad.2019.108671.

Chien MY, Lee PL, Yu CW, Wei SY, **Shih TTF***. Intramyocellular lipids, insulin resistance, and functional performance in patients with severe obstructive sleep apnea. Nature and Science of Sleep, 2020; 12:69-78.

Wu CH, Liang PC, Hsu CH, Chang FT, Shao YY, **Shih TTF***. Total skeletal, psoas and rectus abdominis muscle mass as prognostic factors for patients with advanced hepatocellular carcinoma. JFMA 2021; 120:559-566.

Wu CH, Shao YY, **Shih TTF***. Low skeletal muscle mass are predictive factors of survival for advanced hepatocellular carcinoma. JFMA 2021;120: 781-782.

Shih IL, Yen RF, Chen CA, Cheng WF, Chen BB, Chang YH, Cheng MF, **Shih TTF***. PET/MRI in Cervical Cancer: Associations between Imaging Biomarkers and Tumor Stage, Disease Progression, and Overall Survival. JMRI 2021; 53(1): 305-318.

New Trend of Imaging Biomarkers in Precision Medicine

Hybrid PET/MR scanners are innovative imaging devices that acquire and fuse anatomical and functional data from magnetic resonance (MR), with metabolic information from positron emission tomography (PET). Integrated PET/MR scanners have the potential to greatly impact on medical research and patient management posing the most solid bases for a truly personalized imaging and then push forward the personalized medicine.

Angiogenesis plays a pivotal role in tumor development, progression and metastasis in solid cancers. We successfully use the DCE-MRI as a real-time in vivo image biomarker and demonstrate that angiogenesis measured by DCE-MRI increased in patients with malignancy. An algorithm to assess tumor angiogenesis by measuring the DCE-MRI time-intensity curve pixel by pixel was developed by using the Brix and Toft models, and three distinct parameters: peak enhancement ratio (Peak), to indicate tissue blood perfusion; amplitude (Amp), to reflect vascularity; and volume transfer constant (K_{trans}), to indicate vascular permeability. The image derived image biomarkers could provide prediction of patient outcome; and also provide new therapeutic strategy of monitoring therapeutic response or clinical trials.

Furthermore, the role pf PET/MR would be more important in the near future. Not only the image hybrid, but also the "Hybrid Biomarker" from PET/MRI, such as MTV/ADC_{min} and/or SUV_{max}/Kt_{rans} ratio, could play an important role as imaging biomarker of Precision Imaging. When we face the coming geriatric society and up-rising oncological population, we do need a precise image modality to examine human body; it is important for better compliance and one –stop examination, but also for "Precision Imaging" leading to ear of "Precision Medicine".

Feng-Huei LIN

Professor, Distinguished Investigator and Director, Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Taiwan.

Tel: +886-37-206166 ext:37100

Fax: +886-37-586440

E-Mail: double@nhri.edu.tw / duoble@ntu.edu.tw



Education

1976- 1980	B.S., Department of Materials Sciences & Engineering,
	National Cheng-Kung University, Taiwan.
1983- 1985	M.S., Department of Materials Sciences & Engineering,
	National Cheng-Kung University, Taiwan.
1985- 1989	Ph.D., Biomaterials, National Cheng-Kung University, Taiwan.

Research and Professional Positions Held in Chronological Sequence

2006- 2009	Convener, Division Biomed Eng., National Science Council
2008- 2011	Director, Division of Med Eng., National Health Research Institutes
2007- 2012	Distinguished Prof., Inst. of Biomed.Eng., National Taiwan University (NTU)
2017- 2019	Executive Yuan Member, Science & Technology Program Executive Review Board, Adjunct Research Fellow office of Ministry Science and
2012- present	Technology, Executive Yuan International Fellow, International College of Biomat. Sci & Eng., (ICBSE)
2012 procent	Tenure Distinguished Prof., Inst. of Biomed.Eng., National Taiwan University (NTU)
2014- present	Director, Institute of Biomedical Engineering and Nanomedicine., National Health Research Institutes

Publications

SCI (10-Years)	Top 10 %	Q1	Average IF
159	41	95	4.544

Please refer to National Health Research Institutes Institutional Repository for detailed publications.



Major Honors and Awards Since 2020

Honors/Awards

2000 · 2003 2009 · 2010 2011	Excellent Teaching Award, National Taiwan University
2004 · 2012 2015	Outstanding Teaching Award, National Taiwan University
2004 · 2010 2015	Outstanding Research Award, Ministry of Science and Technology, R.O.C
2005 · 2011 2016	Outstanding Research Award, National Taiwan University
2008	Taiwan Medicine Society, Dr. Cong-Ming Tu Outstanding Research Award
2012	Fellow, International College of Biomaterials Science and Engineering (IFBMSEC)
2012	Chau-Jean Lee Research Scholar Award, Society of Biomaterials & Control Release, Taiwan
2013	Far Eastern Y.Z Hsu Science and Technology Memorial Foundation of Lecture Professor Award
2014	International Fellow, World Federation of Preventive & Regenerative Medicine (WFPRM)
2016	International Fellow, International Society of Blood Biomaterials (ISBB)
2017	Distinguished Administrative Service Contributions, National Health Research Institutes.
2018	Fellow, American Institute for Medical and Biological Engineering (AIMBE)
2018	MOST Outstanding Achievement Case Source of Academia Industry Collaboration by Research Institutes Program.
2019	Outstanding Research Achievement Award of National Health Research Institutes (NHRI)
2019	Chau-Jean Lee Biomedical Engineering Award, Society of Biomaterials & Control Release, Taiwan
2020	Outstanding Research Achievement and Contribution Award, The 30 th Wang Ming-Ning Memorial Foundation
Other honors	Traily mily momentary canadaton
1 2	International reviewer for the National Research Foundation (NRF), Korea International reviewer for EP-7, Europe.
3	International reviewer for National Science Foundation, USA

Fe-doped CaS as Theranostic Biodegradable Magnetic Nanoparticle for Hyperthermia and MRI Imaging Enhancer

In this study, a magnetic iron-doped calcium sulfide (Fe-CaS) nanoparticle was newly developed and studied for the purpose of hyperthermia due to its promising magnetic property, adequate biodegradation rate and relatively good biocompatibility. Fe-CaS nanoparticles were synthesized by a wet chemical co-precipitation process with heat treatment in an N_2 atmosphere, and were subsequently cooled in N_2 and exposured to air at a low temperature. The crystal structure of the Fe-CaS nanoparticles was similar to that of the CaS, which was identified by an X-ray diffractometer (XRD). The particle size was less than 40 nm based on a Debye-Scherrer equation and transmission electron microscope (TEM) examination.

Magnetic properties obtained from the SQUID magnetometer demonstrated that the synthesized CaS was a diamagnetic property. Once the Fe ions were doped, the synthesized Fe-CaS converted into paramagnetism which showed no hysteresis loop. Having been heated above 600° C in N₂, the Fe-CaS showed a promising magnetic property to produce enough energy to increase the temperature for hyperthermia. 10 mg/ml of the Fe-CaS was able to generate heat to elevate the media temperature over 42.5° C within 6 minutes. The area of the hysteresis loop increased with the increasing of the treated temperature, especially at 800° C for 1 hour. This is because more Fe ions replaced Ca ions in the lattice at the higher heat treatment temperature. The heat production was also increasing with the increasing of heat treatment temperature, which resulted in an adequate specific absorption ratio (SAR) value, which was found to be 45.47 W/g at 37° C under an alternative magnetic field of f = 750 KHz, H = 10 Oe.

The *in vitro* biocompatibility test of the synthesized Fe-CaS nanoparticles examined by the LDH assay showed no cytotoxicity to 3T3 fibroblast. The result of *in vitro* cell hyperthermia shows that under magnetic field the Fe-CaS nanoparticles were able to generate heat and kill the CT-26 cancer cells significantly.

Furthermore, the sulfide-based magnetic Fe-doped CaS nanoparticles modified with a silica layer were then investigated. A polyvinyl pyrrolidone polymer was used as the coupling agent. The developed nanoparticles contained 11.6 wt% iron concentration, and their x-ray diffraction pattern was similar to those of CaS and Fe-CaS nanoparticles. The average particle size was approximately 47.5 nm and homogeneously dispersed in aqueous solutions. The major absorption bands of silica were observed from the FTIR spectrum. The magnetic properties and heating efficiency were also examined. The specific absorption ratio of nanoparticles at a concentration of 10 mg/ml at 37°C in an ethanol carrier fluid was 37.92 W/g and the nanoparticles would raise the temperature to over 45°C within 15 min. A cytotoxicity analysis revealed that the nanoparticles had good biocompatibility, which indicated that the nanoparticles did not affect cell viability. The therapeutic effects of the nanoparticles were investigated using in-vitro and animal studies. Cells seeded with nanoparticles and treated under an AC magnetic field revealed a percentage of cytotoxicity (60%) that was significantly higher from that in other groups. In the animal study, during a hyperthermia period of 15 days, tumor-bearing Balb/c mice that were subcutaneously injected with nanoparticles and exposed to an AC magnetic field manifested a reduction in tumor volume. The newly developed Fe-CaS nanoparticles and silica-modified Fe-CaS nanoparticles can thus be considered a promising and attractive hyperthermia thermoseed.

Keywords: Hyperthermia \cdot Iron-doped \cdot Calcium Sulfide \cdot Nanomedicine \cdot Magnetic nanoparticles

Hiroshi KUDO

Professor Emeritus, Tohoku University, Sendai, Japan. President, Radiation Education Forum

Tel: **+81-22-308-8041** E-Mail: kudo.hrs@nifty.com



Education

1964	B.S., Chemistry, Faculty of Science, Tohoku University
1967	M.S., Chemistry, Graduate School of Science, Tohoku University
1971	D.Sc., Tohoku University

Research and Professional Positions Held in Chronological Sequence

1967- 1976	Research Scientist, Japan Atomic Energy Research Institute (JAERI)
1976- 1977	Visiting Scientist, Kernforschunsanlage Jülich (KFA)/ Germany
1979- 1984	Senior Scientist, JAERI
1984- 1988	Principal Scientist, JAERI
1988- 1993	Head, Division of Research and Development, JAERI
1993- 1996	Group Leader, Advanced Science Research Center, JAERI
1994- 2005	Professor, Graduate School of Science, Tohoku University
1994- 2005	Associate Editor, The Journal of Radioanalytical and Nuclear Chemistry
1997- 2005	Editor, The Radiochimica Acta
2002- 2004	President, The Japan Society of Nuclear and Radiochemical Sciences
2005- 2017	Director, Tohoku Radiation Science Center
2007- present	Professor Emeritus, Tohoku University
2008- 2013	Director, Radiation Education Forum
2014- present	Deputy-Director General, Radiation Education Forum

Awards and Honor

Divisional Award of the Chemical Society of Japan (March, 1996) on "Discovery of Hyperlithiated Molecules, and Studies on the Structure and Nature of Bonding"

<u>Publications</u>

Books

Periodic Table with Nuclides and Reference Data; K. Yoshihara, H. Kudo and T. Sekine, Springer-Verlag, Berlin (1985).

*And other 3 papers in books

Review Articles

Research and Development of ⁹⁹Mo Production Technology in Japan: H. Kudo, N. Yamabayashi, A. Iguchi and E. Shikata, Proc. Technical Committee Meeting, Karlsruhe, Oct. 1987, "Fission Molybdenum for Medical Use," IAEA, Vienna (1989) pp. 83-97.

Facilities and Activities in Fusion Nuclear Technology: Japan Atomic Energy Research InstituteM. Seki, H. Yoshida, T. Nakamura, H. Watanabe and H. Kudo, *Fusion Technol.*, 17, 288-298 (1990).

*And other 42 papers

Original Papers

Chemical Effects Associated with β -Decay Process. I. The Chemical Behavior of a Decayed Product, 144Pr, in the EDTA Complex System; T. Shiokawa, H. Kudo and T. Omori, *Bull. Chem.* Soc. Jpn., 38, 1340-1343 (1965).

Study of Hot Atom Effects of Cadmium Phthalocyanine Using a "Daughter-Tracing Technique"; K. Yoshihara and H. Kudo, *Nature*, 222, 1060-1061 (1969).

"Appearance Energy" and Energy Dependence of the Recoil Product Yield in Indium-Ethylenediaminetetraacetate by the 115 In(γ , γ')115mIn Reaction; K. Yoshihara and H. Kudo, *J. Chem. Phys.*, 52, 2950-2953 (1970).

Chemical Behavior of Tritium Produced by the 6 Li(n, α)T Reaction in Lithium Oxide; H. Kudo, K. Tanaka and H. Amano, *J. Inorg. Nucl. Chem.*, 40, 363-367 (1978).

Interaction of OT⁻ with Li⁺ during Diffusion of Tritium in Lithium-Containing Oxide Crystals Irradiated with Neutrons; H. Kudo, *Radiochim. Acta*, 50, 71-74 (1990).

Structure and Energetics of Lin(OH)n–1 (n = 2-5) Clusters Deduced from Photoionization Efficiency Curves; H. Tanaka, H. Kudo and K. Yokoyama, *J. Chem. Phys.*, 114,152-159 (2001).

Structure of [N,N'-bis(3,5-di-t-butyl-salicylidene)-2-benzyl-1,3-propanediaminato]nitridotechnetium(V) Complex, TcN(bzdbsalpn), and Nitrido-Bridged Linear Polymeric Chains inCrystalline syn-Isomer; T. Takayama, Y. Abe, T. Sekine and H. Kudo, *Radiochim. Acta*, 92, 265-269 (2004).

*And other 116 papers

Science in Radiation Education: The New Chemical Element Nihonium and an Old One Nipponium

To enhance the radiation literacy of general public, it seems important to make them interested not only in medical and engineering application of radiation, but also in advancement of basic science associated with radiation.

In 2016, the International Union of Pure and Applied Chemistry (IUPAC) officially announced that Element 113 is named "Nihonium" with its symbol "Nh". This new chemical element was synthesized with a linear accelerator in RIKEN (Institute of Physical and Chemical Research), Wako, Japan by Professor Koske Moria and his colleagues in 2007 for the first time in Asia and then named after the country name of its discovery. Japan is called "Nihon" or "Nippon" in Japanese.

In the past, there was a chemical element "Nipponium" (Np) with its atomic number 43 named by Professor Masataka Ogawa (1865-1930) of Tohoku University, Sendai, Japan. He claimed the discovery of the Element 43 in natural ore "Thorianite" while he stayed in Professor Ramsay's Laboratory in University College, London and reported the finding in English journal *Chemical News* (1908). Unfortunately, however, his discovery was not confirmed by the following experiments because the element 43 does not occur naturally, and the name "Nipponium" has disappered from the table of chemical element. At present, we know that the element 43 is Technetium (Tc), the first artificially synthesized element found in a deuteron-irradiated molybdenum plate by C. Perrier and E. Segré in 1937.

Although Technetium does not occur naturally, we are keeping now a few tons of radioactive 99 Tc ($T_{1/2}$ = 2.1 x 10 5 years) produced in spent nuclear fuel. Short-lived 99 mTc ($T_{1/2}$ = 6 days) is one of the most essential radioisotopes for medical diagnosis and the world's most widely used radionuclide nowadays.

The present author deals with the histories of discovery of Nihonuim as well as Nipponium, including the production and application of ^{99m}Tc from a viewpoint of radiation education.

Kevin Chia-Wen WU

Professor, Director-Division of Strategic Planning, Office of Research and Development, Dept. of Chem. Eng., National Taiwan University, Taiwan.

Tel: +886-2-3366-3064 Fax: +886-2-2362-3040 E-Mail: kevinwu@ntu.edu.tw



Education

2006- 2008	Post-Doc. in Chemistry from Iowa State University, U.S.A.,
2005- 2006	Post-Doc. in Applied Chemistry from Waseda University, Japan,.
2000-2005	Ph.D. in Materials Science and Engineering from The University of
	Tokyo, Japan,
1998- 2000	M.S. in Agricultural Chemistry from National Taiwan University, Taiwan,
1994- 1998	B.S. in Agricultural Chemistry from National Taiwan University, Taiwan,

Research and Professional Positions Held in Chronological Sequence

2012- 2016	Associate Professor-Dept. of Chem. Eng., National Taiwan University,
	Taiwan,
2013- 2016	Vice Chair-The Center of Strategic Materials Alliance for Research and
	Technology (SMART Center), National Taiwan University, Taipei, Taiwan.
2015- 2017	General Secretary-Taiwan Institute of Chemical Engineers.
2010- 2018.	Joint Appointed Assistant Investigator- National Health Research
	Institutes, Taiwan, Aug.
2008- 2012	Assistant Professor-Dept. of Chem. Eng., National Taiwan University,
	Taipei, Taiwan,
2016- present	Professor-Dept. of Chem. Eng., National Taiwan University, Taiwan
2018- present	Professor-Molecular Science & Technology, National Taiwan Univ.
	(NTU-MST), 2018-present
2019- present	Director-Division of Strategic Planning, Office of Research and
	Development, NTU

Awards and Honor

2021	Outstanding Research Award, Ministry of Science and Technology, Taiwan.
2019	ACS Sustainable Chemistry & Engineering Lectureship Award (ACS)
2019	Outstanding Researcher Award (Asia-Pacific Association of Catalysis Societies; APACS)
2018	Outstanding Research Award, Ministry of Science and Technology, Taiwan.
2018	Humboldt scholars, Research Fellowship for Experienced Researchers from Alexander von Humboldt Foundation, Germany, 2018-2020.
2017	Outstanding Young Chemist Award, Chemistry Society of Taiwan.

2017	Lai Zia-Te Award, Taiwan Institute of Chemical Engineers, Taiwan.
2016	The SCEJ Award for Outstanding Asian Researcher and Engineer.
2015	Wu Da-Yu Award, Ministry of Science and Technology (MOST), Taiwan.

<u>Publications:</u> 2018- Present Selective publications:

Jie Wang, Yunling Xu, Bing Ding, Zhi Chang, Xiaogang Zhang*, Yusuke Yamauchi*, and **Kevin C. -W. Wu***. Confined Self-Assembly in Two-Dimensional Interlayer Space: Monolayered Mesoporous Carbon Nanosheets with In-Plane Orderly Arranged Mesopores and High Graphitized Framework. *Angewandte Chemie International Edition.* 2018, 57(11), 2894-2898. **Very Important Paper.**

Yang Li, Jenoghun Kim, Jie Wang, Nei-ling Liu, Yoshio Bando, Abdulmohsen Ali Alshehri, Yusuke Yamauchi, Chia-Hung Hou* and **Kevin C.-W. Wu***. High Performance Capacitive Deionization using Modified ZIF-8 Derived, N-doped Porous Carbon with Improved Conductivity. *Nanoscale*. 2018, 10, 14852-14859. (Selected as **Front Cover**).

Chia-Chen Lee, Chih-I Chen, Yu-Te Liao, **Kevin C.-W. Wu,*** and Chu-Chen Chueh.* Enhancing Efficiency and Stability of Photovoltaic Cells by Using Perovskite/Zr-MOF Heterojunction Including Bilayer and Hybrid Structures. *Advanced Science*. 2019, 6, 1801715. (IF: 12.441) (Selected as **Back Cover**).

Yuyuan Huang, Hannelore Konnerth, Jyun-Yi Yeh, Martin H. G. Prechtl, Cheng-Yen Wen, and **Kevin C.-W. Wu***. De novo synthesis of Cr-embedded MOF-199 and derived porous CuCr2O4/CuO composites for enhanced phenol hydroxylation. *Green Chemistry.* 2019, 21, 1889-1894 (Selected as **Front Cover**)

Chu-Chen Chueh,* Chih-I Chen, Yu-An Su, Hannelore Konnerth, Yu-Juan Gu, Chung-Wei Kung,* **Kevin C.-W. Wu.*** Harnessing MOF materials in photovoltaic devices: recent advances, challenges, and perspectives. *Journal of Materials Chemistry A.* 2019, 7, 17079-17095 (Selected as **Front Cover**)

Chi Van Nguyen, Seulchan Lee, Yongchul G. Chung,* Wei-Hung Chiang,* and **Kevin C.-W. Wu**.* Synergistic effect of metal-organic framework-derived boron and nitrogen heteroatom-doped three-dimensional porous carbons for precious-metal-free catalytic reduction of nitroarenes. *Applied Catalysis B: Environmental.* 2019, 257, 117888.

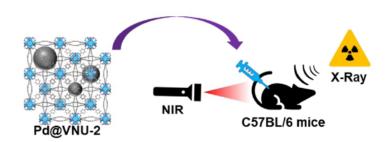
Pd-Loaded Metal-Organic Frameworks (Pd@VNU-2) for Radiation/ Photothermal Combined Cancer Therapy

Radiotherapy is often used in clinic to kill malignant tissues. However, different types cancer might have different sensitivity to radiation. For example, Non-small Cell Lung Cancer and Skin Melanoma are considered radiation resistant, which means that higher dosage must be given during the treatment. Although higher doses of radiation can achieve curative effects, and it will also cause more damage to normal tissues near the tumor. In order to solve this problem, a novel method is to apply radiosensitizers. These sensitizers can be chemotherapy drugs which has synergistic effects with radiotherapy, such as cisplatin or nanomaterials containing high-Z elements such as Hafnium.

In this work, we successfully synthesized a Hf-based Metal-Organic Framework VNU-2 as radiosensitizer. Due to the high electron density of hafnium, when VNU-2 is irradiated by ionizing radiation, it can efficiently generate photoelectrons, secondary electrons and Auger electrons. Besides, its porous structure can avoid the self-quenching of photoelectrons and further improve the diffusion of reactive oxygen species (ROS) generated when electrons react with water molecules, make it more effective to cause direct and indirect damage to cancer cells.

In addition, we also find that the triple-bond structure in the ligand can effectively adsorb noble metal ions. Therefore, we designed to first adsorb the palladium metal ions in the pores of VNU-2, and then reduce the palladium metal ions to Palladium nanoparticles. Since palladium nanoparticles have excellent absorption and photothermal efficiency in the range of UV-Vis and NIR, we use 808 nm NIR laser for photothermal therapy. The cell cycle analysis results show that after photothermal treatment, the proportion of the most radiation-resistant S phase decreases, which further improves the sensitivity of cancer cells to radiation therapy.

Until now, we have conducted in vitro experiments with the skin melanoma cell line B16F10 and the non-small cell lung cancer cell line A549, and obtained good results. Preliminary results of animal study based on skin melanoma model have also been obtained.



Kazuko OHNO

Professor Kyoto College of Medical Science, Japan

E-Mail: kakochan@kyoto-msc.jp



Education

1981- 1987	Faculty of Medicine, Aich Medical University, Japan, awarded the degree of MD
1988- 1992	Doctoral course in medical science, Aich Medical University, awarded the degree of PhD

Research and Professional Positions Held in Chronological Sequence

1987- 1988	Resident, Department of Gynecology, Aich Medical University Hospial
1992- 1998	Fellow, Department of Radiology, Aich Medical University Hospial
1998- 2007	Instructor, Department of Radiology, Aich Medical University Hospial
2006	Lecturer, Department of Radiology, Charité Mitte Humboldt-Universität zu
	Berlin (Germany)
2007- present	Professor of Kyoto Collage of Medical Science

Publications

K. Ohno, T. Kaori., Efficient education of radiation safety for nurses., Radiat Prot Dosimetry (2004), DOI: 10.1093/rpd/nc0000

K Ohno, K Endo., Lessons learned from Fukushima Daiichi Nuclear Power Plant Accident-Efficient education items of radiation safety for general public-., Radiat Prot Dosimetry (2015),165(1-4):510-2. doi: 10.1093/rpd

Watanabe H., Ishii K., Hosono M., Imabayashi E., Abe K., Inubushi M., Ohno K., Magata Y., Ono K., Kikuchi K., Wagatuma K., & Takese T.. Report of a nationwide survey on actual administered radioactivities of radiopharmaceuticals for diagnostic reference levels in Japan. Nucl Med, 30(6), 435-444 (2016).

Yamashita Y., Murayama S., Okada M., Watanabe Y., Kataoka M., Kaji Y.,Imamura K., Takehara Y., Hayashi H., Ohno K., Awai K., Hirai T., Kojima Ki., Sakai S.,Matsunaga N., Murakami T., Yoshimitsu K., Gabata T., Matsuzaki K., Tohno E., Kawahara Y., Nakayama T., Monzawa S., & Takahashi S., The essence of the Japan Radiological Society/Japanese College of Radiology Imaging Guideline. JJR, 34(1), 43-79 (2016).

Ohno K., Establishment of Comprehensive Radiation Education E-learning System for Medical Staff. International Conference of the Public Healthe Foundation of India and Pacific Bacin Consortium (2017).

Sumi Yokoyama, Kazuko Ohno et al., Current situations and discussions in Japan in relation to the new occupational equivalent dose limit for the lens of the eye, 37, 659-683 (2017).

Ohno K., An E-learning System for Medical Staff about Ionizing Radication and Radioactive Materials.A Nuclear Physicians' Approach in Japan. 19th Workshop the German-Japanese Radiological Affiliation. (2018)

How Can Radiologists Mitigate the Public's Fear of Ionizing Radiation and Radioactive Materials? —The Usefulness of an E-learning System—

Introduction: On March 11, 2011, a nuclear accident occurred at the Fukushima Daiichi Nuclear Power Station (FNP-1), operated by Tokyo Electric Power Company. Consequently, there has been widespread skepticism and anxiety about radiation all over the world. In addition to that, many patients in Fukushima prefecture and in the other part of Japan declined radiological examinations despite a doctor's recommendation.

Objectives: It is extremely important for radiologists to encourage every medical staff to have a knowledge to correct prejudiced public understandings on the effects of ionizing radiation on human health, especially at low doses. we have created an E-learning system on radiation for the education of medical staffs.

Methods: We had been taking more than thirty classes for medical staffs from May 2011 to November 2016. Based on questions and answers in these classes. With consideration of the questionnaire results, the contents of this e-learning were chosen.

Result:

To put out accurate information about their questions, we chose the following five contents.

- 01.Radiation All Around Us
- 02. Devices for Measuring Radiation
- 03. Effects on Humans
- 04. Internal Exposure
- 05. Radiation Emergency Medicine

The results of the following test showed that estimations about internal doses were the most difficult to understand.

Conclusion: We created an e-learning for medical staffs. We hope many physicians correct their misunderstandings concerning the effects of ionizing radiation on human health, especially at low doses. (https://radiation-protection.jp/en/)

Keynote Speakers

Feza KORKUSUZ

Professor Hacettepe University Medical Faculty Ankara, Turkey

Tel: +90-312-305-1347

E-Mail: feza.korkusuz@gmail.com



Education

1989- 1990 Department of Orthopedic Surgery, Osaka University

1992- present Postgraduate, Gazi Üniversitesi

(specialized in Orthopedic Surgery and Traumatology)

Research and Professional Positions Held in Chronological Sequence

Dr. Feza Korkusuz compleded his specialized in Orthopedic Surgery and Traumatology in 1992. Between 1989 and 1990, he studied in Osaka University Faculty of Medicine, Department of Orthopedic Surgery and specialized in Spine Surgery and Sports Medicine. He did research on bioceramics, osteomyelitis and periosteal cell culture during his Osaka University Studies. He focused on medical imaging of the musculoskeletal system using ultrasound and magnetic resonance. He also works on biomaterials and biomechanics. In the year 2000, he received the Scientific and Technological Research Council of Turkey Promotion Award in Medical Sciences for his research studies. In 2016, he was the editor of the "Musculoskeletal Research and Basic Science" book. He and his team members wrote several chapters in international books including "Hard-Tissue Biomaterial Interactions" in Encyclopedia of Biomaterials and Biomedical Engineering and "Hard Tissue-Biomaterial Interactions in Biomaterials in Orthopedics". He published more than 90 manuscripts in Web of Science.

He was an active member of the Orthopaedic Research Society between 1995 and 2015. In 2008 he became an active member of the Association of Bone and Joint Surgeons, and since 2006 he has been a member of the corresponding and deputy editor of Clinical Orthopaedics and Related Research. Dr. Korkusuz is the current department head of Sports Medicine at Hacettepe University Medical Faculty and adviser to the president of the Scientific and Technological Research Council of Turkey.

Publications

Torgutalp ŞŞ, Babayeva N, Kara ÖS, Özkan Ö, Dönmez G, Korkusuz F. Trabecular bone score of postmenopausal women is positively correlated with bone mineral density and negatively correlated with age and body mass index (DOI: 10.1097/GME.000000000001375) Menopause (ISSN: 1530-0374) 2019;26:XXX-XXX.

Küçükkubaş N, Korkusuz F. What happens to bone mineral density, strength and body composition of ex-elite female volleyball players: a cross sectional study (DOI: 10.1016/j.scispo.2018.11.006). Science & Sports (ISSN: 0765-1597) 2018;XX:XXX-XXX

Taş S, Korkusuz F, Erden Z. Neck muscle stiffness in participants with and without chronic neck pain: A shear-wave elastography study (DOI: /10.1016/j.jmpt.2018.01.007). J Manipulative and Physiol Therap (ISSN: 0161-4754) 2018;41:580-588

Taş S, Ünlüer NÖ, Korkusuz F. Morphological and mechanical properties of plantar fascia and intrinsic foot muscles in individuals with and without flat foot (DOI: 10.1177/2309499018802482). J Orthop Surg (Hong Kong) (ISSN: 2309-4990) 2018:26(3):2309499018802482

Karanfil Y, Babaeva N, Dönmez G, Diren HB, Eryılmaz M, Doral MN, Korkusuz F. Thirty minutes of running exercise decreases T2 signal intensity but not thickness of the knee joint cartilage: A 3.0-T magnetic resonance imaging study (DOI:https://doi.org/10.1177/1947603518770). Cartilage (ISSN: 1947-6035) 2018:1:1947603518770246.

Taş S, Bek N, Onur MR, Korkusuz F. Effects of body mass index on mechanical properties of the plantar fascia and heel pad in asymptomatic participants (DOI: 10.1177/1071100717702463). Foot & Ankle Int (ISSN: 1071-1007) 2017:38;779-784.

Taş S, Yılmaz S, Onur MR, Soylu AR, Altuntaş O, Korkusuz F. Patellar tendon mechanical properties change with gender, body mass index and quadriceps femoris muscle strength. (DOI:10.1016/j.aott.2016.12.003) Acta Orthop Traumatol Turc (ISSS: 1017-995X) 2017:51:54-59.

Taş S, Yılmaz S, Soylu R, Onur MR, Korkusuz F. Shear wave elastography is a reliable and repeatable method to measure elastic modulus of rectus femoris muscle and patellar tendon (doi:10.7863/ultra.16.03032). J Ultrasound Med (ISSN: 0278-4297) 2017:506;565-570.

Musculoskeletal Imaging Advancements in Magnetic Resonance and Shear Wave Elastography

Functional Magnetic Resonance (MR) was previously used to evaluate brain functional changes before and after exercise [1]. We have recently used this technology to assess and quantify joint cartilage and skeletal muscles [2]. Quantifying dimensions and signal intensity may allow us the early diagnose of diseases and evaluate treatment outcomes. Shear wave elastography (SWE) is another emerging technology that allows quantification of musculoskeletal tissues mechanical properties. This is a reliable and valid methodology [3]. Transmission of ultrasound through tissues can now be used to predict stiffness of skeletal muscles and tendons. We have used this new technology to assess various normal and pathological conditions [4-7]. We would like to highlight opportunities of new developing imaging techniques and how we can use them for evaluating musculoskeletal conditions.

References

Çağlar E, Sabuncuoğlu H, Keskin T, Işıklı S, Keskil S, <u>Korkusuz F</u>. *In vivo human brain biochemistry after aerobic exercise: preliminary report on functional magnetic resonance spectroscopy*. Surg Neurol 2005;64S2:S53-S56.

Karanfil Y, Babaeva N, Dönmez G, Diren HB, Eryılmaz M, Doral MN, <u>Korkusuz F</u>. Thirty minutes of running exercise decreases T2 signal intensity but not thickness of the knee joint cartilage: A 3.0-T magnetic resonance imaging study. Cartilage 2018:1:1947603518770246. Taş S, Yılmaz S, Soylu R, Onur MR, <u>Korkusuz F</u>. Shear wave elastography is a reliable and repeatable method to measure elastic modulus of rectus femoris muscle and patellar tendon. J Ultrasound Med 2017:506;565-570.

Taş S, Yılmaz S, Onur MR, Soylu AR, Altuntaş O, <u>Korkusuz F</u>. Patellar tendon mechanical properties change with gender, body mass index and quadriceps femoris muscle strength. Acta Orthop Traumatol Turc 2017:51:54-59.

Taş S, Bek N, Onur MR, Korkusuz F. Effects of body mass index on mechanical properties of the plantar fascia and heel pad in asymptomatic participants. Foot & Ankle Int 2017:38;779-784.

Taş S, Ünlüer NÖ, <u>Korkusuz F</u>. Morphological and mechanical properties of plantar fascia and intrinsic foot muscles in individuals with and without flat foot. J Orthop Surg (Hong Kong) 2018:26(3):2309499018802482.

Taş S, Korkusuz F, Erden Z. Neck muscle stiffness in participants with and without chronic neck pain: A shear-wave elastography study. J Manipulative and Physiol Therap 2018;41:580-588.

Li-Wei KUO

Associate Investigator
Institute of Biomedical Engineering and Nanomedicine,
National Health Research Institutes, Miaoli County,
Taiwan

Tel: +886 (37) 206166 *37120

E-Mail: lwkuo@nhri.edu.tw

Education

2003- 2008	Ph.D., Department of Electrical Engineering, National Taiwan
	University, Taipei, Taiwan
2001- 2003	M.S., Department of Electrical Engineering, National Taiwan University,
	Taipei, Taiwan
1997- 2001	B.S., Department of Electrical Engineering, National Taiwan University,
	Taipei, Taiwan

Research and Professional Positions Held in Chronological Sequence

Dr. Li-Wei Kuo received his B.S., M.S., and Ph.D. degrees in Electrical Engineering from National Taiwan University in 2001, 2003, and 2008, respectively. He conducted his postdoctoral researches in the Center for Optoelectronic Biomedicine at National Taiwan University College of Medicine and the Advanced MRI section at the Laboratory of Functional and Molecular Imaging in National Institute of Neurological Disorders and Stroke at the National Institutes of Health in USA. Since September 2011, he has joined the National Health Research Institutes in Taiwan and led the MR Neurolmaging Lab (MRNIL). The major objective of Dr. Kuo's laboratory is to develop advanced MRI neuroimaging techniques to facilitate the understanding of the complex structures, physiological functions and network topology of the healthy and pathological brains. The most notable contributions have been in instrumentation innovation and the development of advanced neuroimaging methods. For instrumentation innovation, Dr. Kuo's team has successfully built and integrated an ultrahigh strength gradient system on 3T, and has demonstrated its quality and capability in translational MRI studies between clinical and pre-clinical platforms. This ultrahigh strength gradient system is designed for acquiring the MRI data with high spatial and angular resolution, which is particularly beneficial to brain neuroscience researches. The development of neuroimaging methods is associated with emerging diffusion MRI techniques, including diffusion kurtosis imaging optimization and free water elimination technique. Both studies have significantly improved image clarity to reveal more details relating to tissue microstructures within the brain, and have shown their potentials in preclinical research. His lab has also focused on developing novel brain connectivity analysis

approaches to investigate the structural and functional brain networks. Specifically, the major goal is to demonstrate the capability of MRI neuroimaging biomarkers for identifying alterations in brain structures and functions between different disease states or sub-types. Importantly, Dr. Kuo's team has demonstrated the clinical relevance of brain connectivity analysis on applications of neurological diseases and psychiatric disorders, including Alzheimer's disease, subcortical ischemic vascular dementia, and heroin addiction.

<u>Publications</u>

Min-Chien Tu, Sheng-Min Huang, Yen-Hsuan Hs, Jir-Jei Yang, Chien-Yuan Lin, Li-Wei Kuo*. Discriminating Subcortical Ischemic Vascular Disease and Alzheimer's Disease by Diffusion Kurtosis Imaging in Segregated Thalamic Regions. Human Brain Mapping, 42(7):2018-2031, May 2021, doi:10.1002/hbm.25342.

Min-Chien Tu, Yen-Hsuan Hsu, Jir-Jei Yang, Wen-Hui Huang, Jie-Fu Deng, Shih-Yen Lin, Chien-Yuan Lin, Li-Wei Kuo*. Attention and functional connectivity among patients with early-stage subcortical ischemic vascular disease and Alzheimer's disease. Frontiers in Aging Neuroscience, 12:239, August 2020, doi:10.3389/fnagi.2020.00239.

Ezequiel Farrher*, Farida Grinberg, Li-Wei Kuo*, Kuan-Hung Cho, Richard Buschbeck, Ming-Jye Chen, Hsuan-Han Chiang, Chang-Hoon Choi, N. Jon Shah. Dedicated diffusion phantoms for the investigation of free water elimination and mapping: insights into the influence of T2 relaxation properties. NMR in Biomedicine, 33:e4210, April 2020, doi:10.1002/nbm.4210.

Chia-Wen Chiang, Shih-Yen Lin, Kuan-Hung Cho, Kou-Jen Wu, Yun Wang, Li-Wei Kuo*. Effects of signal averaging, gradient encoding scheme, and spatial resolution on diffusion kurtosis imaging: An empirical study using 7T MRI. Journal of Magnetic Resonance Imaging, 50(5):1593-1603, November 2019, doi:10.1002/jmri.26755.

Li-Wei Kuo**, Pei-Sheng Lin*, Shih-Yen Lin, Ming-Fang Liu, Hengtai Jan, Hsin-Chien Lee, Sheng-Chang Wang*. Functional Correlates of Resting-state Connectivity in the Default Mode Network of Heroin Users on Methadone Treatment and Medication-free Therapeutic Community Program. Frontiers in Psychiatry, 10:381, June 2019, doi:10.3389/fpsyt.2019.00381.

Advanced Diffusion MRI in Neurological and Neurodegenerative Diseases

During the past decade, mapping complex structural and functional networks in living human brain using non-invasive neuroimaging technologies has been widely developed and employed on a variety of cognitive and clinical neuroscience researches. Among all modern neuroimaging technologies, magnetic resonance imaging (MRI) has been considered as one of the most reliable and reproducible neuroimaging modalities for exploring the complex brain networks with adequate spatial and temporal resolutions. In this talk, I will introduce how we develop advanced diffusion MRI techniques and analysis methods to investigate the tissue microstructures, brain structural connectivity, and complex brain networks. The applications on neurological and neurodegenerative diseases will also be introduced and discussed.

Keyword: Neuroimaging, Diffusion MRI, Structural Connectivity, Neurological Disease, Neurodegenerative Disease

Maxim A. SOLOVCHUK

Associate Investigator Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, No. 35 Keyan Road, Zhunan Town, Miaoli County 350053, Taiwan

Tel: +886 (37) 206166 *37156 E-Mail: solovchuk@gmail.com



Education

2007 Ph.D. degree in the Theoretical Physics Department, I. Kant State University

of Russia, Kaliningrad

2004 Master's degree with honours, Theoretical Physics Department, Kaliningrad

State University

Research and Professional Positions Held in Chronological Sequence

2008- 2009	Associate Professor (Docent), Theoretical Physics Department, I. Kant State University of Russia.
2009- 2012	Postdoctoral Research Fellow, National Taiwan University, Taida Institute for Mathematical Science (TIMS), Center for Advanced Study in Theoretical Sciences (CASTS); Department of Engineering Science and
	Ocean Engineering
2012- 2015	Research Associate, National Taiwan University, Taida Institute for Mathematical Sciences (TIMS), Center for Advanced Study in Theoretical Sciences (CASTS)
2015- 2019	Assistant Investigator, Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes
2016- 2020	Assistant Professor (Joint Appointment), National Taiwan University, Department of Engineering Science and Ocean Engineering
2020- present	Associate Principal Investigator, Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes
2020- present	Associate Professor (Joint Appointment), National Taiwan University, Department of Engineering Science and Ocean Engineering
2020- present	Associate Professor (adjunct), National Chung Hsing University, Graduate Institute of Biomedical Engineering, Research Center in Tissue Engineering and Regenerative Medicine

Publications

Maxim A. Solovchuk, Tony W. H. Sheu, Marc Thiriet, Image-based computational model for focused ultrasound ablation of liver tumor, Journal of Computational Surgery, 1:4, 2014 (invited article).

Maxim A. Solovchuk, San Chao Hwang, Hsu Chang, Marc Thiriet, Tony W. H. Sheu, Temperature elevation by HIFU in ex-vivo porcine muscle: MRI measurement and simulation study, Medical Physics, 2014, 41, 052903.

Maxim A. Solovchuk, Tony W. H. Sheu, Marc Thiriet, Multiphysics Modeling of Liver Tumor Ablation by High Intensity Focused Ultrasound, Communication in Computational Physics, 18 (04), 1050-1071, 2015.

Maxim A. Solovchuk, Marc Thiriet, Tony W. H. Sheu, Computational study of acoustic streaming and heating during acoustic hemostasis, Applied Thermal Engineering, 124, 1112-1122, 2017.

K. Zilonova, M. Solovchuk*, T.W.H. Sheu, Bubble dynamics in viscoelastic soft tissue in high-intensity focal ultrasound thermal therapy, Ultrasonics Sonochemistry, 40(A), 900-911, 2018. (among most downloaded papers)

M. Diaz, M. A. Solovchuk*, T.W.H. Sheu, A Conservative Numerical Scheme for Modeling Nonlinear Acoustic Propagations in Thermoviscous Media, J. of Computational Physics, 2018, 363, 200-230.

M. Diaz, M. A. Solovchuk*, T.W.H. Sheu, High–Performance Multi–GPU Solver for Describing Nonlinear Acoustic Waves in Homogeneous Thermoviscous Media, Computers& Fluids, 2018, 173, 195-205.

Zilonova, E. M., Solovchuk, M.*, & Sheu, T. W. H., Simulation of cavitation enhanced temperature elevation in a soft tissue during high-intensity focused ultrasound thermal therapy. Ultrasonics Sonochemistry., 53, 11-24, 2019

Zilonova, E., Solovchuk, M.*, & Sheu, T. W. H.*. Dynamics of bubble-bubble interactions experiencing viscoelastic drag. Physical Review E, 2019, 99(2), 023109.

M. Solovchuk*, P. A. Deng, T.W.H. Sheu, Experimental and numerical study on the temperature elevation in tissue during moxibustion therapy, Evidence-Based Complementary and Alternative Medicine, 2020, Article ID 7514302.

MRI Guided Focused Ultrasound Treatment of Cancer: Treatment Planning and Monitoring

High intensity focused ultrasound (HIFU) is very promising new technology, that has many therapentic application, among them are the treatment of cancer in different organs without major side effects. MRI guided focused ultrasound is completely non-invasive and currently many clinical trials are performed for cancer treatment in different organs. With the ultrasound beam being focused, thermal energy can be added primarily to a small region of tissues with little or no deposition at all on the surrounding tissues. When tissue temperature is higher than 55 °C, thermal coagulation necrosis occurs, which can be used for tumor ablation. MRI provides real-time monitoring capability. Both a necrosed area and temperature elevation during the treatment can be observed. For the further development of the technology multidisciplinary approach is required, which includes optimization of MR imaging and thermal monitoring, characterization of different tissues, modeling of ultrasound propagation through different tissues and optimization of the treatment. We are working on the development of surgical planning platform for a non-invasive focused ultrasound tumor ablative therapy. High performance computing on multiple GPUs is performed for the calculation of ultrasound propagation in a patient specific geometry and optimization of the treatment. Mathematical and computational model is constructed that includes nonlinear ultrasound propagation in heterogeneous tissues, takes into account the effect of blood flow on the thermal therapy and cavitation. Simulations of HIFU tumor ablation in a patient specific liver geometry will be presented and it will be shown that the treatment time can be sufficiently reduced up to several minutes. The presented results will be validated by the invivo and ex-vivo experimental data.

Vuk USKOKOVIC

Visiting Assistant Professor Department of Mechanical and Aerospace Engineering, University of California, Irvine, California, United States of America

E-Mail: vuk21@yahoo.com



Education

1995-2001 B.Sc., and MS, Physical Chemistry, University of Belgrade, Yugoslavia 2003 M.Sc., Materials Science & Engineering, University of Kragujevac, Serbia and Montenegro 2006 Ph.D., Nanoscience and Nanotechnologies, Jožef Stefan International

Postgraduate School, Slovenia

Research and Professional Positions Held in Chronological Sequence

Vuk Uskoković is a Visiting Assistant Professor of Mechanical and Aerospace Engineering at University of California in Irvine. His former affiliations as an assistant professor and research scientist include the Schools of Engineering and Medicine at University of Illinois in Chicago (2013 – 2019), School of Pharmacy at Chapman University in Orange County, California (2016 - 2018), Schools of Medicine, Pharmacy and Dentistry at University of California, San Francisco (2007 – 2013), Center for Advanced Materials Processing at Clarkson University in New York (2006 – 2007), Advanced Materials Department at Jožef Stefan Institute in Ljubljana, Slovenia (2002 – 2006), and the Serbian Academy of Sciences and Arts (2001 – 2002). Dr. Uskoković is the director of the NIH-funded Advanced Materials and Nanobiotechnology Laboratory, whose goal is the development of nanotechnological innovations in the field of biomedicine. Bridging the gap between materials science and life science, the lab specializes in synthesis, characterization and biological testing of materials for the next generation of medical devices. The most influential work to have emerged from it pertains to the use of calcium phosphate nanoparticles for advanced drug and gene delivery applications. Other materials, including magnetic nanocomposites and carbonbased materials, are also engineered and their interface with the biological systems probed, all with the goal of creating clinically effective therapeutics and diagnostics. Socially responsible materials together with in vitro biological assays that substitute for animal testing present an important aspect of research done in the Uskoković Lab. This social responsibility also comes into play through seeing the lab as an incubator of high-tech skills for knowledgebased economy.

Publications

Vuk Uskoković, Sean Tang, Victoria M. Wu – "Targeted Magnetic Separation of Biomolecules and Cells using Earthicle-Based Ferrofluids", *Nanoscale* 11, 11236 – 11253 (2019).

Alessio Adamiano, Victoria M. Wu, Francesca Carella, Gianrico Lamura, Anna Tampieri, Michele Iafisco, Vuk Uskoković – "Magnetic Calcium Phosphates Nanocomposites for the Intracellular Hyperthermia of Cancers of Bone and Brain", *Nanomedicine* 14 (10) 1267 – 1289 (2019).

Vuk Uskoković, Eric Huynh, Sean Tang, Sonja Jovanović, Victoria M. Wu – "Colloids or Powders: Which Nanoparticle Formulations Do Cells Like More?" *Colloids and Surfaces B: Biointerfaces* 181, 39 - 47 (2019).

Victoria M. Wu, Eric Huynh, Sean Tang, Vuk Uskoković – "Brain and Bone Cancer Targeting by a Ferrofluid Composed of Superparamagnetic Iron-Oxide/Silica/Carbon Nanoparticles (Earthicles)", *Acta Biomaterialia* 88, 422 – 447 (2019).

Vuk Uskoković, Valerio Graziani, Victoria M. Wu, Inna V. Fadeeva, Alexander S. Fomin, Igor A. Presniakov, Marco Fosca, Marzo Ortenzi, Ruggero Caminiti, Julietta V. Rau – "Gold is for the Mistress, Silver for the Maid: Enhanced Mechanical Properties, Osteoinduction and Antibacterial Activity due to Iron Doping of Tricalcium Phosphate Bone Cements", Materials Science and Engineering C: *Materials for Biological Applications* 94, 798 – 810 (2019).

Sebastian P. Pernal, Victoria M. Wu, Vuk Uskoković – "Hydroxyapatite as a Vehicle for the Selective Effect of Superparamagnetic Iron Oxide Nanoparticles against Human Glioblastoma Cells", ACS Applied Materials and Interfaces 9 (45) 39283 – 39302 (2017).

Vuk Uskoković – "Entering the Era of Nanoscience: Time to Be So Small", *Journal of Biomedical Nanotechnology* 9, 1441 – 1470 (2013).

Vuk Uskoković, Aljoša Košak, Miha Drofenik – "Preparation of Silica-Coated Lanthanum-Strontium Manganite Particles with Designable Curie Point, for Application in Hyperthermia Treatments", *International Journal of Applied Ceramic Technology* 3 (2) 134 – 143 (2006).

Hyperthermia with Composite Magnetic Nanoparticles as a Cancer Treatment Modality

Magnetic radiation is one of the least harmful and invasive types of radiation used in medicine. Recent results on the design of composite magnetic nanoparticles for the hyperthermia treatments of malignant gliomas and osteosarcomas in alternate magnetic fields will be presented. These nanoparticles are formulated as aqueous, surfactant-free ferrofluids that are administrable parenterally. They are composed of superparamagnetic iron oxide cores, inner shells comprising silica and outer shells made of carbon, having 10 -20 nm in size on average. The nanoparticles preferentially bind to brain cancer cells and exhibit greater toxicity in these cells compared to the primary ones. Even in an ultralow alternate magnetic field, the nanoparticles generate sufficient heat to cause the tumor death. This ability of theirs to selectively target the cancer cell population and cause its effective disintegration in the alternate magnetic field of an ultralow intensity can be harnessed in the design of the next generation cancer therapies. The nanoparticles are also capable of traversing the blood-brain barrier transcellularly and localizing to the brain tissues, while preserving the integrity of this barrier and causing no adverse systemic effects to the animals. Different response of the nanoparticles in the magnetic field depending on whether they are delivered as ferrofluids or as powders will be discussed. In conclusion, these composite nanoparticles show great promise as an anticancer biomaterial for the treatment of different types of cancer and may serve as an alternative or addendum to traditional chemotherapies.

Olga A. KOVAL

Senior scientist, I

Institute of Chemical Biology and Fundamental Medicine, Russia

Assistant Professor

Novosibirsk State University, Russia

Tel: +7-383-3635190 E-Mail: o.koval@niboch.nsc.ru



Education

2003 Ph.D. Institute of Chemical Biology and Fundamental Medicine, Russia

Research and Professional Positions Held in Chronological Sequence

Dr. Koval received her Ph.D. at the Institute of Chemical Biology and Fundamental Medicine, Russia in 2003, where she remains for the present time. In her research Dr. Koval ranged from the study of apoptosis-inducing proteins as anticancer agents to oncolytic viruses and CAR-T cells. She has won the Award of the President of Russian Federation for outstanding achievement in molecular biology in 2006. More recently she has turned her attention to the construction of recombinant vaccinia viruses and investigation of their oncolytic properties. Moreover, in collaboration with physicists she involved in the investigation of the cold atmospheric plasma activity towards to cancer cells as a new anticancer approach.

Publications

Bagamanshina AV, Troitskaya OS, Nushtaeva AA, Yunusova AY, Starykovych MO, Kuligina EV, Kit YY, Richter M, Wohlfromm F, Kähne T, Lavrik IN, Richter VA, Koval OA. Cytotoxic and Antitumor Activity of Lactaptin in Combination with Autophagy Inducers and Inhibitors. Biomed Res Int. (2019) Jun 17;2019:4087160. doi: 10.1155/2019/4087160. eCollection 2019.

Manko N, Starykovych M, Bobak Y, Stoika R, Richter V, Koval O, Lavrik I, Horák D, Souchelnytskyi S, Kit Y. The purification and identification of human blood serum proteins with affinity to the antitumor active RL2 lactaptin using magnetic microparticles (2019). Biomed Chromatogr. (2019) Jul 12:e4647. doi: 10.1002/bmc.4647.

Nushtaeva A, Karpushina A, Ermakov M, Gulyaeva L, Gerasimov A, Sidorov S, Gayner T, Yunusova A, Tkachenko A, Richter V, Koval O. (2019) Establishment of primary human

breast cancer cell lines using "pulsed hypoxia" method and development of metastatic tumor model in immunodefcient mice // Cancer Cell Int, 19:46. https://doi.org/10.1186/s12935-019-0766-5. IF=3.96

Chanyshev MD, Koval OA, Nushtaeva AA, Gulyaeva LF. (2019) Effect of benzo[a]pyrene on the expression of miR-126, miR-190a and their target genesEGFL7,TP53INP1andPHLPP1 in primary endometrial cells // J Biochem Mol Toxicol. 2019;e22314. DOI: 10.1002/jbt.22314. IF=2.61

Koval O., Kochneva G., Troitskaya O., Tkachenko O., Nushtaeva A., Kuligina E., Richter V (2019) Implication of immune system in vaccinia virus-induced cell death // Cell Death Discovery. P. 35-36. – DOI: 10.1038/s41420-018-0128-4.

Golubitskaya E., Chinak O.A., Pyshnaya I.A., Stepanov G.A., Zhuravlev E.S., Richter V.A., Koval O.A. (2019) Boosting of the cytotoxic effect of RNAs by using the pro-apoptotic protein lactaptin for delivery of nucleic acids into cancer cells // Cell Death Discovery. P. 28-29. – DOI: 10.1038/s41420-018-0128-4.

Richter M., Wohlfromm F., Koval O.A., Kähne T., Richter V.A., Lavrik I. (2019) Recombinant analogon RL2 of human κ-Casein induces cell death in breast cancer cell lines // Cell Death Discovery. P. 12. – DOI: 10.1038/s41420-018-0128-4.

Koval O., Volkova O., Kulemzin S., Gorchakov A, Tkachenko A., Nushtaeva A., Kuligina E., Richter V., Taranin A. (2017) NK-cell based delivery of anticancer therapeutics. Annals of Oncology, V. 28, I. suppl 11, doi.org/10.1093/annonc/mdx711.050. IF=13.9

Nushtaeva A.A., Stepanov G.A., Semenov D.V., Zhuravlev E.S., Balahonova E.A., Gerasimov A.V., Sidorov S.V., Savelyev E.I., Kuligina E.V., Richter V.A., Koval O.A. (2018) Characterization of primary normal and malignant breast cancer cell and their response to chemotherapy and immunostimulatory agents // BMC Cancer, V18, P. 728-739. IF=3.28

Matvienko D.A., Kulemzin S.V., Smagina A.S., Belovezhets T.N., Chikaev A.N., Volkova O.Y., Chikaev N.A., Koval O.A., Kuligina E.V., Taranin A.V., Gorchakov A.A. (2018) ANALYSIS OF IN VITRO ACTIVITY OF PSCA-SPECIFIC CARS IN THE CONTEXT OF HUMAN NK CELL LINE YT // Cellular Therapy and Transplantation. T. 7. № 2. C. 70-77. IF=0.15

Novel Therapeutic Approaches Based on Cold Atmospheric Argon and Helium Plasma Irradiation of Biotarget

Along with developing efficacious chemotherapeutic agents to treat malignant neoplasms, much attention is currently being paid to physical methods. Cold atmospheric plasma (CAP) has been shown as potential anticancer tool. CAP is an ionized gas consisting of charged particles, active uncharged particles, an electric field and UV radiation. Two type of CAP treatment was applied to achieve cytotoxic effect on cancer cells: direct irradiation and irradiation of culture medium and both were successful. Here, we analyzed the selectivity of CAP-induced cell death as well as the mechanism of cell death after CAP treatment. The biological effect of plasma-activated cultural medium on the epidermoid carcinoma cells A431, and normal human embryonic kidney cells HEK-293T has been investigated. The medium was exposed to CAP irradiation generated in argon gas for 2-8 min at a voltage of 4.9 kV and then added to the cells. The proliferation of the directly treated cells in real time mode was measured using iCELLigence RTCA. The rate of apoptotic and necrotic cells were analyzed by the flow cytometry. The levels of intracellular reactive oxygen (ROS) and nitrogen (RNS) species, which are known to be the main CAP affectors, were measured with 2',7'-dichlorofluorescin diacetate fluorescent dye. In order to determine the parameters of the cold plasma jet that can be changed to enhance the specific cytotoxic effects, the grounded substrate beneath was introduced into the system. We showed more efficient suppression of the proliferation of cancer cell with the presence of grounded substrate.

To revel the conditions when the selectivity of CAP against tumor cells can be achieved we used a pair of lung cell lines: adenocarcinoma cells A549 and normal fibroblasts Wi-38. The viability of A549 and Wi-38 cells after direct CAP treatment were examined. Under optimized CAP conditions (duration 60 c, voltage amplitude 4.2 kV, 3 L/min in helium) Wi-38 stayed alive and A549 cancer cells were killed. The expression profiles of CAP-treated cells were evaluated by using RNA-seq. Functional analyses were employed to reveal the difference in normal and cancer cell response. The substantial difference of transcription factors response was detected between cancer and normal cells. The data obtained could be a basis for the development of selective CAP treatment of cancer cells. This study was supported by the RSF grant # 19-19-00255.

Antonina V. LEVSHAKOVA

Head of the Department of Computed Tomography and Magnetic Resonance Imaging, Moscow, Russia

Tel: +79031880816 Fax: +74959458020

E-Mail: levshakova71@mail.ru



Education

2004 Ph.D., Russian Medical Academy of Postgraduate Education, Moscow,

Russia (preparation and defense of Thesis)

2011 Dr. Sci., Moscow State Medical and Dental University, Moscow, Russia

(preparation and defense of Thesis)

Research and Professional Positions Held in Chronological Sequence

Antonina Levshakova is head of the Department of Computed Tomography and Magnetic Resonance Imaging, Moscow, Russia. The main direction of his scientific and practical activity is oncoradiology. The Department uses all modern methods of CT and MRI studies necessary to identify, assess the prevalence and effectiveness of treatment of malignant tumors. Scientific directions of the Department are aimed at differential diagnosis of malignant tumors, as well as determining the degree of hypoxia and heterogeneity of the tumor using various imaging methods such as CT perfusion and MR-spectroscopy. Herzen Moscow Research Cancer Institute is the oldest cancer institution in Russia, where the foundations of Russian cancer science were laid.

Publications

Peshkov A.O., Rubtsova N.A., Levshakova A.V., Khomyakov V.M., Utkina A.B., Sidorov D.V., Grishin N.A. Computed tomography and magnetic resonance tomography in peritoneal carcinomatosis diagnosis (lection) // Radiology. Practice (Rus). 2019. Accepted for printing.

Kryaneva Elena V., Rubtsova Natalia A., Levshakova Antonina V., Khalimon Aleksandr I., Leontyev Aleksey V., Kalpinskiy Aleksey S., Nyushko Kirill M., Nikiforovich Petr A., Polyakov Andrey P., Zikiryakhodzhaev Aziz D., Kaprin Andrey D. Rare localization of renal cell carcinoma metastases in the paranasal sinuses and breast: a case report. // Medical Imaging (Rus). 2018;6: 17-22. DOI: 10.24835/1607-0763-2018-6-13-22.

Boiko A.V., Gevorkov A.R., Bolotina L.V., Kornietskaya A.L., Volchenko N.N., Polyakov A.P., Sokolov V.V., Telegina L.V., Rubtsova N.A., Levshakova A.V., Malysheva O.A., Titova O.A., Nikiforovich P.A. Current possibilities of diagnosis and combined treatment in patients with locally advanced nasopharyngeal carcinoma // P.A. Herzen Journal of Oncology (Rus). 2018;3: 42-46. DOI: 10.17116/onkolog/ 20187342.

Kaprin A.D., Rubtsova N.A., Khalimon A.I., Levshakova A.V., Ryabov A.B., Pikin O.V., Amiraliev A.M., Volchenko N.N., Bruslinskaya A.B. Diagnosis and Treatment of Recurrent Malignant Peripheral Nerve Sheath Tumor (Literature Review and Clinical Case) // Radiology. Practice (Rus). 2017;3: 29-38.

CT Perfusion in Differential Diagnosis and Evaluation of the Effectiveness of Treatment of Malignant Tumors

Perfusion computed tomography (CTp) is a imaging technique that provides qualitative and quantitative information about tumor angiogenesis. Changes in perfusion indicators, in particular – a decrease, may indicate the effectiveness of treatment before the tumor size decreases. Other potential benefits include determining the histological subtype of the tumor and predicting potentially aggressive tumors that can help clinicians better plan patient therapy. The Institute conducts research on the use of CT perfusion in assessing the effectiveness of treatment of malignant tumors of different localization using systemic chemotherapy, targeted therapy, as well as after regional chemoembolization. A Protocol of low-dose CT perfusion of the pancreas in case of suspected neuroendocrine tumor was developed. Threshold values of perfusion parameters of benign and malignant kidney tumors and various histopathological types of kidney tumors, including low - and highly differentiated light cell kidney cancer, were determined. A study is conducted to assess the state of renal tissue after resection in the early and late postoperative period, depending on the ischemic method (with renal artery clamping or anoxia against the background of controlled hypotension). We believe that our research will improve the results of treatment of patients with malignant tumors.

Michele IAFISCO

Senior researcher Institute of Science and Technology for Ceramics, National Research Council (CNR) in Faenza (RA), Italy

Tel: +39 0546 699730

Fax: +39 0546 46381

E-Mail: michele.iafisco@istec.cnr.it



Education

2005 B.S. Chemistry, University of Bologna

2009 Ph.D. in Chemical Science, University of Bologna

Research and Professional Positions Held in Chronological Sequence

Michele lafisco is senior researcher at Institute of Science and Technology for Ceramics (ISTEC) of the National Research Council (CNR) in Faenza (RA), Italy. He graduated in Chemistry in 2005 from the University of Bologna. From the same university he obtained the Ph.D. degree in Chemical Science in April 2009. His research interests include biomaterials, biomineralization, nanotechnology, and bioceramics. He has authored more than 100 papers in international peer-reviewed journals, 15 book chapters and 6 patents. H-index=32, total citation: more than 2900, Source: Google Scholar (January 2020). He is member of the editorial boards of several international journals and expert evaluator for the European Commission and for other European research agencies. In 2015 he was recipient of the prize "Ricercatamente 2014" for the best research activity of most promising young researcher "under 35" at the National Research Council of Italy in the field "Chemical Sciences and Materials Technology" and of the IUPAC-2015 Young Chemist Travel Award. He is scientific responsible of the Research Line on "Nanostructured materials for dental and maxillofacial applications" of the ISTEC-CNR.

<u>Publications</u>

Nanotechnological approach and bio-inspired materials to face degenerative diseases in aging. A Tampieri, M Sandri, M Iafisco, S Panseri, M Montesi, A Adamiano, M Dapporto, E Campodoni, S M Dozio, L Degli Esposti, S Sprio. *Aging Clin Exp Res*, 2019, 1-17.

Role of citrate in the formation of enamel-like calcium phosphate oriented nanorod arrays. F Carella, L Degli Esposti, D Barreca, G A Rizzi, G Martra, P Ivanchenko, G Escolano Casado, J Gomez Morales, J M Delgado Lòpez, A Tampieri, M Iafisco. *CrystEngComm*,

2019, 21 (32).

The effect of the repression of oxidative stress on tenocyte differentiation: A preliminary study of a rat cell model using a novel differential tensile strain bioreactor. M-Y Hsiao, P-C Lin, W-H Liao, W-S Chen, C-H Hsu, C-Kun He, Y-W Wu, A Gefen, M Iafisco, L Liu, F-H Lin. *Int. J. Mol. Sci.*, 2019, 20 (14).

Nanomedicine approaches for the pulmonary treatment of cystic fibrosis. C Velino, F Carella, A Adamiano, F Bugli, M Sanguinetti, A Vitali, D Catalucci, M Iafisco. *Front. Bioeng. Biotech.*, 2019, 7.

Influence of Hydroxyapatite Nanoparticles on Germination and Plant Metabolism of Tomato (Solanum lycopersicum L.): Preliminary Evidence. L Marchiol, A Filippi, A Adamiano, L Degli Esposti, M Iafisco, A Mattiello, E Petrussa, E Braidot. *Agronomy*, 2019, 9 (4).

Cardiovascular nanomedicine: the route ahead. M Iafisco, A Alogna, M Miragoli, D Catalucci. *Nanomedicine*, 2019, 14 (18).

Magnetic calcium phosphates nanocomposites for the intracellular hyperthermia of cancers of bone and brain. A Adamiano, V M Wu, F Carella, G Lamura, F Canepa, A Tampieri, M Iafisco, V Uskoković. *Nanomedicine*, 2019, 14 (10).

Bioinspired crystallization, sensitized luminescence and cytocompatibility of citrate-functionalized Ca-substituted europium phosphate monohydrate nanophosphors. J Gómez-Morales, C Verdugo-Escamilla, R Fernández-Penas, C Parra-Milla, C Drouet, M Iafisco, F Oltolina, M Prat, J Fernández-Sánchez. *J. Colloid. Interf. Sci.*, 2019, 538 (7).

A sustainable multi-function biomorphic material for pollution remediation or UV absorption: Aerosol assisted preparation of highly porous ZnO-based materials from cork templates. A Quarta, R M Novais, S Bettini, M Iafisco, R C Pullar, C Piccirillo. *J. Environ. Chem. Eng.*, 2019, 7 (2).

Bioinspired mineralization of type I collagen fibrils with apatite in presence of citrate and europium ions. J Gómez-Morales, R Fernández Penas, C Verdugo-Escamilla, L Degli Esposti, F Oltolina, M Prat, M Iafisco, J Fernández Sánchez. *Crystals*, 2019, 9(1), 13.

Superparamagnetic hybrid microspheres affecting osteoblasts behavior. T M Fernandes Patrício, S Panseri, M Montesi, M Iafisco, M Sandri, A Tampieri, S Sprio. *Mater. Sci. Eng. C*, 2019, 96.

On the Use of Calcium Phosphate Nanoparticles as Agent for Magnetic and Nuclear *In-vivo* Imaging

In recent years, biomimetic calcium phosphate (CaP) nanoparticles (NPs), having chemical similarity with the mineral phase of bone, have attracted a great interest in nanomedicine. To evaluate the therapeutic perspectives of CaP NPs through the mechanisms of action and organs they interact with, the non-invasive monitoring of their in vivo behavior is of paramount importance. To this aim, the feasibility to radiolabel CaP NPs ("naked" and surface-modified with citrate to reduce their aggregation) with two positron emission tomographic (PET) imaging agents ([18F]NaF and 68Ga-NO₂APBP) was investigated. The labeling results with both tracers were fast, straightforward, and reproducible. CaP NPs demonstrated excellent ability to bind relevant quantities of both radiotracers and good in vitro stability in clinically relevant media after the labeling. In vivo PET studies in healthy Wistar rats established that the radiolabeled CaP-NPs gave significant PET signals and they were stable over the investigated time (90 min) since any tracer desorption was detected. Moreover, the identification of alternative biocompatible magnetic NPs for advanced clinical application is becoming an important need due to raising concerns about iron accumulation in soft issues associated to the administration of superparamagnetic iron oxide NPs. Here, we report on the performance of iron-doped CaP (FeCaP) NPs as contrast agent for magnetic resonance imaging (MRI). The MRI contrast abilities of FeCaP and Endorem® (dextran coated iron oxide NPs) were assessed by ¹H nuclear magnetic resonance relaxometry and their performance in healthy mice was monitored by a 7 Tesla scanner. FeCaP applied a higher contrast enhancement, and had a longer endurance in the liver with respect to Endorem® at iron equality. Additionally, a proof of concept of FeCaP use as scintigraphy imaging agent for positron emission tomography (PET) and single photon emission computed tomography (SPECT) was given labeling NPs with 99mTc-MDP. FeCaP efficiency as MRI-T2 and PET-SPECT imaging agent combined to its already reported intrinsic biocompatibility qualifies it as a promising material for innovative nanomedical applications.

Ryuichi TANAKA

Vice President and Secretary Genera NPO Radiation Education Forum, Japan

Tel: +81-027-251-4825

E-Mail: ryutnk@kra.biglobe.ne.jp



Education

1961- 1964 Bachelor Degree in Physics, Tokyo Institute of Technology Doctorate of Engineering degree from Osaka University

Research and Professional Positions Held in Chronological Sequence

1964	Japan Atomic Energy Research Institute (JAERI)
1986- 1999	JAERI, Senior researcher, Head, Adv. Radiation Application Project
1999- 2000	JAERI, Director, Takasaki Radiation Chemistry Research Development
	Establishment
2000- 2004	Representative Director, Beam Operation Co., Ltd.
1998- present	Member, Radiation Education Forum (NPO incorporated in 2000)
	Director (2004~)
2012- present	Vice President and Secretary Genera, NPO Radiation Education Forum

Publications

田中隆一(Ryuichi Tanaka), 電子線に着目したクルックス管観察の学習展開の考察 (Consideration of learning development of observation of crux tube focusing on electron beam), 放射線教育(Radiation Education) 22, 1, 13-22 (2018)

田中隆一(Ryuichi Tanaka), 宮川俊晴(Toshiharu Miyakawa),新教科書による中学校での放射線授業実践の支援 一放射線教育フォーラムの最近の活動から一, (Supporting radiation class practice in junior high school with new textbooks -From recent activities of radiation education forum),エネルギー・環境教育研究(Energy and environmental education research) 11, No.2, 77-82 (2017)

田中隆一(Ryuichi Tanaka), 放射線学習の骨組みを構成するキーワードの要点解説 (Explanation of key points that make up the framework of radiation learning), 放射線教育 (Radiation Education) 16, 1, 57-66

田中隆一(Ryuichi Tanaka), 学習指導要領に基づいた放射線等の取扱いに関する考察 (Consideration about the handling of radiation etc. based on the course of study), エネルギー・環境教育研究(Energy and environmental education research) 3, No.2, 73-79 (2009)

- 田中隆一(Ryuichi Tanaka), 放射線は日本社会でどのように怖がられているか (How is radiation scared in Japanese society) , 放射線教育(Radiation Education) 8, 1, 83-94 (2004)
- 田中隆一(Ryuichi Tanaka), 高速イオンによる放射線法要研究の現状と展望(Present Status and Future Development of Research for Advanced Radiation Application Using Fast Ions), 応用物理(Applied Physics)69, 4, 369 (2000)
- 田中隆一(Ryuichi Tanaka), 神谷富宏(Tomihiro Kamiya), 小林泰彦(Yasuhiko Kobayashi), 渡辺宏(Hiroshi Watanabe), 高エネルギーシングルイオンヒット技術と細胞局部照射への応用 (High-Energy Single Ion Hit Technique and Its Application to Local Irradiation of Living Cells), 応用物理(Applied Physics) 65, 2, 168 (1996)
- R. Tanaka and T. kamiya: The JAERI High Energy, Heavy Ion Microbeam System and Single Ion Hit Technique, *Nucl. Instr. and Methods*, B79 432 (1993)
- R. Tanaka, H. Sunaga and T. Kojima: A Simultaneous Electron Energy and Dosimeter Calibration Methods for Electron Beam Irradiator, Proceedings of a Symposium on High-Dose Dosimetry for Radiation Processing, Vienna 5-9 Nov. (1990)
- R. Tanaka, H. Kaneko, N. Tamura, A. Katoh and Y. Moriuchi: Standard Measurement of Processing Level Gamma Ray Dose Rates with a Parallel-Plate Ionization Chamber, Proceedings of a Symposium on High-Dose Dosimetry, Vienna 8-12 Oct. 1984 IAEA STI/PUB/671 (1985)
- R. Tanaka, S. Mitomo and N. Tamura: Effects of Temperature, Relative Humidity, and Dose Rate on the Sensitivity of Cellulose Triacetate Dosimeter to Electrons and γ -rays, Intern. J. Appl. *Radiat. Isot.* 35, 9, 875
- R. Tanaka, K. Mizuhashi, H. Sunaga, and N. Tamura: A Simple and Accurate Measurement Method of Current Density of Electron Accelerator for Irradiation, *Nucl. Instr. and Methods*, 174, 201 (1980)
- R. Tanaka, H. Sunaga, and N. Tamura: The Effect of Accumulated Charge on Depth-Dose Profile in Poly(methylmethacrylate) Irradiated with Fast Electron Beam, IEEE Trans. *Nucl. Sci.* NS-26 4670 (1979)
- R. Tanaka, H. Sunaga, and H. Hotta: Depth-Dose Distribution in an Aluminam-Blue Cellophane Stack for a High-Intensity Electron Beam in Atmosphere of Helium, Radiation Research 63 14 (1975)

Recent Progress of Radiation Education Support for School Teachers Focusing on the Activities of Radiation Education Forum

Radiation education in Japanese school started in 1951 with science classes at junior high schools, but was canceled in 1977 due to the revision of the course of study. However, the fear of radiation continued to be taught in classes such as social studies and national language from the elementary school stage, related to the atomic bomb disasters in Hiroshima and Nagasaki. To improve these situations, Radiation Education Forum (REF), launched in 1994, made policy recommendations to the Ministry of Education, for the revival of radiation learning. As a result, the guidance of learning has been revived by the FY2007 revision of the course of study after 30 years of radiation education blank, and radiation classes restarted in FY2011 in the third-grade science of junior high school in the context of social studies.

However, the 3.11 accident at the TEPCO Fukushima Daiichi Nuclear Power Station with massive release of radioactive material to the environment occurred happened just before the restart of radiation lessons, and fake and fearful information had spread to television and newspapers along with information from experts, which is generally difficult for ordinary people to understand. These influences of the accident and the 30-year blank in radiation education had led to confusion and hesitation over the lesson practices of school teachers, a lot of them who had never learned and/or been taught radiation. Traditionally, Experts have provided lectures on radiation to school teachers, but the one-way provision of information has not helped students deepen their understanding within a limited class time. The fact that one-way information provision by experts has not helped teachers practice the lesson is also behind their confusion and hesitation.

Based on the above background, Radiation Education Forum has supported the practice of radiation classes mainly in junior high school science. Through the four panel discussions (2013~2016) organized by REF, direct discussions were repeated among many teachers, experts, and supporters,

mainly on how radiation classes should be based on radiation descriptions in new textbooks. As a result of the panel discussions, REF proposed a radiation lesson plan that will be built up in stages throughout the three years of junior high school, in place of the current curriculum that incorporates radiation classes in the second half of the third grade.

REF has also emphasized the importance of scientific understanding of radiation in school education since the establishment, On the other hand, as mentioned earlier, radiation learning in FY2007 revision of the course of study for junior high school science was introduced from a social study perspective. However, in light of the spread of harmful rumors after the 3.11 accident in 2011, the latest revision of the course of study in FY2017 emphasized scientific understanding related to radiation, and radiation learning has newly appeared in the second year of junior high school. This learning guidance will be implemented from FY2021, and is expected to considerably improve radiation education at junior high schools.

Yoshimune OGATA

Associate Professor Radioisotope Research Center Medical Division, Nagoya University, Japan

Tel: +81-52-744-2414

E-Mail: yoshimune.ogata@aichi-med-u.ac.ip



Education

1979- 1983	Science Course, Hokkaido University
1983- 1986	Department of Radiological Technology, Nagoya University
1986- 1990	Department of Engineering, Nagoya Institute of Technology
Degree	Doctor of Environmental Studies (Nagoya University)

Research and Professional Positions Held in Chronological Sequence

1986	Radiological Technologist, Department of Radiological Technology,
1986- 1997	Nagoya University Hospital
1900- 1997	Radiation Safety Manager, Radioisotope Research Center, Nagoya University
1997- 1999	Research Associate, Radioisotope Research Center, Nagoya University
1999- 2015	Assistant Professor, Department of Radiological Technology, Nagoya University School
2015- present	Associate Professor, Radioisotope Research Center Medical Division, Nagoya University

Publications

Determination of ¹³⁴Cs activity by the sum-peak method via a well type Ge detector. Yoshimune Ogata, Hidesuke Itadzu, Sadao Kojima, J Radioanalytical and Nuclear Chemistry, Vol. 316, p.1145-1149, DOI 10.1007/s10967-018-5784-6 (2018)

Estimation of ¹³⁴Cs activity by a new approximation referred to the sum peak method via a well-type Ge detector, Yoshimune Ogata, Hidesuke Itadzu, Sadao Kojima, Applied Radiation and Isotopes, Vol. 134p.172-176 (2018)

Geant4 based Monte Carlo simulation for verifying the modified sum-peak method, Tsukawa Aso, Yoshimune Ogata, Ryuta Makino, Applied Radiation and Isotopes Vol. 134, p.147-150 (2018)

Evaluation of radiocesium concentration in new leaves of wild plants two years after the Fukushima Dai-ichi Nuckear Power Plant accident, Yuki Sugiura, Michihiro Shibata, Yoshimune Ogata, Hajime Ozawa, Tsutomu Kanasashi, Chisato Takenaka, J Environmental

Radioactivity, Vol. 160, p.8-24 (2016)

Development of a high resolution gamma camera system using finely grooved GAGG scintillator, Seiichi Yamamoto, Jun Kataoka, Tsubasa Oshima, Yoshimune Ogata, Tadashi Watabe, Hayato Ikeda, Yasukazu Kanai, Jun Hatazawa, Nuclear Inst. Methods Phys. Res. A, Vol.821, p.28-33 (2016)

Development of the modified sum-peak method and its application, Y. Ogata, H. Miyahara, M. Ishihara, N. Ishigure, S. Yamamoto, S. Kojima, Applied Radiation and Isotopes, Vol.109, p.354-357 (2016)

Development of a Modified Sum-peak Method for Activity Determination of Some Gamma Emitters, Y. Ogata, H. Miyahara, N. Ishigure, M. Ishihara, M. Nishio, S. Yamamoto, Nuclear Inst. and Methods Phys. Res. A, Vol.775, p.34-40 (2015)

High sensitive airborne radioiodine monitor, Yoshimune Ogata, Tadashi Yamasaki, Ryuji Hanafusa, Applied Radiation and Isotopes, Vol.81, p.119-122 (2013)

Fallout by the Disaster of Fukushima Daiichi Nuclear Plant at Nagoya, Yoshimune Ogata, Radiation Measurements, Vol.55, p.96-98 (2013)

Distribution of thermal neutron flux around a PET cyclotron, Yoshimune Ogata, Nobuhito Ishigure, Shingo Mochizuki, Kengo Ito, Kentaro Hatano, Junichiro Abe, Hiroshi Miyahara, Kazuyoshi Masumoto, Hajime Nakamura, Health Physics, Vol.100 (Supplement 2): S60-S66 (2011)

Radioactivity measurement with a plastic scintillation vial, Yoshimune Ogata, J Radioanalytical and Nuclear Chemistry, Vol.273, pp.253-256 (2007)

Tritium separation by electrolysis using solid polymer electrolyte, Yoshimune Ogata, Sakuma Yoichi, Ohtani Nobuo, Kotaka Masahiro, Fusion Science and Tech., Vol.48, No.1, pp136-139 (2005)

Practice of Radiation Education for Nurses

Nurses are the closest to patients among medical professions, and most patients trust and relay upon nurses. Patients may easily talk to nurses at hospitals. However, there is a problem that most nurses have few knowledge about radiation. Nowadays, a lot of diagnoses and treatments using radiation such as X-ray diagnosis, radiation therapy, nuclear medicine, IVR, etc. are performed in medical fields. Modern medical care cannot carry on without use of radiation, and the role of radiation will increase more and more in future. Nurses are expected to respond appropriately not only in medical fields, but also in events of a nuclear or radiation disaster as the closest to the victims among professions. However, there is no education on radiation nursing in the current nurse's training course. Therefore, nurses have little opportunity to systematically learn about radiation. In addition, post-employment education is inadequate. Many nurses have anxious about radiation. For example, in an X-ray portable imaging in a hospital room, nurses may escape to the outside of the room. Such behavior gives anxiety to patients and their families. It is necessary for nurses to overcome excessive radiation anxiety with the correct knowledge of radiation. It leads to the correct explanation to patients with anxiety and the provision of better nursing care. Therefore, we planned the practice of radiation education for nursing staff. We will provide not only lectures but also experiments to make them as easy to understand and as interesting as possible. In the course, they will experience the effect of shielding and distance, and see the radiation track with a cloud chamber. I will present the details of the results of the education at this conference.

Masafumi AKIYOSHI

Associate Professor, Radiation Research Center, Osaka Prefecture University, Japan

Tel: +81-72-254-9852

E-Mail: akiyoshi@riast.osakafu-u.ac.jp



Education

1988	Odawara prefecture high school of Kanagawa.
1991	Tokyo Institute of Technology.
1995	Master Course, Nuclear Engineering Department,
	Graduate School of Science and Engineering, Tokyo Institute of Technology.
1997	Doctoral Course, Nuclear Engineering Department,
	Graduate School of Science and Engineering, Tokyo Institute of Technology.
2001	Dr. defenced.

Research and Professional Positions Held in Chronological Sequence

Research Laboratory for Nuclear Reactors, Tokyo Institute of Technology. (also hold the post of) Visiting Researcher, Advanced Materials Laboratory, National Institute for Materials Science, Japan Research Associate, Department of Material Science and Engineering, School of Engineering and Applied Science, University of Virginia, USA. Postdoctoral research fellow, Oarai Research Center, Japan Nuclear Cycle Development Institute. Research Associate, Department of Nuclear Engineering, Faculty / Graduate School of Engineering, Kyoto University. Associate Professor.	2001	Part time Lecturer,
Visiting Researcher, Advanced Materials Laboratory, National Institute for Materials Science, Japan 2002 Research Associate, Department of Material Science and Engineering, School of Engineering and Applied Science, University of Virginia, USA. 2002 Postdoctoral research fellow, Oarai Research Center, Japan Nuclear Cycle Development Institute. 2004 Research Associate, Department of Nuclear Engineering, Faculty / Graduate School of Engineering, Kyoto University.		Research Laboratory for Nuclear Reactors, Tokyo Institute of Technology.
Advanced Materials Laboratory, National Institute for Materials Science, Japan Research Associate, Department of Material Science and Engineering, School of Engineering and Applied Science, University of Virginia, USA. Postdoctoral research fellow, Oarai Research Center, Japan Nuclear Cycle Development Institute. Research Associate, Department of Nuclear Engineering, Faculty / Graduate School of Engineering, Kyoto University.		(also hold the post of)
Japan Research Associate, Department of Material Science and Engineering, School of Engineering and Applied Science, University of Virginia, USA. Postdoctoral research fellow, Oarai Research Center, Japan Nuclear Cycle Development Institute. Research Associate, Department of Nuclear Engineering, Faculty / Graduate School of Engineering, Kyoto University.		Visiting Researcher,
2002 Research Associate, Department of Material Science and Engineering, School of Engineering and Applied Science, University of Virginia, USA. 2002 Postdoctoral research fellow, Oarai Research Center, Japan Nuclear Cycle Development Institute. 2004 Research Associate, Department of Nuclear Engineering, Faculty / Graduate School of Engineering, Kyoto University.		Advanced Materials Laboratory, National Institute for Materials Science,
Department of Material Science and Engineering, School of Engineering and Applied Science, University of Virginia, USA. 2002 Postdoctoral research fellow, Oarai Research Center, Japan Nuclear Cycle Development Institute. 2004 Research Associate, Department of Nuclear Engineering, Faculty / Graduate School of Engineering, Kyoto University.		Japan
Applied Science, University of Virginia, USA. 2002 Postdoctoral research fellow, Oarai Research Center, Japan Nuclear Cycle Development Institute. 2004 Research Associate, Department of Nuclear Engineering, Faculty / Graduate School of Engineering, Kyoto University.	2002	Research Associate,
2002 Postdoctoral research fellow, Oarai Research Center, Japan Nuclear Cycle Development Institute. 2004 Research Associate, Department of Nuclear Engineering, Faculty / Graduate School of Engineering, Kyoto University.		Department of Material Science and Engineering, School of Engineering and
Oarai Research Center, Japan Nuclear Cycle Development Institute. Research Associate, Department of Nuclear Engineering, Faculty / Graduate School of Engineering, Kyoto University.		Applied Science, University of Virginia, USA.
2004 Research Associate, Department of Nuclear Engineering, Faculty / Graduate School of Engineering, Kyoto University.	2002	Postdoctoral research fellow,
Department of Nuclear Engineering, Faculty / Graduate School of Engineering, Kyoto University.		Oarai Research Center, Japan Nuclear Cycle Development Institute.
Engineering, Kyoto University.	2004	Research Associate,
		Department of Nuclear Engineering, Faculty / Graduate School of
2014 Associate Professor.		Engineering, Kyoto University.
	2014	Associate Professor,
Radiation Research Center, Osaka Prefecture University.		Radiation Research Center, Osaka Prefecture University.

Publications

Investigation of Low-energy X-ray Radiated from the Crookes Tube Used in Radiological Education, DO Duy Khiem, Hirokazu ANDO, Hiroto MATSUURA, Masafumi AKIYOSHI, Radiation safety management, 18 (2019) 9-15.

Validation of miniature test specimens for post-irradiation thermal diffusivity measurement,

M. Akiyoshi, R. Kasada, Y. Ishibashi, L.M. Garrison, J.W. Geringer, W.D. Porter and Y. Katoh, Fusion Engineering and Design, 136 Part A (2018) 513-517.

Radiation degradation prediction for InGaP solar cells by using appropriate estimation method for displacement threshold energy, Y. Okuno, S. Okuda, M. Akiyoshi, T. Oka, M. Harumoto, K. Omura, S. Kawakita, M. Imaizumi, S. R. Messenger, K. H. Lee and M. Yamaguchi, Journal of Applied Physics, 122 (2017) 114901_1-7.

Development of radiological educational program using a Peltier-cooling-type high performance cloud chamber, M. Akiyoshi, H. Ando, Y. Okuno, H. Matsuura, Proc. of The fifth international symposium on radiation education (ISRE2016), 2017, 54-62.

Irradiation effects on thermal diffusivity and positron annihilation lifetime induced by neutron and 30MeV electron, M. Akiyoshi, H. Tsuchida, I. Takagi, T. Yoshiie, Xu Qiu, K. Sato and T. Yano, Journal of Nuclear Science and Technology, 49 (2012) 595-601.

Thermal diffusivity of ceramics during neutron irradiation, M. Akiyoshi, H. Tsuchida and T. Yano, In C. Sikalidis, editor, Advances in Ceramics - Characterization, Raw Materials, Processing, Properties, Degradation and Healing, pp. 39-58. InTech, Rijeka, Croatia, 2011.

Neutron-irradiation effect in ceramics evaluated from macroscopic property changes in asirradiated and annealed specimens, M. Akiyoshi and T. Yano, Progress in Nuclear Energy, 50 (2008) 567-574.

Relation between macroscopic length change and the crystal structure in heavily neutron-irradiated ceramics, M. Akiyoshi, N. Akasaka, Y. Tachi and T. Yano, Journal of Nuclear Materials, 329-333 (2004) 1466-1470.

A structural model of defects in β -Si3N4 produced by neutron-irradiation, M. Akiyoshi, T. Yano and M.L. Jenkins, Philosophical Magazine A, 81 (2001) 683-697.

Radiation Safety Management for Crookes Tubes in Education Field

Crookes tube is widely used in science education, and in Japan, main purpose is to understand the character of electron and current, not for radiological educations. Therefore, most teachers never mind the leakage of X-rays from Crookes tube. On the other hand, it have been turned out that some Crookes tubes radiate large dose of X-rays (most strong case at a distance of 15 cm, $H_P(0.07)$ reaches 200 mSv/h) which energy is about 20 keV. This energy is too low for conventional survey meters to estimate correct dose (even for Nal scintillator), therefore the dosimetry is quite difficult for teachers in education field. In this study, we use CZT detector to estimate energy spectrum and ionization chamber to obtain dose in our laboratory. Furthermore, we send radio-photoluminescence (RPL) dosimeters they are able to be sent by postal mails to measure the dose of X-rays in education field in Japan. With these measurements, we propose a radiological safety guide line for science education using Crookes tubes..

Wei-Hsung WANG

Professor of Center for Energy Studies
Director of Radiation Safety Office, Louisiana State
University, Louisiana State, United States of America

Tel: 225-578-2743 Fax: 225-578-2094 E-Mail: weihsung@lsu.edu



Education

1986	B.S. in Geology, National Taiwan University, Taipei, Taiwan
1992	M.S. in Environmental Health Engineering, Northwestern University,
	Evanston, Illinois, United States
2000	Ph.D. in Health Physics, Purdue University, West Lafayette, Indiana,
	United States

Research and Professional Positions Held in Chronological Sequence

1995- 2000	Graduate Assistant, Purdue University, School of Health Sciences, West Lafayette, IN
2000- 2003	Senior Health Physicist/Laser Safety Officer, Purdue University, Radiological & Environmental Management Department, West Lafayette, IN
2001- 2003	Assistant Professor of Health Sciences, Purdue University, School of Health Sciences, West Lafayette, IN
2003- present	Director, Louisiana State University (LSU), Radiation Safety Office, Baton Rouge, LA
2015- present	Professor, Louisiana State University, Center for Energy Studies, Baton Rouge, LA

Publications

Bastian FO, Lynch J, Wang W-H. Novel Spiroplasma sp. isolated from CWD is an extreme bacterial thermoacidophile that survives autoclaving, boiling, formalin treatment, and significant gamma irradiation. J Neuropathol Exp Neurol (in printing).

Ellwood BB, Nestell GP, Lan LTP, Nestell MK, Tomkin JH, Ratcliffe KT, Wang W-H, Rowe H, Nguyen TD, Nguyen CT, Dang TH. The Permian–Triassic boundary Lung Cam expanded section, Vietnam, as a high-resolution proxy for the GSSP at Meishan, China. Geol Mag (in printing).

Wilson IV CA, Hamideh AM, Matthews II KL, Wang W-H. Determination of uranium series activity before secular equilibrium is established. Heal Phys 117:443-448; 2019.

Wilson IV CA, Hendrickson KR, Hamideh AM, Matthews II KL, Wang W-H. Visualizing highorder decay after disequilibria. Health Phys 115:791-796; 2018.

Elfar El, Ellwood BB, Wang W-H, Bell GL, Sea level and climatic-induced facies variations in the Middle Cambrian House Range Embayment, western Laurentia. Palaeogeography, Palaeoclimatology, Palaeoecology 475:125-139; 2017.

Wilson IV CA, Matthews II KL, Pulsipher AG, Wang W-H. Using geographic information systems to determine site suitability for a low-level radioactive waste storage facility. Health Phys 110(Suppl 1):S17-S25; 2016.

Ellwood BB, Wang W-H, Tomkin JH, Ratcliffe KT, Hassani AE, Wright AM. Testing high resolution magnetic susceptibility and gamma radiation methods in the Cenomanian-Turonian (upper Cretaceous) GSSP and near-by coeval section. Palaeogeography, Palaeoclimatology, Palaeoecology 378:75-90; 2013.

Marceau-Day ML, Teague RE, Wang W-H. The use of photographic film to pin-point accelerator beam losses. Health Phys 101(Suppl 2):S121-S123; 2011.

Wang W-H, Matthews II KL, Teague RE. Dose rates of a cobalt-60 pool irradiator measured with Fricke dosimeters. Health Phys 94(Suppl 2):S44-S50; 2008.

Wang W-H, Matthews II KL. Simulating gaseous iodine-131 distribution in a silver zeolite cartridge using sodium iodide solution. Health Phys 90(Suppl 2):S73-S79; 2006.

Wang W-H, McGlothlin JD, Smith DJ, Matthews II KL. Evaluation of a radiation survey training video developed from a real-time video radiation detection system. Health Phys 90(Suppl 1):S33-S39; 2006.

Wang W-H, McGlothlin JD, Traylor RM. Development of a real-time video radiation detection system and its application in radiation survey and radiation exposure assessment. Radiat Protect Management 19(6):25-31; 2002.

Wang W-H, Zelac RE. The performance of Al2O3:C thermoluminescent dosimeters in compliance with the American national standard specifications for environmental applications. Radiat Protect Management 14:60-64; 1997.

Health Physics Education and Certification in the United States

Health physics, radiological health, and radiological engineering are terms used interchangeably within environmental health engineering and public health to describe the field of protecting individuals, the general public, and the ecosphere by facilitating safe use of ionizing and non-ionizing radiation.[1] Health physicists work in a variety of disciplines, including education, enforcement of government regulations, environmental protection, industry, medicine, and research. Although the health physicist typically concentrates in one of these disciplines, a professional health physicist often performs duties in several areas. The health physicist is responsible for the safety aspects in the design of processes, equipment, and facilities that use radiation sources, as well as for proper disposal of radioactive waste; a goal of the health physicist is to ensure that radiation exposure to personnel and the environment is always maintained within regulatory limits and also as low as reasonably achievable. Thus, the health physicist must keep personnel and the environment under constant surveillance to ensure this goal. If control measures are ever found to be inadequate, the health physicist must assess the severity of the hazard and implement effective corrective actions. Hence, health physicists require critical thinking skills and cross-disciplinary training. This presentation describes vital components of health physics education in the United States, and the role of certification to support the quality of service provided by health physicists.

Health physicists must achieve technical competency in radiological physics and transport, radiation instrumentation, radiation protection including dosimetry, shielding design and facility safety, radiation standards and regulations, radioactive waste management, and health effects of radiation including radiobiology, radioecology, and radiochemistry; this is in addition to fundamental scientific and engineering subjects. Approximately 30 universities in North America award health physics degrees, at the levels of bachelor's, master's and doctoral degrees. Recognizing the demand for a well-trained nuclear workforce, the U.S. Nuclear Regulatory Commission supports nuclear science education by funding of curriculum development, faculty development, undergraduate scholarships, and graduate fellowships.

To demonstrate the qualification and credibility of professional health physicists, the American Board of Health Physics (ABHP) was established in 1959 to evaluate the competency of professional health physicists and grant certificates to its diplomates.[2] Certification indicates that the recipient has completed key benchmarks for education and professional experience, constituting an appropriate foundation in health physics. Examinees must pass two written examinations that test competence in this field. Part I of the examination consists of 150 multiple-choice questions and contains five domains of practice: measurement and instrumentation, standards and requirements, hazard analysis and control, operations and procedures, and fundamentals and education. Part II of the examination comprises two sections: one section contains six questions on four core health physics topics while the other has one question each for eight specialty areas in health physics. Keywords: health physics, education, certification

REFERENCES 1. Cember H. Introduction to Health Physics, 3rd ed. McGraw-Hill, New York (1996). 2. American Board of Health Physics. Prospectus of the American Board of Health Physics. Online: https://www.aahp-abhp.org/abhp/prospectus. Accessed 06 October 2019.

Seiichi SHIBATA

President, Radiation Application Development Association, Japan

E-Mail: shibata3905s@gmail.com



Education

1973- 1976	Doctor Course of Graduate School of Science, Kyushu University
1976	Doctor of Science

Research and Professional Positions Held in Chronological Sequence

1976- 1996	Assistant Professor, Associate Professor, Institute for Nuclear Study,
	University of Tokyo
1979- 1981	Post-Doctoral Research Fellow, Chemistry Department, Carnegie-
	Mellon University, Pittsburgh, Pennsylvania, USA
1996- 2013	Professor, Research Reactor Institute, Kyoto University
2006- 2008	Vice President, Japan Society of Nuclear and Radiochemical Sciences
2008- 2010	President , Japan Society of Nuclear and Radiochemical Sciences
2013	Professor Emeritus, Kyoto University
2013- 2017	Research Adviser, RIKEN Nishina Center for Accelerator-Based Science
2014	Lecturer, Department of Chemistry, College of Humanities and Sciences,
	Nihon University
2014- present	Secretariat Member, NPO Radiation Education Forum
2020- present	Radiation Application Development Association, Japan

<u>Publications</u>

Manganese-53 in the Trenton iron meteorite. S. Shibata, H. Matsuda, S. Umemoto, Y. Takashima, R. Gensho and M. Honda, Memoirs of the Faculty of Science, Kyushu University, Series C, Chemistry 9 (1975) 243-249.

Preparation of manganese-53. S. Shibata, Y. Takashima, R. Gensho and M. Honda, Journal of Radioanalytical Chemistry 36 (1977) 11-18.

Determination of impurities in aluminum metals by proton activation. S. Shibata, S. Tanaka, T. Suzuki, H. Umezawa, J. G. Lo and S. J. Yeh, International Journal of Applied Radiation and Isotopes 30 (1979) 563-565.

Identification of 26-minute Zr-84. S. Shibata and P. J. Karol. Canadian Journal of Chemistry

61 (1983) 754-756.

New upper bound on the electron anti-neutrino mass. H. Kawakami, S. Kato, T. Ohshima, S. Shibata, K. Ukai, N. Morikawa, N. Nogawa, K. Haga, T. Nagafuchi, M. Shigeta, Y. Fukushima and T. Taniguchi, Physics Letters B 256 (1991) 105-111.

Measurements of ¹⁰Be and ²⁶Al production cross sections with 12 GeV protons by accelerator mass spectrometry. S. Shibata, M. Imamura, H. Nagai, K. Kobayashi, K. Sakamoto, M. Furukawa and I. Fujiwara, Physical Review C 48 (1993) 2617-2624.

Yield measurements of ⁷Be and ¹⁰Be produced by photonuclear reactions at intermediate energies: Intercomparison of fragmentation processes between photon- and proton-induced reactions. S. Shibata, M. Imamura, K. Sakamoto, S. Okizaki, S. Shibutani, H. Matsumura, M. Furukawa, I. Fujiwara, H. Nagai and K. Kobayashi, Radiochimica Acta 80 (1998) 181-187.

Preparation of multitracer by thermal neutron fission of ²³⁵U. K. Takamiya, M. Akamine, S. Shibata, A. Toyoshima, Y. Kasamatsu and A. Shinohara, Journal of Nuclear and Radiochemical Sciences 1 (2000) 81-82.

Separation of radionuclides in a multitracer prepared by thermal neutron fission of ²³⁵U. S. Shibata, K. Takamiya, T. Ichihara and T. Sasaki, Applied Radiation and Isotopes 60 (2004) 625-628.

Chemical composition of magnetic spherules collected from deep sea sediment. S. Sekimoto, T. Kobayashi, K. Takamiya, M. Ebihara and S. Shibata Journal of Radioanalytical and Nuclear Chemistry 278 (2008) 319-322.

Application of aerosol formation to radiation dosimetry in high-dose radiation fields. N. Osada, Y. Oki, K. Yamasaki and S. Shibata, Progress in Nuclear Science and Technology 3(2012) 90-93.

Measurements of cross sections for production of light nuclides by 300 MeV proton bombardment of Cu and Y. S. Sekimoto, T. Omoto, H. Joto, T. Utsunomiya, H. Yashima, K. Ninomiya, K. C. Welten, M. W. Caffee, Y. Matsushi, H. Matsuzaki, R. Nakagaki, T. Shima, N. Takahashi, A. Shinohara, H. Matsumura, D. Satoh, Y. Iwamoto, M. Hagiwara, K. Nishiizumi and S. Shibata, Nuclear Instruments and Methods in Physics Research B 294 (2013) 475-478.

Measurement of Fast-neutron Product of ⁶³Ni for Reassessment of Neutron Dosimetry of the Hiroshima Atomic Bomb

In decommissioning the FM/FF cyclotron at Institute for Nuclear Study, University of Tokyo, we measured the residual radioactivities of ⁵⁵Fe, ⁶⁰Co and ⁶³Ni from the viewpoint of the radiation safety control. During the process of these measurements, it was found that the fast-neutron product of ⁶³Ni produced by ⁶³Cu(n,p)⁶³Ni reaction provides a unique measure to estimate the fast-neutron fluence of the Hiroshima atomic bomb. As basic nuclear data for the estimation, the excitation function for ⁶³Cu(n,p)⁶³Ni was measured using the 4.5 MV dynamitron accelerator at Fast Neutron Laboratory of Tohoku University, and then the ⁶³Ni produced in copper samples exposed by the Hiroshima atomic bomb was determined. In this research, the ⁶³Ni was chemically separated and determined by liquid scintillation method. The results obtained for the Hiroshima samples are consistent with the values estimated by Dosimetry System 2002 (DS02).

Yukio YOSHIZAWA

Lecturer, Kashiwa Nursing School of The Jikei. Japan.

Tel: +81-480-93-0828

E-Mail: yogi2000@yahoo.co.jp

Education

1977	Bachelor of Science,	Chemistry, Tok	vo Metropolitan	University, Tokyo,
			.,	, , , ,

Japan

1986 PhD, Microbiology, The Jikei University School of Medicine, Tokyo, Japan

Research and Professional Positions Held in Chronological Sequence

1986- 1988	Postdoctoral Fellow, Microbiology and immunology, Hahnemann
	University School of Medicine, Philadelphia, USA
1988- 2015	Associate Professor, Radioisotope Research Facility, The Jikei University
	School of Medicine, Tokyo, Japan
2015- 2020	Commissioned Researcher, Institute of Clinical Medical Research, The
	Jikei University School of Medicine, Kashiwa, Japan
2020- present	Lecturer, Kashiwa Nursing School of The Jikei, Kashiwa, Japan

Publications

Shinji H, Yosizawa Y, Tajima A, Iwase T, Sugimoto S, Seki K, Mizunoe Y. Role of fibronectin-binding proteins A and B in in vitro cellular infections and in vivo septic infections by Staphylococcus aureus. Infect Immun. 2011; 79 (6): 2215-23.

Ma X X, Ito T, Kondo Y, Cho M, Yoshizawa Y, Kaneko J, Katai A, Higashiide M, Li S, Hiramatsu K. Two different Panton-Valentine leukocidine phage lineages predominate in Japan. J Clin Microbiolo. 2008; 46 (10): 3246-58.

Takiue M, Yoshizawa Y, Fujii H. Cerenkov counting of low energy beta-emitters using a new ceramic with high refractive index. Appl. Rad. Isot. 2004; 61 (6): 1335-7.

Yoshizawa Y, Sakurada J, Sakurai S, Machida K, Kondo I, Masuda S. An Exfoliative Toxim A-converting Phage Isolated from Staphylococcus aureus Strain ZM. Microbial Immunol. 2000; 44 (3): 189-91.

Yoshizawa Y. Isolation and characterization of restriction negative mutants of Staphylococcus aureus. Jikeikai Med. J 1985; 32: 415-21.

Nakahara H, Nagame Y, Yoshizawa Y, Oda H, Gotoh S, Murakami Y. Trace element analysis of human blood serum by neutron activation analysis. J. Radioanal. Chem. 1976; 54 (1-2): 183-90.

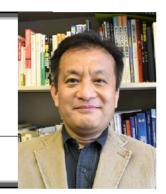
The Importance of Measuring Radon Concentrations as a Cause of Lung Cancer

Radon is a gaseous radioactive element produced from the natural radioactive decay of uranium in rocks and soil. Radon dissolves in groundwater and a hot spring, and then reaches the surface of the ground. Airborne radon activity is the second most common cause of lung cancer after smoking. However, in Japan, radon thermae or hot springs are popular for those who expect radiation hormesis. Radon is a chemically inert gas that can escape easily from the bath water into the air. The gas tends to concentrate in enclosed spaces, such as bathrooms. Samples were collected from 2 famous radon hot springs: Misasa Onsen (Misasa, Tohaku-gun, Tottori Prefecture) and Sarugajo Onsen (Tarumizu, Kagoshima Prefecture). The radon concentrations of the hot springs, measured with a liquid scintillation counter, were 1070 Bq/L and 1470 Bq/L, respectively. The radon concentration of air in these hot springs may exceed 100 Bq/m³, which is the reference level proposed by the World Health Organization because the estimated transfer coefficient of radon between water and air is 1.0 x 10-4.

Soichi HAYASHI

Associate Professor, Department of Applied Physics, Faculty of Science, Fukuoka University, Fukuoka, Japan

E-Mail: soichi@fukuoka-u.ac.jp



Education

1986	Master of Science, RIKKYO University, Tokyo
1989	Master of Science, RIKKYO University, Tokyo
2019	Doctor of Philosophy (Ph.D.), Tokyo University of Science, Tokyo

Research and Professional Positions Held in Chronological Sequence

1987-1999	Teacher of Science (Physics), Rikkyo Senior High school
2000- 2017	Teacher of Science (Physics), Rikkyo Niiza (junior and senior) High
	School,
2017- present	Associate Professor, Department of Applied Physics, Faculty of Science,
	Fukuoka University

Publications

Books

Newly revised for the new teaching guidelines "Teaching Methods of Science for Junior and senior High School" Edited by Takeo Samaki and Akira Yoshida, Tokyo Shoseki (2019)

Learn it well! Basic physics. Supervisor Yasufumi Kawamura / Editors Kiyoshi Torizuka, Soichi Hayashi, Tomofumi Funada, YoshikiYamashita, And 15 authors, Denki Shoin Co. (2014)

*And other books

Textbooks / Miscellaneous

Physics for High School (Revised). Approved Textbook by Ministry of Education, Culture, Sports, Science and Technology, Tokyo Shoseki (2017) / 文部科学省検定教科書 高等学校 改訂 物理 東京書籍(2017)

Fundamentals of Physics for High Scholl (Revised / Large size). Approved Textbook by Ministry of Education, Culture, Sports, Science and Technology, Tokyo Shoseki. (2016) / 文部科学省検定教科書 高等学校 改訂 物理基礎(大判) 東京書籍(2016)

Fundamentals of Physics for High Scholl (Revised / Small size). Approved Textbook by Ministry of Education, Culture, Sports, Science and Technology, Tokyo Shoseki. (2016) / 文部科学省検定教科書 高等学校 改訂 物理基礎(小判) 東京書籍(2016)

Papers / Articles

Soichi HAYASHI. A Study on the Present Situation and Problems of Radiation Learning in High Schools. Doctoral Thesis, Tokyo University of Science (2019)

Soichi HAYASHI, Yasufumi KAWAMURA. A study based on the teaching of radiation throughout three years of junior high school. Journal of Energy and Environmental Education, Vol. 12, No.1, 19-31 (2018)

Soichi HAYASHI, Yasufumi KAWAMURA, History of radiation education in secondary school textbooks. Radiation Education VOL.19 3-12 (2016)

Soichi HAYASHI, Yasufumi KAWAMURA and Satoshi MURAKAMI. A follow-up study on high school physics Experiments for radiation study. Journal of the Physics Education Society of Japan Vol.63 No.3 191-196 (2015)

Soichi HAYASHI. Development of physics teaching materials on the theme of aurora borealis for high school classes. bulletin of Japan Institute of Private School Education, No.51 17-20 (2015)

And other articles

Description of Radiation in the New Curriculum Guidelines - How Radiation is Treated in Japanese Language and Social Studies Textbooks in Primary and Junior High Schools

In Japan, the curriculum guidelines for elementary schools will be revised in 2020 and for junior high schools in 2021, and classes will begin using new textbooks. Before the revision, Japanese and social studies textbooks only mentioned radiation in terms of the atomic bombs used in wars and the nuclear accidents caused by the Great East Japan Earthquake (Higashinihon Daishinsai), and taught only negative images of radiation. How are the peaceful using of radiation in science and medicine, or radiation in nature, described in the new textbooks based on the New Curriculum Guidelines? I report on a survey of these textbooks actually in use. I hope that students will not only be taught negative images of radiation, but also positive ones.

Chun-Yi WU

Assistant Professor Department of Biological Imaging and Sciences, National Yang Ming Chiao Yung University, Taiwan

Tel: +886-2-2826-7000 ext.67215

Fax: +886-2-2820-1095 E-Mail: chunyiwu@nycu.edu.tw



Education

2001- 2005	B.S., Dept. Medicine Radiation Technology, National Yang-Ming
	University, Taipei, Taiwan
2005- 2007	M.S., Dept. Biomedical Imaging and Radiological Sciences, National
	Yang-Ming University, Taipei, Taiwan
2009-2013	Ph.D., Dept. Biomedical Imaging and Radiological Sciences, National
	Yang-Ming University, Taipei, Taiwan

Research and Professional Positions Held in Chronological Sequence

July, 2006	Visiting Student, Department of Experimental Diagnostic Imaging, MD Anderson Cancer Center, Houston, TX
2008- 2009	Research Assistant, Molecular and Genetic Imaging Core, NRPGM, Taipei, Taiwan
2013- 2014	Operator / Research Fellow, Cyclotron Center, Global Medical Solutions Taiwan, Ltd.
2014- 2020	Assistant Professor, Department of Biological Imaging and Science, China Medical University
2020- present	Assistant Professor, Department of Biological Imaging and Sciences, National Yang Ming Chiao Tung University

Publications

Chao-Cheng Chen, Yang-Yi Chen, Yi-Hsuan Lo, Ming-Hsien Lin, Chih-Hsien Chang, Chuan-Lin Chen, Hsin-Ell Wang and *Chun-Yi Wu. Evaluation of Radioiodinated Fluoronicotinamide/Fluoropicolinamide-Benzamide Derivatives as Theranostic Agents for Melanoma. *Int. J Mol. Sci.* 2020;21:6597

Shin-Lei Peng, Han Chiu, **Chun-Yi Wu**, Chiun-Wei Huang, Yi-Hsiu Chung, Cheng-Ting Shih, Wu-Chung Shen. The effect of caffeine on cerebral metabolism during alpha-chloralose anesthesia differs from isoflurane anesthesia in the rat brain. **Psychopharmacology 2019**;**236**(6):1749-1757

Chin-Ho Tsao, Chun-Yi Wu, Chi-Wei Chang, Hsin-Ell Wang, Bing-Fu Shih, Ren-Shyan Liu.

Micro-PET imaging of [¹⁸F]fluoroacetate combined with [¹⁸F]FDG to differentiate chronic Mycobacterium tuberculosis infection from an acute bacterial infection in a mouse model: a preliminary study. *Nucl Med Commun.* 2019;40(6)639-644

Wei-Ying Kuo, Hung-Ju Hsu, Chun-Yi Wu, Hong-Sen Chen, Yu-Chi Chou, Yueh-Liang Tsou, Hung-Pin Peng, Jhih-Wei Jian, Chung-Ming Yu, Yi-Kai Chiu, Ing-Chien Chen, Chao-Ping Tung, Michael Hsiao, Chia-Lung Lin, Yong Alison Wang Andrew H-J. Wang, An-Suei Yang. Antibody-drug conjugates with HER2-targeting antibodies derived from synthetic antibody libraries are highly potent against HER2 positive human gastric tumor in xenograft models. *MAbs.* 2019;11(1):153-165

Wei-Ying Kuo, Jia-Jia Lin, Hung-Ju Hsu, Hong-Sen Chen, An-Suei Yang, *Chun-Yi Wu. Noninvasive assessment of characteristics of novel anti-HER2 antibodies by molecular imaging in a human gastric cancer xenograft-bearing mouse model. *Sci Rep.* 2018;8(1):13735-13744.

Chun-Yi Wu, Jo-Hsin Tang, Pei-Chia Chan, Jia-Je Li, Ming-Hsien Lin, Chih-Chieh Shen, Ren-Shyan Liu, Hsin-Ell Wang. Monitoring tumor response after liposomal Doxorobicin in combination with liposomal vinorelbine treatment using 3'-deoxy-3'[18F]fluorothymidine PET. *Mol Imag Biol 2017 Jun;19(3):408-420*.

Wei-Ying Kuo, Luen Hwu, **Chun-Yi Wu**, Jhih-Shian Lee, Chi-Wei Chang, Ren-Shyan Liu. STAT3/NF-κB-regulated lentiviral TK/GCV suicide gene therapy for cisplatin-resistant triplenegative breast cancer. *Theranositics* 2017;7(3):647-663.

Yo-Liang Lai, **Chun-Yi Wu**, K. S. Clifford Chao. Biological Imaging in clinical oncology: radiation therapy on functional imaging. *Int J Clin Oncol.* 2016;21(4):626-632. (*IF*=1.806, 17/203, ONCOLOGY)

Wei-Ying Kuo, *Chun-Yi Wu (co-first author), Luen Hwu, Jhih-Shian Lee, Cheng-Han Tsai, Kang-Ping Lin, Hsin-Ell Wang, The-Ying Chou, Chun-Ming Tsai, Juri Gelovani, Ren-Shyan Liu. Enhancement of tumor initiation and expression of KCNMA1, MORF4L2, and ASPM genes in the adenocarcinoma of lung xenograft after vorinostat treatment. *Oncotarget* 2015;6(11):8663-8675. (IF=6.627, 164/213, ONCOLOGY)

*Pei-Chia Chan, *Chun-Yi Wu (co-first author), Lin-Shan Chou, Chung-Hsien Ho, Chi-Wei Chang, Shih-Hwa Chiou, Wuu-Jyh Lin, Fu-Du Chen, C. Allen Chang, Jeng-Jong Hwang, Ren-Shyan Liu, Hsin-Ell Wang. Monitoring tumor response after histone deacetylase inhibitor treatment using 3'-deoxy-3'[¹⁸F]-fluorothymidine PET. *Mol Imag Biol 2015;17:394-402. (IF=3.095, 25/120, RADIOLOGY, NUCLEAR MEDICINE & MEDICAL IMAGING)*

Development of Theranostic Boron-containing Gold Nanoparticles for Boron Neutron Capture Therapy

Successful boron neutron capture therapy (BNCT) requires sufficient and specific delivery of boron atoms to malignant cells. Gold nanoparticles (AuNPs) have been used as a useful delivery system for selectively releasing cytotoxic payloads in the tumor. However, studies demonstrating the in vivo distribution or pharmacokinetics of boron-containing AuNPs via noninvasive imaging are lacking. We aim to develop theranostic AuNP-boron cage assemblies (B-AuNPs) and evaluate its feasibility for BNCT. The commercial citratecoated AuNPs were subjected to PEGylation, azide addition, and carborane modification on the surface. To further arm the AuNPs, we conjugated anti-HER2 antibody (61 IgG) with boron-containing PEGylated AuNPs to form 61-B-AuNPs. After the 3-step modification, the diameter of B-AuNPs increased by ~25 nm, and antibody conjugation did not affect the diameter of AuNPs. Radioactive iodine (I-123) was introduced in AuNPs by Click chemistry under copper catalysis. The radiolabeling efficiency of ¹²³I-B-AuNPs and ¹²³I-61-B-AuNPs was approximately 60 ± 5%. MicroSPECT/CT imaging showed that the tumor-to-muscle (T/M) ratio of ¹²³I-B-AuNP-injected mice reached 1.91 ± 0.17 at 12 h post-injection, while that of ¹²³I-61-B-AuNP-injected mice was 12.02 ± 0.94. However, the increased uptake of AuNPs by the thyroid was observed at 36 h after the administration of ¹²³I-61-B-AuNPs, indicating antibody-mediated phagocytosis. The T/M ratio, assessed by ICP-MS, of B-AuNPand 61-B-AuNP-injected mice was 4.91 ± 2.75 and 41.05 ± 11.15, respectively.

Ömer UĞUR

Professor, MD, FEBNM Head of Department of Nuclear Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey

Tel: +90-312-305-1336 Fax: +90-312-309-3508 E-Mail: ougur@hacettepe.edu.tr



Education

1989 Hacettepe University Medical Faculty

1995 Postgraduate / Specialty

Department of Nuclear Medicine, Hacettepe University Medical Faculty

Research and Professional Positions Held in Chronological Sequence

Dr. Uğur became Associate Professor in 1998 and Professor in 2004. He carried out research studies in 1992 and 2001 at Memorial Sloan-Kettering Cancer Center. He was awarded Turkish Society of Nuclear Medicine Prof. Dr. Suphi Artunkal Award in 1995 and 2004, Hacettepe University Science Encouragement Award in 2003, The Sicentific and Technological Research Council of Turkey Science Encouragement Award in 2002 and Turkish Academy of Sciences Young Scentist Award Programme in 2003. His professional interests are nuclear oncology and positron emission tomography.

Publications

Ugur O, Scott AM, Kostakoglu L, Hui TE, Masterson ME, Febo R, Sgouros G, Rosa E, Mehta BM, Fisher DR, Cheung NKV, Larson SM. Calculated and TLD-based absorbed dose estimates for I-131 labeled 3F8 monoclonal antibody in a human neuroblastoma xenograft nude mouse model. Nucl Med Biol 1995; 22: 87-93.

Ugur O, Kostakoglu L, Hui TE, Fisher DR, Garmestani K, Gansow OA, Cheung N-K.V, Larson SM. Comparison of the targeting characteristics of various radioimmunoconjugates for radioimmunotherapy of neuroblastoma: Dosimetry calculations incorporating cross organ beta doses. Nucl Med Biol 1996; 23: 1-8.

Ugur O, Kothari PJ, Finn RD, Zanzonico P, Ruan S, Guenther I, Maecke HR, Larson SM. Ga-66 labeled somatostatin analogue DOTA-DPhe¹-Tyr³-octreotide as a potential agent for positron emission tomography imaging and receptor mediated internal radiotherapy of somatostatin receptor positive tumors. Nucl Med Biol 2002; 29: 147-157.

Uğur O, Gedik GK, Atilla B, Rubello D. Radiosynovectomy: current status in the management of arthritic conditions. Nucl Med Commun. 2008;29:755-8.

Gedik GK, Ugur O, Atilla B, Dundar S. Is corticosteroid coinjection necessary for radiosynoviorthesis of patients with hemophilia? Clin Nucl Med. 2004 Sep;29(9):538-41

Gedik GK, Ugur O, Atilla B, Pekmezci M, Yıldırım M, Seven B, Varoğlu E. Comparison of extraarticular leakage values of radiopharmaceuticals used for radionuclide synovectomy. Ann Nucl Med 2006; 20: 183-188.

Caglar M, Bozkurt FM, Akca CK, Vargol SE, Bayraktar M, Ugur O, Karaağaoğlu E. Comparison of 800 and 3700 MBq iodine-131 for the postoperative ablation of thyroid remnant in patients with low-risk differentiated thyroid cancer. Nucl Med Commun. 2012;33:268-74

Peynircioğlu B, Cil B, Bozkurt F, Aydemir E, Uğur O, Balkanci F. Radioembolization for the treatment of unresectable liver cancer: initial experience at a single center. Diagn Interv Radiol. 2010;16:70-8.

Bozkurt MF, Salanci BV, Uğur Ö. Intra-Arterial Radionuclide Therapies for Liver Tumors. Semin Nucl Med. 2016; 46:324-39

Radionuclide Therapy for Benign and Malignant Skeletal System Disorders

Nuclear medicine techniques are increasingly used in the treatment of musculoskeletal system diseases. Bone pain palliation and radiosynovectomy are the routinely used nuclear medicine therapies. Painful bone metastases are a life debilitating condition in patients with advanced cancers. Analgesics, hormonal therapies and bisphosphonates are also effective in bone pain palliation but have side effects. External radiation therapy provides palliation however, in patients with widespread bone metastases effective palliation is not possible. In these patients, systemic radionuclide therapy provides palliation in all metastatic bone sites. The introduction of new radiopharmaceuticals like Lu177/Y-90-PSMA or Lu177/Y-90-EDTMP used in conjunction with other methods of treatment for bone metastases will further improve the patient benefit.

Radiosynovectomy is performed by intraarticular injection of radionuclides having beta radiation like Y-90 labelled with citrate or silicate. The main aim is to destroy hypertrophied synovium by local high radiation. Most commonly used in rheumatoid artritis and chronic hemophilic synovitis.

Poster Sessions

評審委員: 林峯輝、林明芳、洪三和、栗文治、陳博洲、陳清輝、吳嘉文 (依姓氏筆劃排列)

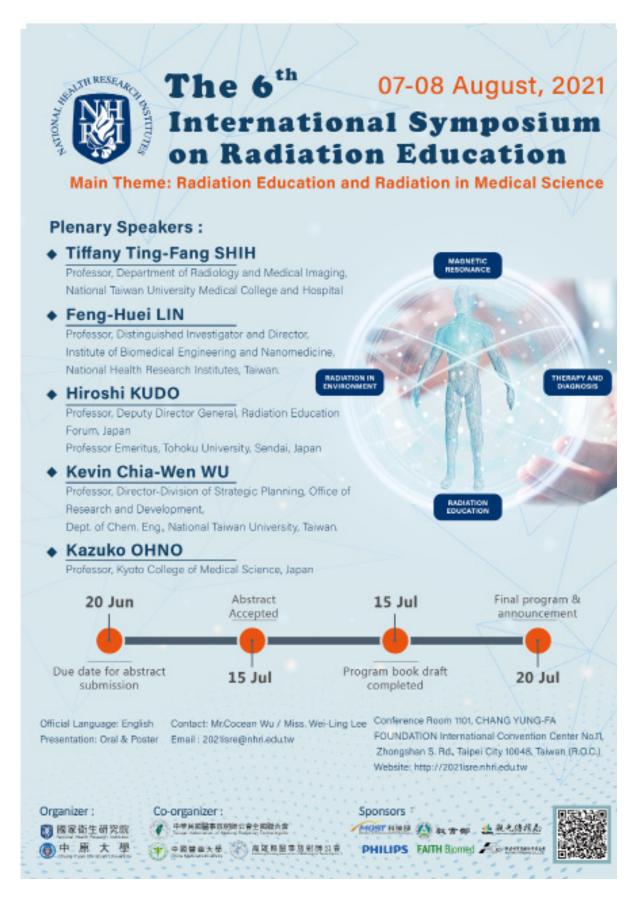
壁報論文解說時段:Aug 7

Topic	Authors	Institute
Carboplatin-loaded Thermogelling Hydrogel with Radiation for Mice Gliomas Therapy	Tzu-Chien Chen ^{1,8} , Hsiang- Kuang Tony Liang ^{1,2,3,4} , Xue- Shi Lai ¹ , Ming- Feng Wei ² , Szu- Huai Lu ² , Wen- Fen Wen ⁵ , Sung- Hsin Kuo ^{2,3,6} , Chung-Ming Chen ¹ , Wen-Yih Isaac Tseng ⁷ , Feng-Huei Lin ^{1,8,*}	1 Institute of Biomedical Engineering, National Taiwan University, Taipei 10617, Taiwan 2 Division of Radiation Oncology, Department of Oncology, National Taiwan University Hospital, Taipei10002, Taiwan 3 Radiation Science and Proton Therapy Center, National Taiwan University College of Medicine, Taipei10002, Taiwan 4 Department of Neurology, National Taiwan University Hospital, Taipei 10002, Taiwan Department of Pathology, National Taiwan University Hospital, Taipei 10002, Taiwan Graduate Institute of Oncology, National Taiwan University Hospital, Taipei 10002, Taiwan Institute of Medical Device and University College of Medicine, Taipei 10051, Taiwan Institute of Medical Device and Imaging, National Taiwan University College of Medicine, Taipei 10051, Taiwan Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli County 35053, Taiwa
Development of ROS- Generated Nanoparticles with Gamma Radiation for Lung Cancer Therapy	I-Hsuan Yang ^{1,2} , Min-Hua Chen ¹ , Feng-Huei Lin ^{1,2,*}	¹ Department of Biomedical Engineering, National Taiwan University, Taipei 10617, Taiwan. ² Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli County 35053, Taiwan.
	Carboplatin-loaded Thermogelling Hydrogel with Radiation for Mice Gliomas Therapy Development of ROS- Generated Nanoparticles with Gamma Radiation for	Carboplatin-loaded Thermogelling Hydrogel with Radiation for Mice Gliomas Therapy Tu-Chien Chen 1.8 Hsiang-Kuang Tony Liang 1.2.3.4 Xue-Shi Lai¹ Ming-Feng Wei² Suu-Huai Lu² Wen-Fen Wen⁵ Sung-Hsin Kuo².3.6 Chung-Ming Chen¹ Wen-Yih Isaac Tseng³ Feng-Huei Lin¹.8.* Development of ROS-Generated Nanoparticles with Gamma Radiation for Tu-Chien Chen¹.8 Hsiang-Kuang Tony Liang¹.2,3.4 Xue-Shi Lai¹ Ming-Feng Wei² Sung-Huai Lu² Wen-Fen Wen⁵ Sung-Hsin Kuo².3.6 Chung-Ming Chen¹ Wen-Yih Isaac Tseng³ Feng-Huei Lin¹.8.*

P-A3	Tb3+ doped LaF3 Nano Particles in Combination with Photosensitizer Through X-ray Irradiation in Brain Cancer Therapy	Yu-Chia Chou, ^{1,4} Min-Hua Chen, ^{1,2} Yi-Jhen Jenh, ¹ Sheng-Kai Wu, ¹ Yo-Shen Chen, ¹ Nobutaka Hanagata, ^{2,3} and Feng-Huei Lin, ^{1,4}	¹ Institute of Biomedical Engineering, National Taiwan University, Taipei, 10051 Taiwan ² Nanotechnology Innovation Station, National Institute for Materials Science, Tsukuba, Ibaraki, 3050047 Japan ³ Graduate School of Life Science, Hokkaido University, Sapporo, Hokkaido, 0600808 Japan ⁴ Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli County, 35053 Taiwan
P-A4	Development of Cedoped TiO2 as a Photosensitizer Activated by Low-dose X-rays for The Generation of ROS to Enhance Photodynamic Therapy in Lung Cancer Therapy	Wei-Ting, Kuo ¹ , Chun-Chen Yang ² , Yu-Jun Sun ¹ , Pei-Hsuan Chung ³ , Wei-Yao Chen ⁴ , Wojciech Swieszkowski ⁵ , Weiming Tian ⁶ , Feng-Huei Lin ^{1, 7, *}	1 Department of Biomedical Engineering, National Taiwan University, Taipei 10617, Taiwan, ROC 2 Department of Materials Science and Engineering, National Taiwan University, Taipei 10617, Taiwan, ROC 3 Department of Animal Science and Technology, National Taiwan University, Taipei 10672, Taiwan, ROC 4 Institute of Biotechnology, National Taiwan University, Taipei 10672, Taiwan University, Taipei 10672, Taiwan University, Taipei 10672, Taiwan, ROC 5 Faculty of Materials Science and Engineering, Warsaw University of Technology, Warsaw 02-507, Poland 6 School of Life Science and Technology, Harbin Institute of Technology, Harbin 150001, China 7 Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli 35053, Taiwan, ROC
P-A5	X-ray Induce Rare-Earth Doped Calcium Carbonate Activated Reactive Oxygen Species as Cancer	<u>Yi-An Li</u> ^{1,3} , Chun- Chen Yang ² , Feng- Huei Lin ^{1,3,*}	¹ Department of Biomedical Engineering, National Taiwan University, Taipei 10617, Taiwan.

	Therapy		 Department of Materials Science and Engineering, National Taiwan University, Taipei 10617, Taiwan. Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli County 35053, Taiwan.
P-A6	Reactive Oxygen Spices Enhanced Photodynamic Treatment by X-ray Irradiation Activated Carbon-doped TiO2 Contribute to Cancer Therapy.	Jhih-Ni Lin ^{1,3} , Chun-Han Hou ² , Feng-Huei Lin ^{1,3*}	¹ Institute of Biomedical Engineering, National Taiwan University, Taipei 10617, Taiwan; ² Department of Orthopedic Surgery, National Taiwan University, Taipei 10617, Taiwan ³ Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli County 35053, Taiwan.
P-A8	Statistics on Nutrition and Health Education of all kind of Cancer Patients in Different Clinics	Shu-Han Yang ¹ , Jun-Yan Wang ¹ , Chih-Jen Huang _{1,2*}	 Department of Radiation Oncology, Kaohsiung Medical University Hospital, Taiwan Department of Radiation Oncology, Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Taiwan
P-B1	Development of Novel Sonosensitizer using ROS Generating C- doped TiO2 Nanoparticles for Cancer Treatment	Minal Thacker ^{1,3} , Chun-Chen Yang ² , Feng-Huei Lin ^{1,3,*}	¹ Department of Biomedical Engineering, National Taiwan University, Taipei 10617, Taiwan. ² Department of Materials Science and Engineering, National Taiwan University, Taipei 10617, Taiwan. ³ Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli County 35053, Taiwan.
P-B2	A Safe and Easy Experiment to Measure Natural Radiation using Charcoal Filter and Underground Water.	Kazuko ONISHI ¹ , Shiori OKADA ² , Masahiro KAMATA ²	

Proceedings of the ISRE 2021







Carboplatin-loaded thermogelling hydrogel with radiation for mice gliomas therapy





Tzu-Chien Chen^{1,8}, Hsiang-Kuang Tony Liang^{1,2,3,4}, Xue-Shi Lai¹, Ming-Feng Wei², Szu-Huai Lu², Wen-Fen Wen⁵, Sung-Hsin Kuo^{2,3,6}, Chung-Ming Chen¹, Wen-Yih Isaac Tseng⁷, Feng-Huei Lin^{1,8}

- Institute of Biomedical Engineering, National Taiwan University, Taipei 10617, Taiwan
- Division of Radiation Oncology, Department of Oncology, National Taiwan University Hospital, Taipei10002, Taiwan Radiation Science and Proton Therapy Center, National Taiwan University College of Medicine, Taipei10002, Taiwan
- Department of Neurology, National Taiwan University Hospital, Taipei 10002, Taiwan
- Department of Pathology, National Taiwan University Hospital, Taipei 10002, Taiwan
- Graduate Institute of Oncology, National Taiwan University College of Medicine., Taipei 10051, Taiwan
- Institute of Medical Device and Imaging, National Taiwan University College of Medicine, Taipei 10051, Taiwan Institute of Biomedical Engineering and Nano-medicine, National Health Research Institutes, Miaoli County 35053, Taiwan

Abstract

Glioblastoma multiforme (GBM) is a highly malignant brain tumor with a more than 90% 5-year mortality. The treatment of GBM is a combination of surgical radiotherapy and oral chemotherapy. Carboplatin is a platinum-based antineoplastic agent, which is commonly combined with radiotherapy (RT) for clinical cancer treatment. In this study, carboplatin-loaded thermogelling hydrogel has been investigated that combined with rt for mice glioma treatment. For mice administered hydrogel carboplatin/RT versus those administered aqueous carboplatin/RT, the 24-day tumor growth control rate and 104-day recurrence-free survival rate were 100% and 50% versus 100% and 66.7% (p//0.648), respectively. However, mice receiving other treatments showed tumor progression by Day 24 and died within 40 days of tumor cell implantation. The carboplatin-loaded hydrogel can not only simplify drug delivery in GBM, but also have potential for clinical applications.

Introduction

Gliomas are the most common primary intracranial tumors, accounting for 81% of brain tumors, and the most common malignant glioma histology is glioblastoma, accounting for 45% of all gliomas. Current treatment strategies to improve local control of glioblastoma through intratumoral drug delivery include carmustine wafer implantation and carboplatin infusion through convective enhanced delivery (CED). Carboplatin is a platinum anti-tumor drug, usually combined with radiotherapy (RT) for clinical cancer treatment. Here, we assume that the sustained release of a single injection of hydrogel carboplatin simplifies intratumoral administration, and compared with multiple injections of aqueous carboplatin, it still has a synergistic effect with RT.

Materials & Methods

The materials and reagents used to prepare hydrogel carboplatin are: hyaluronic acid, sodium tetraborate decahydrate, t-butyl carbamate (t-BC), adipic acid dihydrazide (ADH), sodium bicarbonate, chlorinated Sodium, ethylene glycol, sodium periodate (NaIO4), dialysis bag MWCO 6000e8000 and PARAPLATIN® (carboplatin in water, 10 mg/mL) (Bristol Myers Squibb Company, New York, USA). The characterization of oxi-HA/ADH hydrogel and the detection of hydrogel carboplatin passed the Fourier transform infrared (FTIR) test. The biocompatibility of oxi-HA/ADH hydrogel was evaluated by testing the extraction medium with 3T3 cells. Using six-week-old male C57BL/6 mice, ALTS1C1 glioma cells transfected with the luciferase reporter gene were injected subcutaneously into their right thighs. When the tumor diameter reaches about 3-4mm (suitable for intratumoral injection of drugs), the mice are divided into different treatment groups.

Results

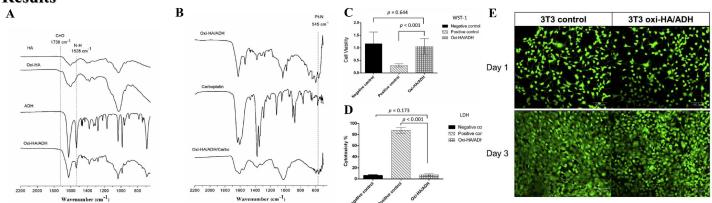
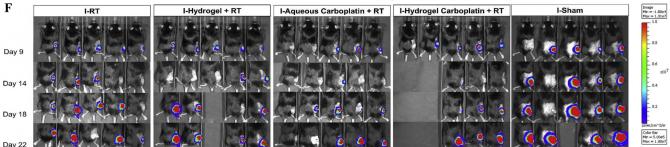


Illustration of FTIR spectra: (A) the peak at 1730 cm1 of oxi-HA disappeared after mixing oxi-HA with ADH and a new forming peak associated with oxi-HA/ADH appeared at 1528 cm1 and (B) that associated with the formation of carboplatin-loaded oxi-HA/ADH hydrogel at 545 cm $^{-1}$.

(C) WST-1 analysis demonstrated that the cell viability of 3T3 cells cultured in oxi-HA/ADH hydrogel extraction ium (D) LDH assay indicated that the cytotoxicity of oxi-HA/ADH is not significantly different from that in the negative control group (E) The LIVE/DEAD staining demonstrated that nearly all 3T3 cells were viable in the oxi-HA/ADH hydrogel after 3 days of cultivation.



(F) First-stage in vivo experiment with different combinations of low-dose carboplatin and RT. Compared with the sham group, BLI demonstrated relatively delayed tumo progression in all other treatment groups.

Conclusion

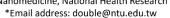
In this study, through comprehensive research including biological materials, cells, and animal experiments, the sustained-release properties of hydrogel carboplatin have been demonstrated that simplify the frequency of administration and maintains the synergistic effect of radiotherapy on malignant gliomas.



Development of ROS-generated nanoparticles with gamma radiation for lung cancer therapy

I-Hsuan Yang^{1,2}, Min-Hua Chen¹, Feng-Huei Lin^{1,2},

¹ Department of Biomedical Engineering, National Taiwan University, Taipei 10617, Taiwan.
² Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli County 35053, Taiwan.





1. Abstract

Photodynamic therapy (PDT) is a treatment that producing cytotoxic reactive oxygen species (ROS) and free radicals to kill cancer cells by exposing a photosensitizer to a specific light wavelength. However, PDT is limited to the treatment of the deeper tumors, due to the limited penetration depth of visible light. In this study, we developed the ROS-generated nanoparticles, hafnium-doped hydroxyapatite (Hf:HAp), which could enhance ROS generation when particles are irradiated with gamma rays for anti-cancer treatment. Hf:HAp nanoparticles were synthesized by doping Hf ions to substitute Ca²⁺ in HAp lattice through wet chemical precipitation. The developed Hf:HAp particles were nano-sized rod-like shapes and with pH-dependent solubility. The efficacy of ionizing radiation on Hf:Hap nanoparticles were evaluated both in vitro and in vivo using A549 cell line. The 2',7'-dichlorofluorescein diacetate (DCFH-DA) assay showed that HF:HAp could significantly generate ROS in cells after gamma irradiation. Both cell viability (WST-1) and cytotoxicity (LDH) assay showed consistent results that A549 lung cancer cell lines were damaged with changes in the cells' ROS level. In the *in vivo* study, mice were treated at days 0 and 7 by intratumoral injection accompany by 5 Gy of gamma rays irradiation. The results showed that the tumor growth is inhibited owing to the cell apoptosis when Hf:HAp nanoparticles were bombarded with ionizing radiation. This finding demonstrates a potential therapeutic method of interacting Hf:HAp nanoparticles with ionizing radiation for lung cancer therapy.

2. Scheme lonizing radiation 1.

0

- Endocytosis of hafniumdoped hydroxyapatite (Hf:Hap) into A549 cells.
- 2. Degradation of Hf:Hap in acidic organelles.
- Enhanced ROS generation under excitation of gamma rays.
- 4. Inhibit tumor growth.

3. Results and discussion

3.1 Phase composition of Hf:HAp nanoparticles

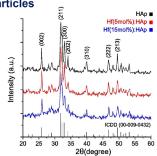


Fig. 1. XRD patterns of HAp, Hf (5 mol%):HAp, Hf (15 mol%):HAp, and the standard data of HAp quote from ICDD file No. 00-009-0432.

3.2 Chemical composition of Hf:Hap nanoparticles

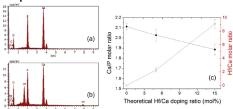


Fig. 2. EDX spectrum of (a) HAp and (b) Hf (15 mol%):HAp; (c) the composition of Ca/P and Hf/Ca molar ratio with varied concentration of Hf ions dopant.

3.3 Lattice parameters of Hf:HAp nanoparticles

Table 1. Unit cell parameters for synthesized HAp, Hf (5 mol%):HAp and Hf (15 mol%):HAp.

Samples	a-Axis (Å)	b-Axis (Å)	c-Axis (Å)	Grain size (nm)	Unit cell volume (ų)
ICDD (00-009-0432)	9.418	9.418	6.884	-	528.8
НАр	9.413	9.413	6.898	27.191	529.3
Hf (5 mol%):HAp	9.394	9.394	6.878	25.234	525.7
Hf (15 mol%):HAp	9.396	9.396	6.849	23.761	523.7

3.4 Morphology and size distribution of Hf:Hap nanoparticles

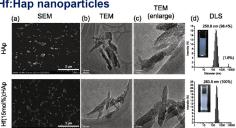


Fig. 3. Morphology and size distribution of HAp and HAp (15 mol%):HAp. (a) FE-SEM micrographs; (b and c) TEM images; and (d) DLS distribution and photography of particles suspended in culture medium.

3.5 Solubility of Hf:Hap nanoparticles

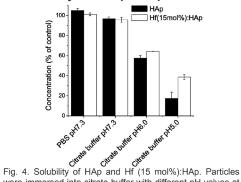


Fig. 4. Solubility of HAp and Hf (15 mol%):HAp. Particles were immersed into citrate buffer with different pH values at pH7.3, pH6.0 and pH5.0. After 1 min of incubation, the concentration was measured by UV spectrophotometer.

3.6 In vitro ROS generation of Hf:HAp nanoparticles with ionizing radiation



Fig. 5. DCF fluorescence intensity of HAp and Hf (15 mol%):HAp of relative ROS concentration in gamma rays irradiated (5 Gy) by using the DCFH-DA assay. Non-irradiated particles at various concentrations were regarded as control groups. (p < 0.05, *, compared to HAp.)

3.7 *In vitro* cytotoxicity of Hf:HAp nanoparticles with ionizing radiation

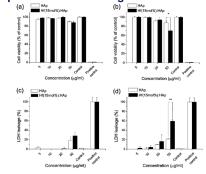


Fig. 6. The impact of HAp and Hf (15 mol%):HAp without (a, c) or with (b, d) 5 Gy of gamma rays irradiation in A549 cell line. After 24 h incubation, cells viability and cytotoxicity were determined by using (a, b) WST-1 assay and (c, d) LDH assay. Cells treated with PBS buffer were used as control groups and cells exposed to 1% Triton X-100 were regarded as positive control of cytotoxicity. (*p < 0.05, **p < 0.01.)

3.8 In vivo anti-tumor effect

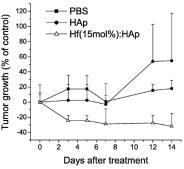
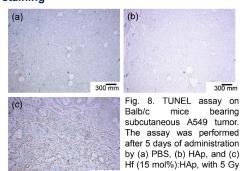


Fig. 7. A relative tumor growth of A549 xenograft in Balb/c nude mice. Mice were received the treatment of PBS, HAp, or Hf (15 mol%):HAp, plus 5 Gy of gamma rays exposure at day 0 and 7, followed by monitoring their tumor growth until day 14.

3.9 *In vivo* histologic examination by TUNEL staining



4. Conclusion

 We successfully synthesized ROS-generated nanoparticles by doping Hf ions to substitute Ca²⁺ in HAp lattice. The Hf:HAp particles are in nano-sized with pH-dependent solubility.

300 mm of gamma rays.

- Hf:HAp lead to an increase in the significant quantities of ROS level in cells when particles are bombarded with gamma rays.
- The cytotoxicity, demonstrated by WST-1 and LDH assays, is consistent with intracellular ROS level.
- The *in vivo* studies also point to the same result that tumor growth is inhibited by cell apoptosis when particles are bombarded with radiation.
- This study provides a novel therapeutic approach in systemic disease and deeper tumor treatment in place of PDT, and offers a new strategy in cancer palliative treatment for patient after the surgical operation.

5. Acknowledgment





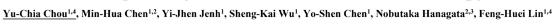






Tb3+ doped LaF3 Nano particles in combination with photosensitizer through X-ray irradiation in brain cancer therapy







- 1. Institute of Biomedical Engineering, National Taiwan University, Taipei, 10051 Taiwan 2. Nanotechnology Innovation Station, National Institute for Materials Science, Tsukuba, Ibaraki, 3050047 Japan
 - 3. Graduate School of Life Science, Hokkaido University, Sapporo, Hokkaido, 0600808 Japan
 - 4. Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli County, 35053 Taiwan

Photodynamic therapy (PDT) has become a promising treatment for various kinds of tumors. By applying the specific wavelength of light to the photosensitizer, it can trigger oxidative reaction and cause PDT-induced cytotoxicity to malignant tumor cells. However, when it came to the brain tumor, the difficulty of PDT increased dramatically. First, the light source (usually the optical fibers) should be placed into brain during craniotomy; second, these optical fibers should be leave an open wound for future treatments. In this study, we investigated an innovation idea for non-invasive PDT treatment for glioma cell line. By using Tb3+-doped LaF3 scintillating nanoparticles (LaF3:Tb) combined with meso-tetra(4-carboxyphenyl)porphyrin (MTCP) as photosensitizer, followed by activation with soft X-ray (80 kVp), the scintillating LaF3:Tb nanoparticles, with sizes of approximately 25 nm, were fabricated. These nanoparticles sized around 25nm and can form good aqueous solution with high biocompability. However, significant cytotoxicity was observed in the glioma cells while the LaF3:Tb nanoparticles with MTCP were exposed under X-ray irradiation. The study has demonstrated a proof of concept as a non-invasive way to treat brain cancer in the future.

Introduction

Malignant gliomas are the most common type of primary brain tumors with the average life expectancy at 5 years is not higher than 5% in Taiwan. Due to its location and the blood-brain barrier (BBB), the malignant gliomas is very difficult to treat. Despite the advances in conventional approaches, including surgery, radiotherapy, and chemotherapy, the effectiveness of treatment in these patients remains limited. Many of the current treatments in malignant gliomas have inadequate drug delivery and cause damage to healthy brain tissue.

Photodynamic therapy (PDT) is based on the concept of proceeding through the activation of photosensitizer by a specific light wavelength (620-690 nm) to produce the predominant cytotoxic agent, such as free radicals and singlet oxygen (102). The use of PDT in the treatment of brain tumors has produced exciting results in clinical trials over the past decade due to its selective cytotoxicity to target infiltrating malignant brain tumor cells and induces a cytotoxic reaction only in the light-exposed areas. However, the limited penetration range of light causes the assessment of the light distribution and tumoricidal effects of PDT inside the brain to be difficult. Currently, all of these treatments require the external optical fibers be placed within the brain tumors. Consequently, there exists the need for a minimally invasive brain cancer PDT.

An attractive non-invasive option is to use scintillating nanoparticles with photosensitizer through X-ray irradiation to enable the light source to reach a higher tissue penetration depth in the range of 8-14 cm. The scintillating nanoparticles, such as Tb3+-doped LaF₃ crystal (LaF₃:Tb), can locally convert X-ray into light and the emitted luminescences are able to activate the photosensitizers on the mechanism of fluorescence resonance energy transfer (FRET), further resulting in activating photosensitizer to induce IO2 for cancer therapy.

X-ray-excited PDT which based on scintillating nanoparticles, was first introduced by Chen and Zhang in 2006 and recently several studies have demonstrated this effect into proof of concept. For future clinical applications, the photosensitizers can be loaded onto nanoparticles, which can lead to a more direct and specific localization of the photosensitizer to the brain tumor sites and increase the efficiency and selectivity in treatment. More importantly, X-ray not only can penetrate the tissue much deeper than the laser light source but also can extend the popularity of PDT to resourcelimited hospitals because the X-ray system is widely used in the clinic for both diagnosis and therapy.

Here we demonstrate a proof of concept as a non-invasive PDT on glioma cell line (9L) by the treatment of soft X-ray (180 kVp) and photosensitizer, meso-tetra(4-carboxyphenyl)porphyrin (MTCP), employing scintillating nanoparticles. Although scintillating nanoparticles have been studied in PDT, to the best of the authors' knowledge, the non-invasive PDT concept of using scintillating nanoparticles in brain cancer cells has not been described.

Materials & Methods

Characterization of LaF2: Th Nanoparticles

The morphology of particles was observed by dropping onto a copper grid using a transmission electron microscopy (TEM; Hitachi H-7100, Japan). Energy-dispersive X-ray spectroscopy (EDX) system attached to TEM was used to analyze the composition of ions in particles. X-ray diffraction (XRD; Geiger Flex, Rigaku) was utilized to identify the crystalline phase composition using Cu Κα radiation ($\lambda = 0.15406$ nm) with the potential at 30 kV and the current at 20 mA.

The viability of LaF3: Tb particles on the fibroblast cell line (3T3) was evaluated by cell proliferation reagent (WST-1, Roche). 3T3 cells were exposed to different concentrations of LaF3: Tb particles, followed by 4 h of incubation period. Later, the media was replaced with fresh media and further incubated for another 24 or 72 h. After that, cells were rinsed once for WST-1 assay and measured by the absorbance at 450 nm. Positive controls were cells exposed to 1% Triton X-100 solution. In Vitro Effect of LaF3:Tb

9L glioma cells grown in DMEM media supplemented with 10% FBS and 100 units/ml of penicillin were seeded in 96-well plates (5000 cells/well) and cultured overnight. Then, cells received the treatment of mixed solution of LaF3; Tb (1 mg/ml) with MTCP (0.5 mg/ml) for 4 h (n = 5). Subsequently, they were washed with phosphate-buffered saline (PBS) twice and then exposed to portable Xray systems (PX-80M, PoYe, Taiwan) for 1 min. The X-ray source was set at 10 mA and 80 kVp with 50 cm of exposed distance from generator to sample. The effect was evaluated after cell incubation for 24 h and analyzed by WST-1 assay (Roche) according to the manufacturer's protocol. Cells treated with PBS were used as control groups. All values were presented as mean ± standard deviation (SD) in quintet repeat. Statistical analysis was performed using Student's t test. Values of p < 0.05 were considered as statistically significant.

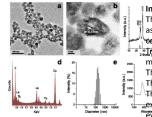
Purpose of study

To find a possible non-invasive method for malignant gliomas treatment

Results

Materials Characterization

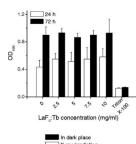
Characterization of LaF₃:Tb particles. a TEM images; b crystal lattice planes; c XRD pattern and with standard data quote from JCPDS file no. 32-483; d EDX spectrum; e hydrodynamic size distribution of particles suspended in culture medium supplemented with 10% FBS; and ${\bf f}$ photoluminescence spectrum of particles obtained in water using an excitation wavelength of 260 nm

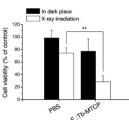


In Vitrô Effect of LaF₃:Tb Nanoparticles

The viability of LaF₂:Tb nanoparticles, LaF₂:Tb nanoparticles assessed in 3T3 cells were determined using various concentrations by use of the WST-1 assay. Cells exposed to 1% mean £ SD in triplicate

The impact of LaF₃:Tb-MTCP nanoparticles with X-ray irradiation. The particles of LaF₃:Tb-MTCP were assessed in 9L glioma cells. The X-ray source was set at 10 mA and 80 kVp with 50 cm of exposed distance from generator to sample. The effect was evaluated after cell incubation for 24 h and analyzed by WST-1 assay. Values are mean \pm SD for quintet repeat. **p < 0.01 vs. control by Student's t test





Conclusions

According to our preliminary finding, LaF₃:Tb nanoparticles could find biological applications, for they have been obtained in nanoscale (approximately 25 nm in physical size), water-dispersible, and with high biocompatibility. However, it shows cytotoxicity on the 9L glioma cell line only when nanoparticles with photosensitizers are exposed under the X-ray exposure. Thus, we believe scintillating nanoparticles in combination with X-ray could be a potential approach for non-invasive PDT in brain cancer for future clinical applications, even though an ideal scintillating nanoparticle that processes the energy transfer from Xray to photosensitizers efficiently will still be an important issue for practical applications. We will further investigate the in vivo study in the following research.

The 6th International Symposium on Radiation Education

Development of Ce-doped TiO₂ as a photosensitizer activated by low-dose X-rays for the generation of ROS to enhance photodynamic therapy in lung cancer therapy

Wei-Ting, Kuo ¹, Chun-Chen Yang ², Yu-Jun Sun ¹, Pei-Hsuan Chung ³, Wei-Yao Chen ⁴, Wojciech Swieszkowski ⁵, Weiming Tian ⁶, Feng-Huei Lin ^{1,7,*}





1 Department of Biomedical Engineering, National Taiwan University, Taipei 10617, Taiwan, ROC 2 Department of Materials Science and Engineering, National Taiwan University, Taipei 10617, Taiwan, ROC 3 Department of Animal Science and Technology, National Taiwan University, Taipei 10672, Taiwan, ROC

4 Institute of Biotechnology, National Taiwan University, Taipei 10672, Taiwan, ROC

5 Faculty of Materials Science and Engineering, Warsaw University of Technology, Warsaw 02-507, Poland

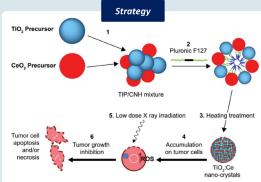
6 School of Life Science and Technology, Harbin Institute of Technology, Harbin 150001, China

ute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli 35053, Taiwan, R



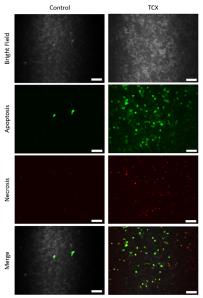


Photodynamic therapy (PDT) is limited by its penetration depth because of the selection of photosensitizer and light source. Therefore, novel alternatives to serve as photosensitizers in PDT are required to overcome the penetration depth limitation and lower the radiation dose. In this study, Ce-doped TiO_2 (TiO_2 :Ce) was synthesized as photosensitizers activated by low-dose X-rays to generate ROS for deep-seated tumor treatment.



TiO₂:Ce particle preparation and *in vivo* delivery via subcutaneous injection. The multiple steps and mechanisms by which TiO₂:Ce produces more ROS under low-dose X-ray irradiation and further inhibits tumor growth.

Effect of synthesized TiO₂:Ce under X-ray irradiation on apoptosis/necrosis

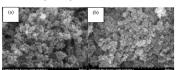


Apoptosis/necrosis of A549 cells in the $TCX_{in-vitro}$ group. Cells undergoing apoptosis are in green and those undergoing necrosis are in red (scale bars: $100 \, \mu m$)

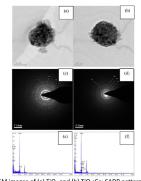
Based on the results, the synthesized $\rm TiO_2$:Ce exposed to X-ray radiation could induce A549 apoptosis and necrosis, leading to cell death. The oxidative stress caused by the increase in ROS levels was involved in the triggering of apoptosis that caused cell death.

150,CG 150,CG 150,CG 160,CG 16

XRD patterns of TiO₂ and TiO₂:Ce synthesized by modified sol-gel method



SEM images of synthesized (a) TiO₂; (b) TiO₂:0

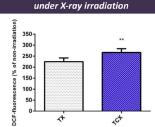


TEM images of (a) TiO_2 and (b) TiO_2 :Ce; SADP pattern of (c) TiO_2 and (d) TiO_2 :Ce; and EDX of (e) TiO_2 and (f) TiO_2 :Ce

These results showed that the cerium addition did not change the crystal structure and average grain size. ${\rm TiO_2}$ and ${\rm TiO_2}$:Ce presented as uniform spheroid-like aggregated particles. The nano-sized ${\rm TiO_2}$:Ce with an average crystal size of 15 nm determined by FWHM calculation and TEM examination were successfully synthesized by a modified sol-gel method.

Material characterization

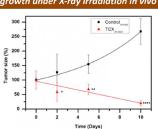
ROS generation of developed TiO₂ and TiO₂:Ce



DCFH-DA assay for relative ROS concentration induced by the synthesized TiO $_2$ and TiO $_2$:Ce under low-dose X-ray radiation (one-way ANOVA, mean \pm SD, n = 6, **: p-value < 0.01)

The results of the DCFH-DA assay indicated that TiO_2 :Ce under low-dose X-ray irradiation could generate more ROS. The A549 cells treated with TiO_2 :Ce produced more ROS than those treated with TiO_2 . Cerium can separate electron and hole pairs by grasping electrons and then releasing H⁺ to react with H₂O to generate ·OH and H₂O₂.

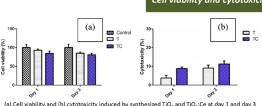
Effect of the synthesized TiO₂:Ce on tumor growth under X-ray irradiation in vivo



Relative tumor growth in BALB/c nude mice injected with TiO₂:Ce and exposed to low-dose X-ray radiation (one-way ANOVA, mean \pm SD, n = 4, \pm : p-value < 0.05, **: p-value < 0.01, ****: p-value < 0.0001)

Tumor growth inhibition was higher in the $TCX_{in-vivo}$ group than that in the Control_{in-vivo} group, which indicated that TiO_2 :Ce and X- rays had a great synergistic effect. Thus, Ce ions could be an applicable dopant to strengthen the effect of host materials under ionizing radiation exposure.

Cell viability and cytotoxicity



Based on these results, we believe that the synthesized TiO₂ and TiO₂:Ce would pose no potential risk to cultured cells.

Conclusion

The nano-sized TiO₂:Ce with an average crystal size of 15 nm determined by FWHM calculation and TEM examination were successfully synthesized by a modified sol-gel method. The WST-1 and LDH assays showed that, alone, TiO₂:Ce had no significant impact on cell viability and was not cytotoxic. However, the cell viability significantly decreased with TiO₂:Ce exposure under low-dose X-ray irradiation. Furthermore, the TiO₂:Ce produced more ROS under low-dose X-ray irradiation. These results indicate that the TiO₂:Ce produced significant ROS under low-dose X-ray irradiation and promoted apoptosis/necrosis of A549 cancer cells. In the *in vivo* study, the TiO₂:Ce can enhance the efficacy of X-ray-induced PDT, and tumor growth was inhibited. These findings suggested that the TiO₂:Ce nanocrystals could serve as photosensitizers in PDT activated by low-dose X-rays for ROS generation as a potential treatment of deep-seated tumors/ cancer.

Acknowledgements: National Science Council, Taiwan (103-2221-E- 002-040-MY3) and National Health Research Institute, Taiwan (106- 0324-01-10-07)

The 6th International Symposium on Radiation Education

X-ray induce Rare-Earth Doped Calcium Carbonate Activated Reactive Oxygen Species as Cancer Therapy

Yi-An, Li ¹, Chun-Chen Yang ², Wei-Yun Wang ², Feng-Huei Lin ^{1, 3, *} Chun-Han Hou ⁴



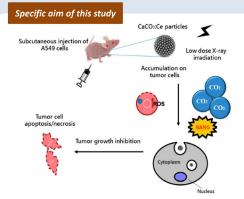
Department of Biomedical Engineering, National Taiwan University, Taipei 10617, Taiwan, ROC
 Department of Materials Science and Engineering, National Taiwan University, Taipei 10617, Taiwan, ROC
 Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli 35053, Taiwan, ROC
 Department of Orthopedic Surgery, National Taiwan University, Taipei 10617, Taiwan, ROC





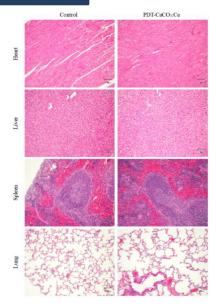
Acknowledgements: National Health Research Institutes, Taiwan (BN-108-PP-01)

Due to the photosensitizer and light source, traditional photodynamic therapy (PDT) is limited by its penetration depth. In this study, we developed X-ray-induced photodynamic therapy, which uses X-rays as a light source to activate Ce-doped CaCO3 (CaCO3:Ce) to produce intracellular reactive oxygen species that kill cancer cells (ROS). The A549 cell line was used as an in vitro and in vivo model to evaluate the efficacy of X-ray-induced CaCO3:Ce. CaCO3: Ce exposed to X-rays, the cell viability significantly decreased, and the cytotoxicity is broadly increased. In the treatment of tumors, it is not as harmful as radiotherapy. CaCO3: Ce produces a large amount of ROS under X-ray irradiation and promotes the death of A549 cancer cells. CaCO3: Ce can enhance the efficacy of X-ray-induced PDT and inhibit tumor growth in vivo. Blood analysis and hematoxylin and eosin staining (H&E) staining fully support the safety of treatment. The mechanism of CaCO3:Ce activated by X-ray radiation to produce ROS and CO2 to cause cytotoxicity and inhibit tumor growth was discussed. These discoveries and advances are very important to provide a novel treatment method as an alternative tumor treatment.



The mechanism of CaCO3:Ce activated by X-ray to generate ROS and CO2 for tumor growth inhibition.

Histological analysis

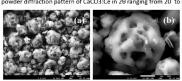


H&E-stained slices of major organs harvested from scarified BALB/c nude mice at the end of the animal study and examined under optical microscope (scale bar: $50 \mu m$).

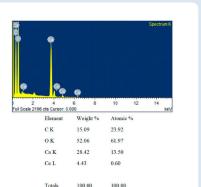
Hematoxylin and eosin stain (H&E) examination were used for safety assessment of the mice. Based on the results, there was no significant difference between the experimental group and control group, including no observable signs of side effects on normal tissues from H&E staining.

Material characterization

 30 2 theta (diffraction angle) 50 50 X-ray powder diffraction pattern of CaCO3:Ce in 2 θ ranging from 20 $^{\circ}$ to 60 $^{\circ}$.



SEM images of CaCO3:Ce particles



Spectra and chemical composition chart of CaCO3:Ce particles.

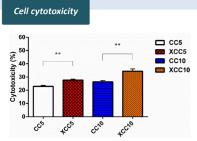
X-ray diffraction (XRD), field-emission scanning electron microscopy (FESEM), and energy dispersive X-ray spectroscopy (EDX) were performed for crystal structure identification, surface morphology observation, and composition analysis, respectively. CaCO3:Ce was successfully synthesized using the co-precipitation method and confirmed by crystalline phase identification. The CaCO3:Ce particle was spherical with a diameter of $1-3~\mu m$ and surface of the particles was very rough and consisted of a large number of pores and channels.

The generation of ROS of CaCO3:Ce particles under X-ray irradiation



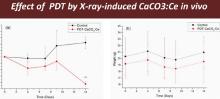
The generation of ROS of CaCO3:Ce particles under X-ray irradiation determined by the degradation of methylene blue (t-test, mean \pm SD, n = 6, ****; p-value < 0.0001).

The degradation of methylene blue (MB) was evaluated to examine the generation of ROS. This result indicated the significant generation of ROS from CaCO3:Ce when exposed to X-ray irradiation.



Cell cytotoxicity induced by CaCO3:Ce under X-ray irradiation (t-test, mean \pm SD, n = 6, **: p-value < 0.01).

The in vitro PDT effects of CaCO3:Ce activated by X-ray irradiation were evaluated using LDH assay with A549 lung cancer cells. The result indicated the cellular death caused by CaCO3:Ce after exposure to X-ray irradiation.



The tumor size (a) and body weight (b) in BALB/c nude mice injected with CaCO3:Ce and subjected to X-ray irradiation (t-test, mean \pm SD, n=4, **: p-value < 0.01).

Tumor-induced BALB/c nude mice were used to in vivo PDT treatment. We chose CaCO3:Ce under X-ray irradiation, indicated as PDT-CaCO3:Ce, as the main experimental group. The results indicated that CaCO3:Ce could be a promising photosensitizer activated by X-ray to great anti-tumor effect.

Conclusion

The CaCO3:Ce particle was synthesized by the co-precipitation method and confirmed by crystalline phase identification in the vaterite phase. The cytotoxicity increased when CaCO3:Ce was activated by X-ray, and cell death was induced via necrosis or apoptosis in human lung adenocarcinoma A549 cells. The result was consistent with ROS detection by the degradation of MB. The in vivo study also showed tumor growth inhibition based on the cell death mechanism induced by the overproduction of ROS and CO2. A safety assessment by blood/serum analysis and H&E examination indicated that CaCO3:Ce is not toxic and causes no side effects to normal tissues. This study provides a novel therapeutic approach as an alternative tumor treatment.



Reactive oxygen spices enhanced photodynamic treatment by X-ray irradiation activated carbon-doped TiO2 contribute to cancer therapy





Jhih-Ni Lin¹, Chun-Han Hou², Feng-Huei Lin^{1,3*}

- 1 Institute of Biomedical Engineering, National Taiwan University, Taipei 10617, Taiwan;
- 2 Department of Orthopedic Surgery, National Taiwan University, Taipei 10617, Taiwan
 3 Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli County 35053, Taiwan



Abstract

Photodynamic therapy (PDT) has been a common method of clinical tumor lesion treatment. However, the penetration depth of visible light restricted the application. Even the light source has been changed to near-infrared, infrared light still unable to overcome the penetration barrier and only effective on the tumor surface. In this study, we used X-ray as a light source coupled with carbon-doped TiO₂ (TiO₂:C) for deep-seated tumor treatment. TiO₂ is a particle with a narrow band gap, which would produce reactive oxygen species (ROS) when exposed to soft X-rays. With the synergistic effect of ROS, X-ray-induced PDT may overcome the limitations of penetration depth with a lower radiation dose. The results showed that the synthesized TiO₂:C particles were identified as crystal structures of anatase and could be activated effectively by soft X-rays to produce ROS, which could degrade methylene blue reach 30.4%. Once TiO₂:C was activated by X-ray irradiation, the death rate of A549 cells in in vitro testing was up to 16.57%. In the animal study, the tumor size gradually decreased after treatment and declined nearly half of its initial volume, while the control group was twice. When the endpoint of the experiment, blood and major organs will be harvested for further analysis and examination. Based on the current results, we believe that X-ray irradiation activated TiO₂:C has the potential to overcome the limitation of penetration depth and improve PDT effects by inhibiting tumor growth effectively.

Synthesis of TiO₂:C Particles

Titanium (IV) isopropoxide (TIP; Ti(OCH(CH₃)₂)₄) was the precursor of TiO₂, and d-(+)-glucose (C₆H₁₂O₆) was used as the carbon source. Two grams of Pluronic F-127 was dissolved in 40 mL of absolute ethanol with magnetic stirring, and 5 mL of TIP was added and dissolved in the mixture. Three grams of glucose were slowly added into the solution and stirred until it dissolved completely. The solution was kept in a static state, for precipitation. The precipitate was collected by centrifugation at 5,000 rpm, washed three times with absolute ethanol, and dried at 100 °C for 20 min. The obtained powder was calcined at 400 °C for 2 h. Exam the product through XRD, SEM, EDS, TEM and XPS

Results

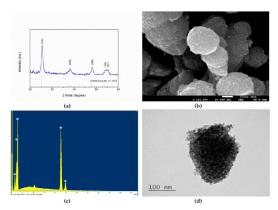


Figure 1. Characterization of the synthesized TiO2:C nanoparticles. (a) XRD pattern compared with the underlined reference of JCPDS card no. 21-1272 for anatase; (b) SEM image; (c) energy-dispersive X-ray spectroscopy (EDX) spectrum; and (d) TEM image.

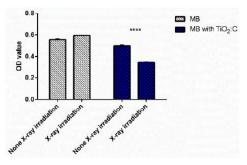


Figure 3. The generation of ROS of the synthesized TiO2:C under X-ray irradiation determined by the degradation of methylene blue. The measurement was performed at a wavelength of 664 nm. The concentration of TiO2:C particles and MB were 1 mg/mL and 10 ppm, respectively. The exposure of X-ray irradiation is 100~s (t-test, mean SD, n=6, ****: p-value < 0.0001).

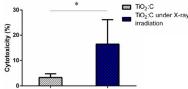


Figure 4. The in vitro photodynamic therapy effects of TiO2:C activated by X-ray irradiation was evaluated using LDH assay with A549 lung cancer cells. Without X-ray irradiation, the developed TiO₂:C showed no significant toxicity (as low as 3.38° 1.48% on day 2). When TiO₂:C was applied with X-ray irradiation, the death rate of A549 cells increased to 16.57 9.63%. (t-test, mean SD, n= 6, *: p-value < 0.05)

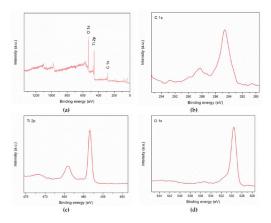


Figure 2. X-ray photoelectron spectroscopy (XPS) analysis of the synthesized nanoparticles. (a) General XPS spectrum; (b) deconvoluted XPS spectrum of C 1s; (c) de-convoluted XPS spectrum of Ti 2p; and (d) de-convoluted XPS spectrum O 1s.

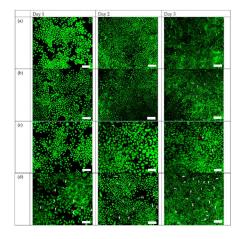


Figure 5. The PDT efficacy of TiO2:C exposed to X-ray irradiation, evaluated by live/dead staining of (a) control group; (b) X-ray-treated group; (c) TiO2:C-treated group; and (d) TiO_2 :C-X-ray group (scale bars: 200 μ m), where green represents living cells and red represents dead cells.

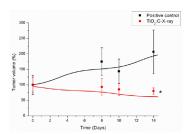


Figure 6. Tumor size in BALB/c nude mice injected with TiO2:C and subjected to X-ray irradiation (t-test, mean SD, n = 4, *: p-value <

Conclusion

This study have developed TiO2:C particles activated by X-rays as a promising approach to produce ROS and enhance PDT. The particles were synthesized at the nano-scale in the anatase phase. The band gap was effectively reduced by doping with C, which could be easily activated by X-rays to generate ROS. And based on the current research evidences it is believe that Xray irradiation activated TiO2:C has the potential to overcome the limitation of current penetration depth and improve PDT effects by inhibiting tumor growth effectively.

Statistics on nutrition and health education of all kind of cancer patients in different clinics

Shu-Han Yang¹, Jun-Yan Wang¹, Zheng-Fu Li¹, Cheng-Han Jiang¹, Yi-Zi Chen¹, Pei-Ying Xie¹, Chih-Jen Huang ^{1,2*}

Department of Radiation Oncology, Kaohsiung Medical University Hospital, Taiwan
 Department of Radiation Oncology, Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Taiwan



[Purpose]

Cancer patients are prone to loss of appetite and changes in taste due to their own disease factors and during radiotherapy or chemotherapy, which seriously affect the nutritional intake of patients, leading to nutritional loss, weight loss, and malnutrition. Through the intervention of nutrition and health education, nutrition evaluation and diet guidance for patients receiving radiotherapy, and continuous tracking and problem solving for malnourished patients with significant weight loss and reduced food intake. If there is an eating disorder, intestinal nutrition is taught the use of products, the preparation of filling formulas and the correct amount of diet to improve the nutritional status of cancer patients. Nutritional health education intervention can increase the nutritional intake of patients, thereby improving leukocytes and chemotherapy indicators and maintaining patient weight, allowing patients to continue to receive chemotherapy and radiotherapy, reducing side effects and infection rates during cancer treatment, and improving the prognosis of the disease.

[Methods]

(A) Cancer Center Nutrition Counseling Clinic Mainly referrals and appointments by physicians and individual managers.

Consultation object:

- (1) Patients with head and neck cancer receiving CCRT for the first time.
- (2) Inpatients with high risk of malnutrition and discharged BMI<18.5.
- (B) Nutrition and Health Education Clinic/ Consultation

The referral is mainly based on the nutrition note issued by the doctor, and the patient needs to receive consultation in the outpatient nutrition classroom at his own expense.

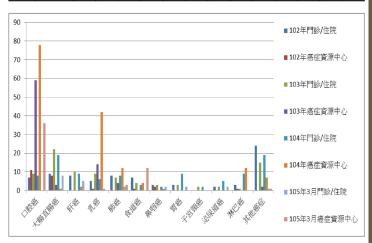
- (1)Consultation target: After the doctor's assessment, according to the patient's nutritional needs before, during and after cancer treatment, a nutritional note will be proposed.
- (2) Consultation project: Cancer diet and nutrition note.

Consultation management: nutrition consultation <48 hours completion rate.

[Results and discussion]

Table 1. Statistics on nutrition and health education of all kind of cancer patients in different clinics.

		口腔癌	大腸直腸癌	肝癌	乳瘤	肺癌	食道癌	鼻咽癌	日信	子宮頸癌	泌尿道 癌	淋巴癌	其他癌症	總數
102	門診住院	7	9	8	5	8	7	3	3	0	2	3	24	102
年	癌症資源中心	11	8	0	1	0	1	2	0	0	0	1	0	103
103	門診住院	9	22	10	9	7	4	3	3	2	2	1	15	100
年	癌症資源中心	59	3	0	14	4	0	0	0	0	0	0	2	169
104 年	門診/住院	8	19	9	6	8	3	2	9	2	5	9	19	258
	癌症資源中心	78	1	2	42	12	4	1	0	0	0	12	7	230
105 年3 月	門診/住院	0	8	5	1	2	0	2	2	0	2	0	1	75
	癌症資源中心	36	0	0	0	3	12	0	0	0	0	0	1	13



 $\label{eq:fig1.Statistics} \textbf{Fig1.Statistics on nutrition and health education of all kind of cancer patients in different clinics.}$

[Conclusion]

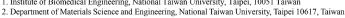
In addition to improving nutritional status and quality of life, the intervention of nutrition education can also enhance the efficacy of cancer treatment. The period of radiotherapy is a critical period of nutritional decline. If the patient's nutritional status can be maintained or improved during this critical period, the patient's tolerance to the treatment can be increased while reducing the incidence of infection, mortality and comorbidities. This is the main reason why cancer patients need active nutritional support.



Development of novel sonosensitizer using ROS generating C-doped TiO₂

nanoparticles for Cancer Treatment





3. Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli County, 35053 Taiwan



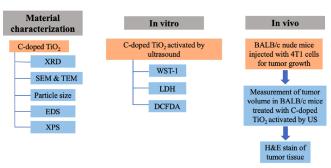
ABSTRACT

Sonodynamic therapy (SDT) is an emerging approach that involves eradicating solid tumors in a site-directed manner with the help of sonosensitizers and low intensity ultrasound. Ultrasound penetrates deep into the target tissue and activates the sonosensitizers to produce reactive oxygen species (ROS) that generate the cytotoxic effect. Titanium dioxide has gained much attention as nanosensitizer due to its varied properties. Hence, in this study spherical carbon doped titanium dioxide nanoparticles were synthesized by sol-gel process. The formation of C-Ti-O bond lowers the bandgap energy of TiO₂ which would be beneficial for the phenomenon of sonoluminescence to improve the effectiveness of SDT. DCFDA, WST-1, LDH and live/dead assay result exhibits good biocompatibility of the synthesized carbon-doped TiO₂ nanoparticle. Additionally, the antitumor efficacy of C-doped TiO₂ nanoparticles under ultrasound irradiation (SDT group) was evaluated using a mice model injected with 4T1 cells. SDT group could decrease the tumor growth significantly on seventh day of the treatment. Moreover, H&E staining results confirmed the effectiveness of SDT to cause the death of 4T1 cells in the tumor tissues.

INTRODUCTION

Cancer has been the leading cause of death in the US or 40 consecutive years. Even though there are effective cancer treatments like chemotherapy, radiotherapy, immunotherapy etc., they not only kill cancer cells but harm the healthy cells as well. Thus, an alternative therapy with fewer side effects called "Sonodynamic therapy (SDT)" was proposed. SDT consists of three elements: ultrasound, sonosensitizer and oxygen molecules. Activated sonosensitizer generates ROS which may cause the death of tumor cells. Hence, in this study, the sonosensitizer C-doped TiO₂ was synthesized through doping carbon into the anatase structure of TiO₂ to diminish the bandgap. A square wave of the ultrasound at a resonant frequency of 1.0 MHz, intensity of 0.33 MPa and duty cycle of 50% was used to induce the inertial cavitation and generate sonoluminescent light to activate the synthesized C-doped TiO₂.

MATERIALS & METHODS



RESULTS

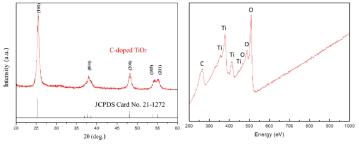


Figure 1: XRD and XPS pattern of C-doped TiO₂

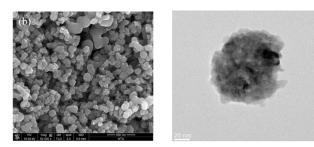


Figure 2: SEM and TEM images of C-doped TiO₂

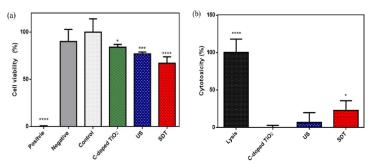


Figure 3: Cell viability and cytotoxicity induced by C-doped ${\rm TiO_2}$ activated by US evaluated by WST-1 and LDH assay respectively

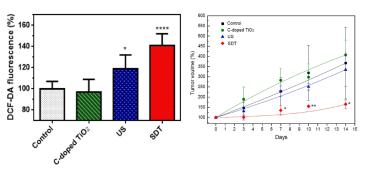


Figure 4: DCFDA cellular ROS detection Figure 5: Relative tumor volume in BALB/c assay (n=6) mice

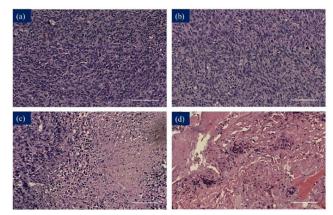


Figure 6: H&E stained images of tumor tissue (a) Control group (b) C-doped ${\rm TiO_2}$ ${}^{\odot}$ US group (d) SDT group

CONCLUSION

This study demonstrated that C-doped ${\rm TiO_2}$ nanoparticles could be viewed as sonosensitizers in SDT activated by low-intensity ultrasound for ROS generation as an effective strategy for alternative cancer treatments in the future.

A safe and easy experiment to measure natural radiation using charcoal filter and underground water

¹Kazuko ONISHI, ²Shiori OKADA, and ²Masahiro KAMATA

Advanced Support Center for Science Teachers, Tokyo Gakugei University, Faculty of Education, Tokyo Gakugei University 4-1-1 Koganei, Tokyo, 184-5801, Japan

1. Purpose of research

In this work, we explored the possibility of using underground water which could be easily obtained in many places. By using a plastic bottle and a charcoal filter cartridge, a safe and inexpensive apparatus was developed for collecting low concentration of radon in water phase in short time [1]. Our method makes it possible to observe the decay of radon and the production of its offspring species even if we use ordinary tap water coming from underground water source.

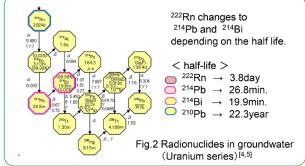
2. Radon and activated carbon

Radon is contained in small amounts in underground water [2]. We collected Radon using activated carbon [3]. Because of the halflife, the radiation dose rate changes with time. We developed a method that makes it easy to investigate.

3. About underground water in Japan

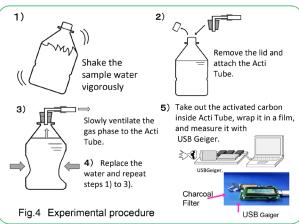
In Japan, there is underground water that naturally springs. Some of them are capable of collecting water freely. (Fig.5)

Charcoal ²²²Rn ²¹⁴Pb detector Fig.1 Radon and activated carbon



4. Experimental equipment and Experimental procedure







2) Spring water of Nukui shrine (Koganei, Tokyo)

3) Kita-machi park well pump (Kokubunji, Tokyo)

Fig.5 Underground water in Japan

5. Experimental results and calculated value

Fig.6 is experimental result. At the start of measurement, the count rate is low. Activated carbon collects radon, but radon emits only alpha rays. Since this measuring device measures only beta rays, the count rate does not increase. After a while, the count rate increases as its daughter nuclide, ²¹⁴Pb and ²¹⁴Bi, are produced. These are to emit β -rays. The half-lives of these nuclides are 26.8 min. for 214 Pb, and 19.9 min. for 214 Bi. By the radioactive equilibrium, indicating

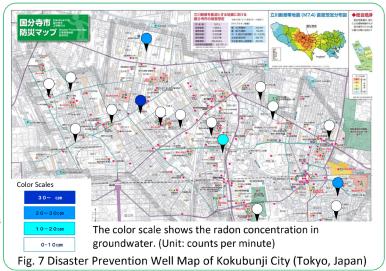
Kitamachi Park well (Kokubunji City, Tokyo .. ≨ 100 Fig.6 Experimental result

that the count rate becomes constant at about 2 hours.

This map is a disaster prevention well map of Kokubunji City in Tokyo (Fig.7) The color scale is the result of radon concentration in groundwater studied by this research. As you can see, the concentration of radon varies from well to well even in groundwater in the city. This may be due to the depth of the groundwater and the stratum through which the groundwater flows. We believe that this research will lead to not only radiation education but also learning about groundwater.

6.Conclusion

- -The radon contained in trace amounts in the groundwater was able to be collected efficiently using a charcoal filter for cigarettes.
- -It can be confirmed that these radionuclides are attenuated.
- And good agreement was also confirmed with the theoretical value.
- -We believe that familiar groundwater can be used as a teaching material for radiation education.



7. References

- [1] Kazuko ONISHI, Yukiko UONO, Masahiro KAMATA, Journal of Science Education in Japan Volume 43,
- [2] Masaaki SAITO, Shigaru TAKADA, RADIOISOTOPES, 43, 507-514 (2014)
- Masahiro KAMATA, Chiharu WATANABE . Chemical education , 48, 524-527 (2000)
 "ATOMICA" Nuclear Encyclopedia http://www.rist.or.jp/atomica/data/pict/08/08010312/07.gif
- [5] "Radioisotope Pocket Data Book 10th Edition, Japan Radioisotope Association (2011)

8. Acknowledgements

This work was supported by JSPS KAKENHI Grant Number JP 21H04061.



































國家衛生研究院 中原大學 National Health Research Institutes





中國醫藥大學 China Medical University



高雄縣醫事放射師公會



中華民國醫事放射師公會全國聯合會 Taiwan Association of Medical Radiation Technologists









