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Institute of Nuclear Energy Research Atomic Energy Council, Executive Yuan 2013 Annual Report

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INER 2013 Annual Report

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New start, new mission The Institute of Nuclear Energy Research – Forever rising, everlastingly evolving

The Institute of Nuclear Energy Research (INER), founded in 1968, is a government agency dedicated to atomic energy and radioactive application. The vision of INER is to provide complete technical solutions for national energy security, environmental protection and national health. Meeting the needs of the national energy policy development, the INER has expanded its researches in recent years to the development of new and renewable energy, energy conservation and carbon reduction, in addition to participating in economic policy research. Results of these endeavors have received high recognition.

In corporation with the government organization reform, the Nuclear Energy Institute will now be a subsidiary of the "Ministry of Economic and Energy Affairs" under a new name -the Institute of Energy Research. We will continue to assist the government in the implementation of Taiwan's energy policies --- assuring nuclear safety and waste reduction, building up green energy and low carbon environment, working toward a nuclear-free homeland. Reorganization signifies a new start and new mission for us. Our goals remain to improve on professional knowledge, innovation and service in order to provide the

best solutions to energy related issues and to contribute to the future development of the country.

In addition to technological research on nuclear energy development and applications, we have gained remarkable achievements in the fields of new energy, renewable energy and radiation application research and development. A number of the accomplishments are provided as follows:

Achieving high recognitions in the Taipei International Invention and Technology Trade Show in 2011, 2012, and 2013: For three consecutive years from 2011 to 2013, the Nuclear Energy Institute won a total of twenty-nine high honors for its projects at this venue: one platinum, thirteen gold, three silver and twelve copper prizes. In addition, we completed a total of thirty-eight projects in technology contracts; specifically, two in technology licensing, nineteen in developing cooperation, four in technical services, ten in intent of cooperation, one in technology transfer and two in early participation. All research and development performance continues to progress with impressive results.

Our nuclear medicine research and development projects won numerous awards at national competitions:

1. The 9th National Innovation Awards:

Development of 188Re-Liposome Therapeutical Radiopharmaceuticals

Development and clinical application of I-123-ADAM SERT imaging agent for diagnosing major depression disorder

2. The 10th National Innovation Awards:

INER Hepatic Receptor Image

Development of a high-end medical device-the INER positron emission imager dedicated for breast cancer imaging

3. In the National Invention and Creation Awards 2013 Silver Award:

Solid oxide fuel cell and the fabrication methods

In the industrial application of pioneering technologies, we made authorization contracts for the manufacturing technology with the industry in Solid Oxide Full Cell (SOFC): ceramic substrate supported unit cell and the fabrication techniques. Specifications of mass production can be expected within six months. This technology will be a significant addition to the international industry chain of SOFC after a third party product certification.

We developed the only engineering magnification and multiple feed pretreatment technology of biomass alcohol (rice straw, bagasse) in Asia, which compared with the original process is much more effective in terms of cost savings for materials and initial setup. The technology of concentrating solar cell module that we developed is the only product in the world that has won the UL certification, the IEC 62108:2007 product certificate and the UL8703 product safety certificate all at the same time. Having these certifications will greatly promote the product into the international market. Vertical axis fan analysis technology, in the meantime, has been listed as the CNS (Taiwan) and GB (China) standards. It is also listed as the small fan JSWTA0001 reference standard in Japan.

We engage in comprehensive evaluation of the needs of the country and strive to develop along the direction set by government policies. With the substantial experiences in research of energy technology and energy strategy analysis that we have accumulated, we are committed to continue to be the research institute that provides complete strategy and technical solutions to the nation's energy security, environmental protection and ultimately the wellbeing of the nation.

Director-General



2 Human Resources and Budgets

(Time of data: December, 2013)



Statistics of Educational Background for Research Staffs





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41.2% 41.2% Associate Researcher 56 persons (15.1%) Associate Researcher 153 persons (41.2%) Assistant Researcher 78 persons (21.0%) Research Assistant 84 persons (22.7%) Research Staffs 371 persons

Statistics of Job Category for Research Staffs

2013 Annual Budget	Unit : Thousand NTD	
Administration and Safety	1,250,714	56.28%
Management, Operation and Maintenance	104,622	4.71%
R&D Projects	728,896	32.80%
Nuclear Safety Technologies	165,427	7.44%
Environment and Energy Technologies	362,166	16.30%
Radio-biomedical Research	201,303	9.06%
Technology Promotion and Service	137,970	6.21%
Total	2,222,202	100.00%



Bevents of the Year

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The Introduction and Annual Achievements of the Center of Energy Economics and Strategy Research

According to the increasing of diversity and complexity on global energy issues, government and authorities would enhance on the research of energy economics, not only reinforce on mid- and long-term planning analysis and energy research, but also continue devoting human resources in related areas. Therefore, Institute of Nuclear Energy Research (INER), Atomic Energy Council, established Center of Energy Economics and Strategy Research in January, 2014. The new center has four divisions, includes energy system, energy economics, energy strategy and energy information and statistics. It consists of 24 members including doctors and masters from different professional areas, and will focus on the following research objectives:

- 1. Researching for energy policy and strategy
- 2. Planning for energy industry roadmap

3-1

3. Developing 3E (energy, economy and environment) model and database platform

In 2013, following to the nuclear power policy "Ensure nuclear energy security, steadily reduce dependence on nuclear energy, create a friendly low-carbon green energy environment, and gradually move towards a nuclear-free homeland". The center has accomplished 29 analysis reports for Executive Yuan as references. And the report focus on the evaluation of cost and benefit which go along with different policy alternatives and energy mix, providing policy makers to perform diverse assessment and cross-validation.

In the study of Taiwan Power Planning and CO₂ Mitigation Analysis - Zero Growth in Electricity Demand, we analyze the cost of electricity generation and CO₂ emissions in Taiwan during 2010 to 2050 by MARKet ALlocation-Elastic Demand (MARKAL-ED) model with different scenarios based on excluding CCS power plants and zero growth in electricity demand. The feasibility of the government's CO₂ reduction target has also been assessed. It is both important and beneficial to perform power planning analysis in order to make the allocation of government's resources as cost-effective as possible and to reach the mitigation target. The analytic result implicates that the ambitious CO₂ reduction target could hardly be achieved. Furthermore, ambitious target might cause unaffordable economic impact. It is recommended that the government might consider adjusting the target. Otherwise, in order to reach the ambitious target, it is necessary to further enlarge renewable policy objectives, to develop CCS power plants or more nuclear plants, or to reduce total electricity demand further.

On the other hand, the price elasticity of energy service demand is a set of critical parameters in MARKAL-ED model. Due to variations of national geographic, socio-economic backgrounds, the principle of the price elasticity setting requires to consider the difference between the region, countries, and various energy service demands. If the price elasticity of energy service demand was overvalued, it may overestimate the effect of government price policies (eg. energy tax policy), and then it would be too optimistic to look the reduction from of greenhouse gas emissions contributed by the demand side. In contrary, if the price elasticity was undervalued, it may underestimate the energy saving contribution of energy demand side to carbon policy, and then energy policy will be oriented toward energy-supply side, such as CCS, renewables, and nuclear power plants. This paper applies the local energy statistic data to estimate the price elasticities of energy service demand for different sectors in Taiwan. The reasonable parameters are helpful for the localization of MARKAL-ED model; furthermore, it makes the policy evaluation more realistic. The center have renewed the price elasticity of energy service demand since 2012, and already finished to evaluate in sectors of residential/commercial, industry, transport and so on.



Looking to the future, with the organizational reform of the Executive Yuan, INER will be a subordinate organization to the Ministry of the Economic and Energy, and rename to Institute of Energy Research. The center will need more professional human resources and research methods in related area. Consequently, the current model of MARKAL are going to be upgraded to advanced TIMES model, also enhance CGE model to facilitate future research and policy assessment.

3-2 INER BreastPET won the 10th National Innovation Award

Let innovation to be seen. Let innovation to change the world- Institute of Nuclear Energy Research (INER) developed a patented, dedicated breast positron emission tomography (BreastPET) apparatus, which not only met the IEC 60601 regulations but also was validated by clinical tests. This high-end medical device won the 10th National Innovation Award hosted by Institute for Biotechnology and Medicine Industry, which is paramount honor of Biotechnology innovation in Taiwan.



▲INER BreastPET won the 10th National Innovation Award

People believed that the European and American women are more likely to cause breast cancers. However according to the latest statistics provided by Ministry of Health and Welfare in Taiwan, the morbidity rate of women breast cancers in Taiwan is 4.8 times higher than 20 years ago, ranking second in Asia after Singapore. Currently morbidity and mortality rates of breast cancers are the top one in the female cancer list and the morbidity rate of young women suffering from breast cancers is higher than older women. Moreover, female Taiwanese had a predilection of incidence ages during 41 to 50, which is 10 year, in average, earlier than ages of European and American women. Therefore, precaution examination of Breast cancers cannot be ignored.

If breast cancers were found in the early stage, it is highly possible to be cured thoroughly. Nevertheless, the current X-ray mammography is more difficult to find the presence of lesions in dense breasts. Because breast density of Oriental women is usually higher than that of Western women, and dense breasts can make mammograms more difficult to interpret. The ultrasound is highly relied on experiences of operators, and is more often applicable to lesions larger than 0.5 cm. On one hand, MRI provided high sensitivity but took longer examination time and higher costs. On the other hand, the high sensitivity of MRI has been criticized for producing false positives as well. Current breast cancer examination in the United States had 86% false positives rate, which costs the U.S. healthcare system approximately \$2.45 billion annually. Breasts dedicated positron emission tomography instrument INER developed is expected to provide solutions to these problems. The high resolution and capabilities of distinguishing benign tumors from many others enhance the ability to detect early breast cancers and help pre-treatment assessment and treatment efficacy.

In 2012, the overall global market of medical imaging reached \$38 billion dollars, 52% of which was radiography products. INER had radiation detection and imaging experiences for over 15 years and leveraged the experiences to develop Women healthcare apparatus – INER BreastPET, a customized medical instrument for oriental women. INER BreastPET not only meets customized medicine demand but also avoids competition with international companies, which are aim to tap in biotech blue ocean.

In this contest of National Innovation Award, INER BreastPET is highly favored by jury due to the creativity and competitiveness of this system. Moreover, the whole system was original design manufacture. Until the end of February in 2014, 9 patents were granted in the United States and Japan and other 8 patents were pending. Core patented technology "A method for reconstructing threedimension images from two-dimensional planar imaging data" of INER BreastPET is that this system used special limited angle 2D angiography imaging technology to create 3D images. Data from 2 nonrotating detectors are combined with physical models and acceleration techniques to create 3D images and maintain both high accuracy and computational efficiency. The invented method won the gold medal of 2013 Taipei Int'l Invention Show & Technomart. The other patented design of INER BreastPET is the gantry which can effectively increase the detective area of breast region and reduce dead area of the chest-wall detection. Moreover, INER BreastPET requires no compression to patients' breasts during scan and axillary lymph node metastasis detection mode can ascertain the likelihood of breast cancer metastasis. Others such as patented efficiency correction and modified geometry can effectively reduce background noise and improve the image quality of INER BreastPET, which are value-added features for system optimization.



Examination postures when patients use INER BreastPET

Overall patent portfolio is the key to inspire vendor's ambition to embrace the dedicated technology of breast cancer diagnosis. The technologies of INER BreastPET already transferred to domestic companies in 2012 for commercialization.

Performances of Preliminary clinical trials are promising

Before the first human trials conducted at National Taiwan University Hospital (NTUH), the image results of INER BreastPET was compared to those of body positron emission tomography instrument. Figure 3 shows INER BreastPET have a fairly good resolution. In August 2013, INER BreastPET was used in clinical trials hosted by Director of Department of Nuclear Medicine - Dr. Kai-Yuan Tzen and Director of Breast Surgery & Breast Center - Prof. Chiun-Sheng Huang in the NTUH. Compared to conventional X-ray mammogram, ultrasound and positron emission tomography (PET/CT) examination, INER BreastPET can detect more 11.5% of small tumors, which can help pre-surgery and treatment assessment. Figure 4 shows a left breast of 72-year-old woman. PET / CT and ultrasonography found an approximate 1.9 cm tumor while INER BreastPET found another 0.5 cm tumor in addition to the 1.9 cm tumor. A pathological section confirmed the 0.5 cm tumor is malignant. Since this small tumor in the location close to the chest wall, which proved INER BreastPET to be capable of near chest-wall detection.





▲ (a) Photograph of the micro-Derenzo phantom used for imaging validation, (b) a reconstructed image of GE Discovery ST-16, and (c) a reconstructed image of INER BreastPET I.



(a) a 1.9 cm tumor was detected by INER BreastPET I and current imaging methods,
(b) an additional 0.5 cm tumor was detected by INER BreastPET I.

Chronicle of INER BreastPET development:

- 2009 Ministry of Economic Affairs, R.O.C. grand funding support and the team developed the prototype and continued to optimize the system and ran the preclinical trials
- 2010 Electronics Testing Center, Taiwan (ETC) granted certificates of IEC 60601-1 and IEC 60601-1-2 to INER BreastPET.
- 2011 Technology transfer contracts were signed with domestic companies to develop commercialized type of INER BreastPET.
- 2012 Both the Taiwan Food and Drug Administration(TFDA), Ministry of Health and Welfare, Taiwan and Institutional Review Board(IRB) of NTUH granted the approvals to run clinical trial program of INER BreastPET in the NTUH.
- 2013 INER BreastPET was used in clinical trials hosted by Director of Department of Nuclear Medicine –Dr. Kai-Yuan Tzen and Director of Breast Surgery&Breast Prof. Center - Chiun-Sheng Huang in the NTUH. The initial results showed INER BreastPET can detect extra 11.5% breast cancers than the conventional PET/CT did. With further collection of more clinical data in the future, it is expected the BreastPET may contribute to patient management.



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3-3 Plasma Coatings on Application Research and Development of Smart Energy-saving Living

To conform to the governmental policies on environmental protection and energy saving in residential/commercial sectors, the plasma coating technologies being the core and cleaning process in INER were utilized to develop the thin film devices with lightweight and flexible energy-saving functions, including the thin film solar cells, electrochromic films and low-emissivity films. They are all solid state and easy to integrate into the innovative systems used in the home energy-saving living and as well as zero carbon buildings. The highlights of 2013 are as follows:

1. High Quality Low-emissivity Coatings

The overall technology of low-e coatings for heat isolation and energy saving at INER is implemented in one go from design and simulation of device mechanism, through mass production processes and system equipment integrated development, to the output of roll products. It is completely indigenous and self-supported. At the 2013 Taipei International Invention Show & Technomart (INST 2013), we exhibited an energy-saving glass window module of 800mm×1200mm sticking with low-e films and a hollow type window module of 400mm×1600mm which a low-e film was suspended in the middle. The crowd at the show can experience the great thermal insulation effect with high transparency. INER

now has contracted with Taiwan's largest company in color films for early involvement in high-end flexible energy-saving films. It marks a big step in spreading the high threshold roll-to-roll plasma coatings to the high quality energy saving industry.





2. Electrochromic (EC) Energy-saving Films

INER has used the core plasma technology to develop electrochromic thin film devices and has accomplished the electrochromic WO3 and NiO thin film module units by plasma sputtering. These units were driven by 2.4 V and their optical variation were 40% (the transmittance varied between 70% and 30%). 6 pieces of the units were assembled to make an energy-saving window module exhibited at the INST 2013. The crowd at the show can experience the application reality of energy-saving window, letting the energy saving technology infuse into home life. The relevant patent gained Bronze Medal at INST 2013. INER now has contracted with a technology company for the cooperative development of electrochromic modules and an optoelectronics company for the technology service of electrochromic modules.





Electrochromic window module of 800mmx1000mm.



Flexible thin film solar cell module of 1500mmx900mm.

3. Flexible Solar Cell Modules

INER has used the home-made roll-to-roll plasma process technology to develop flexible thin film solar cells to bring the manufacturing cost of solar cells down. The flexible solar cells were collocated with home applications, such as windows, blinds, balconies and interior lighting to provide the real experience of residential energy saving and to speed up the promotion of renewable energy in energy saving. We have accomplished the encapsulation of a single flexible solar cell at 135°C this year. 24 pieces of flexible solar cells of 250mm×250mm were assembled to make a flexible solar cells module of 1200mm×1500mm, 25 W and 18 pieces of the ones were assembled to make a flexible solar cell module of 900mm×1500mm, 21 W. The modules can generate power with the projection of interior LED lighting, showing the lightweight, thin and flexible characteristics and the energy-saving concept of interior lighting resource recycling. They were exhibited at INST 2013.

Upon upgrading the plasma technology to high-performance energy saving applications, the preliminary effect has been noticed. In 2013, we developed the particular properties of flexible energysaving devices. The individual device function was exhibited in household energy saving applications at a preliminary stage. We are looking for the industry to involve and perfect the development. Then the practical energy-saving products could be further developed. Next step, we will integrate all of the different devices. For example, the flexible thin film solar cell will be integrated into the EC device for smart-window applications. The solar cell can provide sufficient electric power to operate the EC window, having smart function of transmission tuning. Another is the integration of the solar cell into the thin film battery to be a mobile power which provides next generation applications of flexible 3C products. Both of the two kinds of planning are the future development direction of new green energy saving industry.

3-4 Open the Door for Cellulosic Ethanol Industry

Institute of Nuclear Energy Research (INER) has long-term dedicated to the research and development of cellulosic ethanol technology according to national biofuel-promoting policy, use non-food biomass as the raw materials for lowering the dependence on petroleum, reducing carbon dioxide emission and establishing emerging low-carbon industries. Recently, INER has led in aggressively flexible strategy, and has achieved quite significant progression in opening the first light to promote INER's cellulosic ethanol technology to be commercialized.

Currently, the developed cellulosic ethanol technology has already been international competitiveness, but the acquisition of biomass feedstocks is still the bottle-neck for establishing cellulosic ethanol industry. Since the domestic bioethanol policy is still under debate and the collection and transportation technologies or procedures for massive agro-wastes have not yet been established, hence the co-construction with existing factory to build cellulosic ethanol plant and utilize the lignocellulosic wastes produced by that factory is proposed for promoting the commercialization. So as to create a triple-winning operation mode to simultaneously solve wastes disposal problem, show new value of the wastes, and reduce cost of collecting cellulosic feedstock. Based on this strategy, different industries such as chemical, plywood, paper, and oil companies have come to discuss about cooperation and technology-authorization, and a plywood company has agreed to cooperate with INER. It is expected the wood residues of that company will be converted into ethanol or chemicals using domestic developed technology, and a benchmark cellulosic ethanol commercial plant will be built in south-east Asia within 3~5 years.

In another way, more applications for utilizing non-food biomass feedstocks are developed under above mentioned co-construction idea in this year. Due to the lack of reuse methods to treat large amount of domestic kitchen wastes, Neihu Refuse Incineration Plant, Department of Environmental Protection, Taipei City Government has requested INER for study of kitchen-waste ethanol and assistance in establishing this conversion technology in order to find an innovative and value-added method for solving such environmental problem. INER has applied the experience in the research and development of cellulosic ethanol core technologies to help establish the conversion process and its diversified utilization demonstration platform. This accomplishment has not only promote to the planning of building a mesoscale kitchen-waste ethanol demonstration plant in 2015, but also become a policy-making basis for using kitchen wastes to produce ethanol in the future. It has been paid much attention by several media, CommonWealth magazine has introduced that Taipei City Government acquired INER's kitchen-waste ethanol technology in its No. 533 periodical published in October 2013, and has also reported about INER's continuous effort to promote bioethanol industry through the development of cellulosic ethanol technology and has tested various biomass feedstocks. This further showed the application value and potential of the cellulosic ethanol technology implemented by INER.

The above means INER has made a major breakthrough in commercializing its cellulosic ethanol technology. Besides keeping on lowering production cost and establishing engineering scale-up technology of key equipments, INER would help the industry build cellulosic ethanol commercial plant. INER is planning to expand the applications of the cellulosic ethanol core technologies to establish the conversion process which can use various cellulosic feedstocks to co-produce biofuel and bio-based chemicals and generate bio-power. So that to help create domestic bio-refining industries featured in both low-carbon and high-value products.



Current Major R&D Activities

I. Nuclear Safety Technologies

President Ma declared new energy policies of Taiwan on November 3rd, 2011. Among those to ensure nuclear energy security and to reduce nuclear energy dependence steadily are two main purposes. To achieve those, the security of the 4th Nuclear Power Plant must be ensured prior the commercial operation. Meanwhile, no extension to life spans of existing plants, and the decommissioning plan should be launched as planned.

The institute of nuclear energy research is the top research institute on nuclear science and engineering in Taiwan over past four decades. The INER will continue its efforts to the technologies and assessments of nuclear regulatory as well as operation safety. It also devoted various research achievements being applied to the nuclear power life cycle.

The INER followed the governmental new energy policies and sustained its R & D efforts to support the security of nuclear power in Taiwan, and actively developed nuclear back-end technologies so as to effectively mitigate the issue of radioactive wastes. Consequently Taiwan will move towards nuclearfree homeland, and achieve an all-win goal–energy security, environmental preservation and economic prosperity.

The main achievements of the nuclear safety technology research in the INER in 2013 are as follows:

- (1) Nuclear Regulation Technology Support: An assessment methodology of environment associated fatigue for class 1 components in ABWR environment was established and the soil structure interaction (SSI) analysis were performed so as to enhance the seismic analysis accuracy.
- (2) Radwaste Management for Nuclear Power System Lifecycle: A spent fuel pool water treatment unit was established. The hot test of uranium sludge stabilization and the proficiency test for measurement and analysis of clearance samples were completed. Some special liquid radwaste treatment technologies were developed.
- (3) Clearing Legacy Nuclear Facilities: The cleanup technology for high-activity spent resin was established. Solidification of evaporator concentrate technology was studied. A remote suction device for underground-stored high-activity spent resins was developed.
- (4) Construction of Nuclear Industry Platform: The stretch power uprate for the Kuosheng nuclear power plant was achieved. The development of welding overlay technology for the nuclear power plants was completed. The licensing technology development for safety-related instrumentation and control and the dry storage system development program were continued.

Current Major R&D Activities



Major Activities

1

This study investigated the structural safety of the nuclear components and the mechanical properties of the fuel claddings. On the aspect of the structural integrity of the reactor pressure vessel, we perform the detail calculation of the stress field of the nozzle component subjected to various loads in different service levels according to the ASME (American Society of Mechanical Engineers) code. The study of fuel claddings is mainly focused on the fracture toughness tests of the Zircaloy-4 fuel claddings after heat treatments. Relevant research results can be used to enhance the technical bases for the regulatory measures taken by AEC. Details are described as follows:

(1) Build the analysis models of nuclear component based on the realistic dimensions and geometry using ANSYS FEM codes. Perform both the thermal transient and mechanical analyses for the component under a variety of service conditions specified in the design specifications. Develop the three-dimensional stress analysis standard procedure of the nuclear component.



▲ Nuclear component (nozzle) drawing and thermal analysis of a transient event

- (2) With an aim to guarantee that the component can perform its intended functions as well as to ensure the RPV integrity in plant service life, we execute both the stress- and fatigue-limit checks in accordance with the relevant requirement specified in Section III Division 1 NB-3200 of the ASME Boiler and Pressure Vessel (B&PV) code.
- (3) Establish the assessment methodology of environment-associated fatigue for nuclear class 1 components in ABWR (Advanced Boiling Water Reactor) environment in accordance with both NRC Regulatory Guide 1.207 and NUREG/CR-6909.
- (4) Build the detailed finite element model of the Lungmen NPP (Nuclear Power Plant), and perform the soil-structure interaction (SSI) analysis using SASSI software to increase the accuracy of SSI analysis.
- (5) Measure the hydrogen contents of the hydrided Zircaloy-4 fuel claddings, and execute the fracture toughness tests of the claddings under different heat treatment conditions and methods.

Development and Prospect

(1) Considering the complicate geometry and design loads of the nuclear components, the 3-D model and analysis technique provide better accuracy than the simplified 2-D model and method. The

study has successfully applied the 3-D stress analysis technique to the stress analyses of the seal drain nozzle (SD) of Lungmen NPP. The evaluation results indicate that the SD nozzle design is complied with the requirement the ASME code.



▲ Deformation contour (left) and stress contour (right) in a 3-D full-model

- (2) This study has established the fatigue assessment technique for nuclear components considering the environmental effects. The technique was successfully used to evaluate the fatigue life reduction of the RPV feedwater nozzle in Lungmen NPP due to the effects of LWR environment. Four specific environmental parameters are considered: service temperature, strain rate of material, dissolved oxygen level in water, and sulfur content of the steel. The results show that the environmental cumulative usage factor of feedwater nozzle has the maximum value of 0.3326 in 60 years of service life. This guarantees the structural safety of feedwater nozzle considering the effects of reactor coolant environment, and ensures the structural integrity of the reactor pressure vessel.
- (3) The simulation of the soil-structure interaction (SSI) of Lungmen NPP shows that the detailed model gives more accurate results than the traditional stick model. It is thus suggested to use the detailed model for the SSI calculation hereafter.



SASSI model for SSI analysis of Lungmen NPP- Detailed Model

(4) On the study of the cladding property, the main objective is to investigate the heat treatment effect on the fracture toughness of hydrided Zircaloy-4 fuel claddings. With increasing hydrogen content (150-800 wppm H), the fracture toughness of hydride SRA (Stress Relief Annealed) and RXA (Recrystallization Annealed) cladding decreases at both 25 and 300°C. However, with the same testing conditions, the value of fracture toughness for RXA claddings is better than that of SRA ones at both 25 and 300°C. The results suggesting that the mechanical properties of fuel cladding can be enhanced by RXA heat treatment. A paper with thorough discussion of the experiment design and results has been published on the Journal of Nuclear Materials.



2



▲ Jmax against hydrogen concentration for SRA and RXA Zircaloy-4 cladding tested at 25 and 300°C

The Development and Application of Radwaste Management Technologies for Nuclear Power System Lifecycle

The nuclear energy user is under the obligation to fulfill the commitment of reducing radioactive wastes. A valid waste management can enhance operation safety of a nuclear facility and mitigate the public anxious feeling of radioactive contamination to living environment.

This project is aimed to develop and verify novel radioactive waste management technologies for the necessity of nuclear power system lifecycle. The strategy is to achieve the waste treatment requirement form the operation and decommissioning for existed facilities in INER at first. Then the established technologies will support the radioactive waste management of domestic nuclear power plants for both operation and management of theirs decommissioning activities in the future.

In 2013, three subprojects including, (1) "The study of volume-reduction technologies for decommissioning radwaste", (2) "The study of treatment technologies for special liquid radwaste", and (3) "The development and application of radwaste final disposal technologies" will be conducted. To develop and apply the core technologies of radwaste treatment and disposal are the main value of this project. Through the valuation and validation process, the developed technologies will ensure the safety and domestic possession while they are applied to the nuclear power plant decommissioning.

2-1 The Study of Volume-reduction Technologies for Decommissioning Radwaste

This project is aimed to develop radioactive waste minimizing technologies required for nuclear facilities. At first, applications are focusing on clearing INER research facilities. In the future, the developed technologies will also meet the decommissioning requirement from domestic nuclear power plants. For year 2013, the major accomplishments are as follows,

- Completion of safety assessment of TRR biological shielding block waste storage building,
- Establishment of spent fuel water treatment unit ,
- Completion of uranium sludge stabilization hot test,
- Completion of proficiency test for measurement and analysis of clearance samples.

Removal of suspended solids from the TRR spent fuel pool water using inorganic coagulant

During the decommissioning phase of TRR , fuel pool water was contaminated by Cs-137 > Sr-90 > actinides and suspended solids. Hence, to remove the radioactivity and turbidity from the pool is the major concern. Traditionally, organic materials such as filters, ion exchange resins and polymer coagulant aid were widely employed to purify the contaminated water. However, most of the organic media are degraded under strong ionization radiation, so further stabilization of the spent radioactive media is usually required. Currently, the radiation resistance of inorganic media has attracted considerable attention pertaining to their application in liquid radioactive waste treatment. In the previous study, diatomite-based ceramic filter and aluminosilicates have been employed to remove the radioactive contaminants, and also the purification units have been established.

Directly separating the suspended solids from the pool water without pretreatment leads to the filter clogged and derives the higher backwash frequency and lifetime reduction. Coagulation processes are widely employed for the treatment of water before filtration processes to avoid the problem above mentioned. An inorganic reagent, polyferric sulfate (namely PFS) incorporated with alkali, was successfully employed to remove the suspended solids from the pool water without polymer coagulant aid. When PFS was mixed with modeling turbid water in the presence of either Ca (OH)₂ or Na₃ (PO)₄, the turbidity of water was reduced from 139 NTU to 0.6 NTU. After the proper dosage of PFS and lime reacted with the TRR spent fuel pool water, the turbidity of water was reduced from 5.0 NTU to 0.6 NTU. After the coagulation treatment, the supernatant may contain calcium and ferric ions. The adsorption abilities of aluminosilicates in pool water, supernatant and slurry solutions were assessed, and the results indicated no obviously negative effect.

In this work, the inorganic coagulation reagent is successfully developed to remove the suspended solids, so the filter lifetime extension and waste reduction is remarkable. Furthermore, the products of coagulation have minor effect on the adsorbent, so the reagent is compatible with the other purification

units. In the near future, dewatering and solidification techniques for the treatment of sludge will be investigated to reach the goals of wastes volume reduction and safe storage.

of suspended solids

 Appearance and morphology of the sludge generated by PFS+Ca(OH)₂ in the presence



The removal of suspended solids using PFS incorporated with different alkali (initial turbidity 139 NTU, pH 6.5~7.0)





The adsorption of beta-emitters from the pool water, supernatant and slurry by aluminosilicate





▲ The removal of suspended solids from the TRR spent fuel pool water using PFS incorporated with lime

Proficiency test for measurement and analysis of clearance samples

Based on the experiences of foreign countries, the routine running and decommissioning of nuclear power stations will produce a lot of low-level solid radioactive waste. Most of them can be categorized as non-radioactive waste after a certain clearance measurement with quality assurance procedures. To effectively solve the pressure of temporary radioactive storage warehousing and low-level radioactive waste disposal site, the aforementioned very low-level radioactive waste can be released by following the "Regulations on Clearance Level for Radioactive Waste Management" enacted by the Atomic Energy Council (AEC). Looking into the competence requirements of laboratories dealing related measurements and referring to the technology criteria draft for the radiation waste clearance measurements, the National Radiation Standard Laboratory (NRSL) ran this proficiency test for measuring instruments used in clearance.

The measurements of the instruments were in two forms: barrel and box. The detector types included the plastic scintillation detectors and the germanium detector. The density of the tested sample was ~ 1.0 g/cm³, the activity range was 0.01 Bq/g ~ 1.0 Bq/g. The dominant radionuclides were Co-60 and Cs-137. The test box was a stainless steel container of 34 cm length, 34 cm width, 36 cm height and 0.2 cm thickness. The test barrel was an iron container with an internal height of 86 cm, a 56 cm diameter and 0.2 cm thickness. Standard test pieces were tested for uniformity, and the uncertainty evaluation for the reference activities of Co-60 and Cs-137 were $\leq 0.50\%$ (k = 1), and $\leq 0.75\%$ (k = 1), respectively.

The judgment criteria in this proficiency test was (1) Bi \cdot -0.25 ~ +0.50, (2) En \leq 1, Uci \leq 20% and (3) weighing bias \leq 10%.

Three laboratories took part in the proficiency test workshop by offering 7 measuring instruments. All the results were acceptable for bias and traceable to the national standards and the minimum detectable activity (MDA) values of Co-60 and Cs-137 met the release limit of 0.1 Bq/g defined by the IAEA.



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2-2 The Study of Treatment Technologies for Special Liquid Radwaste

To treat the problematic radioactive liquid waste produced from various research institutions or nuclear facilities in Taiwan, INER has successfully developed several effective treatment technologies and promising green processes such as AC-GA inorganic adsorbent, solar-driven evaporator and auxiliary fuel incineration process. Through the evaluation test with actual radioactive waste, the superior performance of the developed technologies has been verified. Furthermore, they will be applied to treat related waste existed in INER.

Inorganic adsorbent with high selectivity for Sr

Participant Code

Using the domestically synthesized inorganic adsorbent (AC-GA) to remove Sr^{2+} nuclide from radioactive wastewater was implemented in this project. AC-GA showed excellent adsorption capability at extensive operation range of pH (from pH = 3 to 11). It also demonstrated higher removal efficiency (99.5%) and adsorption equivalent (4.3 meq g⁻¹) than commercial adsorbents, respectively. Through the column tests using processing wastewater (22.96 Bq mL⁻¹), the removal of Sr-90 radionuclide via AC-GA was over 99.9%, and the water quality of effluent completely met the regulation requirement.





Participant Code

AC-GA performance in a wide pH range





Hot commissioning of the experimental evaporation equipment for the high-conductivity liquid radwaste treatment

The experimental solar-driven evaporation equipment has been installed and successfully implemented hot commissioning for treating the high-conductivity liquid radwaste containing tritium stored in Building 015B of INER. The results showed that the effluent's quality completely met the discharge standards except tritium nuclide, and the main activity concentrations of Cs-137 and Sr-90 were below minimum detectable activity (MDA). The maximum temperature of the steam separator is up to above 120°C. The output rate of the distillate is approximately 20 L/h, and the overall thermal efficiency of the experimental solar evaporator is 24%. In terms of the industrial and radioactive safety, no accidents happened during the hot commissioning period. Moreover, this equipment will routinely treat the high-conductivity liquid radwaste containing tritium after the Safety Analysis Report of the Latest Edition in Building 015B of INER, which includes this hot commissioning report, is approved by the relevant administration.



Experimental solar evaporator

U type vacuum-tube collector

The study of radioactive organic wastewater treatment of INER

The radioactive organic liquid waste has separated into two layers including aqueous layer and organic solvent layer after long time storage in INER's waste treatment facility. The organic layer may occupy 24% of the total volume and the aqueous layer may occupy 76% of the total volume. Due to miscible and similar calorific value with diesel, organic waste solvent can be used as an auxiliary fuel of radioactive incinerator. The treatment of waste solvent by this manner is expected to effectively save fuel diesel consumption and well solve of waste problem.

Using radioactive organic solvent as auxiliary fuel, this project has finished the treatment test of 1,000 L waste solvent by auxiliary combustion system. The results confirm that the process is successful and the concentration of exhaust gas is far below the regulation limitation.



▲ Waste solvent auxiliary combustion system

2-3 The Development and Application of Radwaste Final Disposal Technologies

To conform the operating requirements of low-level radioactive final disposal, we are trying to establish an operation platform for waste drum inspection to meet the ongoing accept standard for disposal, to build the certificating technology for waste characteristics, and to modify present analysis technology for nuclides. At the same time, the project is focused on developing nuclides releasing prevention technology to block pollutants distribution for maintaining environmental radiation safety. The goals of safe management of radioactive waste, such as maintaining an excellent ecological quality, ensuring public health, and enhancing public trust are thus achieved.

The major work is to complete the installation of mechanic equipment of inspection operation platform to provide the outlook inspection, ventilation and image taking & recording with which the inspection is performed. In respect to radwaste characterization, the automated solid phase extraction (SPE) technique for sample pretreatment has been established, and the analytical methods of the waste sources with high radioactivity and TRU wastes have also been identified by ISOCS. Furthermore, determination of Tc-99 and TRU was performed using the SRM 4359 (Standard Reference Materials) for method validation of automatic system, which improved the separation effectiveness and provided fast measurements of radwastes with the same activities. Also, the optimization and modification of suction and injection technology are developed to evaluate how to decrease groundwater radioactivity as an effective method to block pollutants releasing and distribution.

The function of inspection operating platform can distinguish the normal and reinforcing-required drums from the outlook, and recording the inspection procedures as the archive. As to the detection results of nuclides, the estimation of scaling factors for total activity concentrations of Cs-137 and Sr-90 relative to that of gross β - was finished. The activity concentration of Sr-90 could be derived mainly using the direct measurement of Cs-137 and gross β -. In this study, the positive correlation existed for gross β - and (Cs-137 + Sr-90), indicating that the range of concentration activity for hard-to-measure radionuclide, Sr-90 could be quickly estimated. According to the research on the solute concentration of the groundwater by flow rate versus suction and injection treating groundwater, the efficiency of suction and injection treatment will be strongly influenced by the rainfall and original soil moisture. Thus, the rainfall and soil moisture sectional variation will be subsequently observed to analyze the retention time of leaching to non-confined water-contained level of ground water and its relative water level increase.



▲ Mechanic equipment for 55 gallon waste drum Inspection platform

▲ Outlook inspecting on inspection operation platform



 Establishment of radionuclides characterization for outer tubes of TRR spent fuel with high activities in the 55 gallon waste drum

 The positive correlation curve between activities of gross β- and (Cs-137+Sr-90)



Establishment of pumping- treatment- injection to decrease the solute concentration in the groundwater



The established technologies will be implemented in the practical waste treatment operation in the next fiscal year. The contaminated fuel pool water of TRR would be treated in situ and then transferred to the liquid waste treatment plant for further polishing. The stored organic liquid waste would be treated with the aid of incineration and the novel inorganic ion-exchanger pellets are going to implement the plant site long term test. Furthermore, the preparation facility for waste drums will be continued to complete the equipment installation and software establishment. The hydrology investigation results of ground water and its remediation method for radiological contamination would be improved and verify the efficiency and accuracy.

3

Clearing Legacy Nuclear Facilities

Most of the major nuclear application countries have established a general consensus that, to meet the safety requirement of preventing radioactive contaminants from proliferation and to meet the internal need of reuse the facility site, nuclear facility shall be clear up at its end of life. The facility owner would gain privileges from both economic and social responsibility point of view on implementation of nuclear facilities clearing. INER is the first organization that has the problem of legacy nuclear facilities which stop operating. To comply with government's nuclear safety policy, INER sets up a project to proceed with nuclear facilities clearing step by step. The work scope of this project for year 2013 includes "cleanup and improvement of nuclear reactor and affiliated facilities" and "minimization and safe storage of radioactive waste". The former aims to release the public from worries in uncertainty to the radiation contamination while the latter focuses on decreasing the amount of radioactive waste and consequential decrease of radioactive waste treatment and disposal costs. The achievements made in this year are good for the subsequent tasks.

3-1 Cleanup and Improvement of Nuclear Reactor and Affiliated Facilities

The major accomplishments of this project for year 2013 include establishment of cleanup technology of high-activity spent resin, approval of use permit of greater than class C waste container, and installation of monitoring system for dismantling building structure. The major accomplishments of are as follows.

The cleanup technology of high-activity spent resin

The cleanup of TRR spent fuel pool is one of the most important working items of the TRR decommissioning project. The radioactive wastes stored in spent fuel pool must be removed as planned to meet the regulatory requirement. The spent ion exchange resins are classified as greater than class C (GTCC) waste and are required to be stabilized before final disposal. Yet, the stabilization technology is still on the way of developing. In order to accelerate the cleanup of spent fuel pool, the technology to safely remove spent resins are required.

The cleanup framework of spent resins has been planned follow the acceptance criteria at INER. The cleanup technologies include the drying process designed and storage container licensed. The drying process of high radiation and GTCC wastes was paten applied in Taiwan and US. The storage container has been certificated by US DOT and IAEA, and it also has been employed to the storage of GTCC wastes in foreign nuclear facility decommissioning sites. The container equips with filter vent and lead-shield liner, so it meets the requirement of safe storage. Furthermore, the container is stackable so that the storage space is more compact.

The container of GTCC has been permitted by the authority. Expectably, the storage space of the warehouse will be efficiently used by applying this container to solve the GTCC wastes storage problem during the decommissioning of TRR. The cleanup technology and container were successfully used to remove parts of the spent resins. Currently, there are 14 drums of the spent resins have been drying and packing. All of the spent resins will be removed on 2014 and transported to the First Storage Warehouse at INER pending for the stabilization process established. Therefore, the treatment and removal of the pool water could be further performed.



▲ The cleanup framework of spent resins



 Method of drying high-level radioactive wastes and device



Monitoring system for dismantling building structure

To enhance the storage safety of TRR biological shielding waste, a 10-year reassessment of dismantling building is completed and a structure monitoring system is installed in 2013. The dismantling building structure monitoring system was under the TRR biological shielding waste monitoring system. Several devices are added in monitoring system, such as tiltmeters, 3-axis strain gauges, and 1-axis strain gauges. The system monitors the verticality and structural stress of dismantling building and also performs structural safety evaluation of dismantling building in the same time. The system could provide early precaution against hazard.



▲ Monitoring tiltmeter of dismantling building structure



 Monitoring data recorder of dismantling building structure

3-2 Minimization and Safe Storage of Radioactive Waste

The major accomplishments of this project for year 2013 include completion of treating combustible radioactive wastes more than planned amount, development of remote suction device for underground-stored high-activity spent resins, and completion of solidification of evaporator concentrate study. Their descriptions are as follows.

The setup of the remote suction device for underground-stored highactivity spent resins

In order to condition the high-activity spent resins stored in underground vaults, the remote suction device had been developed. In 2012, this device, which includes the cyclone dust collector, the intermediate holding box, and the filter assembly, had been set up, and the cold test of this device had been finished successfully. In 2013, the follow-up hot test of this remote suction device and its accessories dealing with one drum of low-activity spent resins was finished to ensure the device's

function. This device will further deal with the highactivity spent resins stored in the underground vaults to ensure their safety storage in the next few years.



 Remote suction device for underground-stored high-activity spent resins



A view of remote sucking-out test with low-activity spent resins

A study of solidification of evaporator concentrate

Evaporation is one of the adoptable technologies applied to wastewater treatment, for it gives high volume reduction factor as well as high contamination factor. The distillates could be recycled. However, evaporator concentrates containing various nuclides require proper solidification to immobilize the nuclides in stable waste forms. Cementation is a widely applied technique for conditioning of low and intermediate level radwaste. Beside, bentonite, which is inexpensive and widely used as the buffer material, could solve the bleeding problem of waste form due to its ability to form gels with water. In this study, the solidification agents are categorized as type CB (Portland cement and bentonite), type CBFS (50wt% Portland cement/ bentonite, 30 wt% fly ash and 20wt% blast-furnace slag), type CBF (70 wt% Portland cement/bentonite, 30 wt% fly ash) and type CBS (60wt% Portland cement/bentonite and 40wt% blast-furnace slag), respectively. Simulation solutions are categorized as tape water (symbolized as No.1), sodium solution with the concentrations of 3.23M (symbolized as No.2) and 4.03M (symbolized as No.3), respectively. For instance, CB-3 represents that simulation solution adopts 4.03M sodium solution and the solidification agent is type CB. Experimental results indicated that the recommended operational conditions of the solidification are as follows. When simulation solution is tap water, the optimal solid-liquid ratio is 1, and the additive bentonite amount is 10 wt% of water content. Under this condition, the average compressive strength after 28-day curing of waste form is 71 kg/cm², the average compressive strength after weather resistance is 84 kg/cm², and the average compressive strength after water resistance is 92kg/cm². Similarly, when the simulation solution is 4.03M sodium solution, the optimal solid-liquid ratio is 2, and the additive bentonite amount is 25 wt% of water content. Under this condition, the average compressive strength after 28-day curing of waste form is 230 kg/cm², the average compressive strength after weather resistance is 245 kg/cm², and the average compressive strength after water resistance is 280 kg/cm². All these above-mentioned test results meet the regulation limits, 15 kg/cm². Hence, the developed solidification recipes give the advantages of high volume reduction, prevention from bleeding, and good water resistance of waste form.



▲ Three-component diagram of solidification



▲ The relations between compression strength and curing time for CB-1 and CB-2



▲ The relations between critical bentonite/ water ratio and solid/liquid ratio for type CB-3



▲ The relations between compression strength and solid/liquid ratio for CB-1 and CB-3



On the bases of nuclear decommissioning and radioactive waste management technologies that INER has developed, and under the premises of safety and environment protection, this project steadily proceeds with nuclear facilities clearing and minimization of radioactive waste. The project aims to solve the domestic physical problems, to upgrade technologies in the process of on-site exercises, and to cultivate nuclear decommissioning talents. All of the lesson learned could also be used in the nuclear power plants decommissioning industry in the future.

4 Construction of Nuclear Industry Platform

The main objective for constructing the nuclear industry platform is to enhance the domestic technology associated with safety evaluation and operational maintenance & repair. This will not only promote the performance of domestic nuclear power plant operation, but also prevent foreign technology from monopolizing the nuclear market. Major work scope in this project includes power uprating program, replacement of large-scale equipments and components, water chemistry, licensing technology for safety-class instrumentation & control, and dry storage design and cask analysis technology for spent fuel pool etc.

Major Achievement and Results

(1) Stretch Power Uprate Program Development for Kuosheng Nuclear Power Plant Units 1 and 2

The program provides Taipower with support and service for implementing Stretch Power Uprate (SPU) in both Kuosheng unit 1 and unit 2. Major task in this program is to provide licensing support for Design Change Request (DCR) associated with SPU implementation. The core thermal power is projected to be increased from current 2943 MWt to 3001 MWt, i.e., 2% increase in core thermal power. The annual electrical energy output is predicted to increase approximately 300 million kW-hour, which is equivalent to fossil fuel replacement cost saving of 860 million NT dollar and carbon dioxide emission reduction of approximately 252,000 tons / year. The goal of effectively reducing carbon dioxide and saving energy has been achieved through the completeness of the project.

(2) Development of Welding Overlay Technology for Nuclear Power Plants

A welding overlay technology for nuclear power plant application has been established. The technology not only solves the timing and safety issues associated with replacement and repair of large-scale equipments and components, but also induces the development of domestic maintenance and repair technology applicable to the operating nuclear power plants.

(3) Licensing technology development for safety-related instrumentation and control

The program has been executed to cooperate with German TUV Rheinland company. A licensing procedure applicable to safety function integration for the safety-related control system has been established. This procedure has also been licensed internationally with SIL-3 high reliability level.

(4) Dry Storage System development Program

Domestic technology for the dry storage system design and analysis has been developed. The manufacturing and installation of the system has also been completed. The technology has been

applied in the aspect of spent fuel dry storage for domestic operating plants.

Since the Fukushima nuclear disaster happening on March 2011, countries owning nuclear power plants had extensively reviewed their nuclear policies. Our government also announced its new energy policy, which emphasized on reducing the nuclear activities gradually and stably. However, this is to be accomplished in conjunction with three principles, including no electricity restriction, reasonable electricity price, and fulfillment of international commitment on carbon dioxide emission reduction. In view of this, a project "Development of Key Technology for Improving Safety in Nuclear Power Plant Management and Operation" has been initiated. The project is proposed in such a way that that its development is in line with the governmental energy policy, particularly with respect to safe operation of existing nuclear power plants. Overall, the goal of the project is aimed at:

- (1) Assuring the operational safety of each operating power plant during its design life, and maintaining a stable supply of domestically produced energy;
- (2) Effectively preventing the complex-type severe accidents from occurring by enhancing the safety features and self-defensive capability for each operating plant, and
- (3) Studying and formulating an effective radiation protection measure against severe accidents, through which the impact on the environment will be minimized.





- Power Ascension Test Histogram during implementation of Stretch Power Uprate for Kuosheng Unit 1
- Proceeding with the Functional Test by Installing the Hot Leg Welding Equipment on the Mockup Facility



Product and Technology Presentation for SCS-2000 Safety Control System by Taiwan Nuclear Instrumentation & Control System Company



Cask Measurement Simulation and Background Measurement

II. Research on Environmental and Energy Technologies

With the enormous consumption of fossil fuel, released toxic materials and emitted carbon dioxide pollute the environment and deteriorate the global warming. To meet the double considerations of less dependence on fossil fuels and of environmental protection, the technological developments of energy saving, new and renewable energy have become an imminent issue. In addition to the research and development of nuclear related technologies, INER has actively thrown itself into technologies of energy saving, new and renewable energy, including environmental plasma, photovoltaic system, solid oxide fuel cell (SOFC) power system, clean carbon, microgrid, wind power, cellulosic ethanol mass production, and assessment of energy, technology, industrial policy. Fruitful results of relevant studies mentioned above have provided the green industrial technology development of Taiwan with substantial benefits in recent years.

The main features and results of the fiscal year of 2013 are summarized as follows: firstly, in the aspect of environmental plasma technologies of energy saving, INER utilized the key plasma technologies to produce the following merchandises and effectively applied the research outcomes to the civilian applications and energy saving. For example: insulating window film with low emissivity, electrochromic (EC) film for regulating light transmission, flexible thin film solar cells powered by low illumination, and roll-to-roll thin film. Secondly, the development of photovoltaic technologies, the efficiency of HCPV micro-module and polymer solar cell reached the international level, i.e., 34.43% and 9.6%, respectively. In addition, the efficiency of CZTS solar cell made by selenization of e-beam evaporated precursors reached 5%, and also CPC Corporation had consigned INER to develop the sputteringrelated CZTS solar cell process. As to the development of SOFC technology, which is one of the most highlighting developments of INER, the output power of INER's stack cell reached 384.3 W. With regard to the conventional ceramic cells, relevant patent rights of the fabrication process of ceramic substrate membrane electrode assembly had been empowered to domestic company (Leatec). A kilowatt grade prototype SOFC power system was built up in the China Steel Corporation and accomplished a 500hour trial test with all the BOP components functioned normally. About the development of clean carbon technologies, the key point was to establish an integrated test facility for demonstration, to showcase the practical capability of INER, and to continuously develop technologies of CO₂ capture for high performance and low cost. Concerning the development of microgrid technology, besides establishing the 100kW grade microgrid test field, INER had enthusiastically studied the technologies of electrical integration engineering, electrical- and electronic-related energy, intelligent control, and energy management, to elevate the electricity quality, stability, and reliability of regional grid, and to reach the goal of cultivating the technology capacity of establishing self-controlled microgrid. For the development of wind turbine technology, via technique services and technology transfer, INER had assisted domestic small scale wind turbine vendors to create the technology capability of design and assessment. Moreover, INER had effectively helped local companies pass the rigorous international gualification and certification, and benefited Taiwan's products of the small scale wind turbine to become internationalization. In relation to the development of the mass production technology for cellulosic ethanol, The process developed by INER can produce about 220~250 liter ethanol from one ton dry bagasse. The yield is at the same level to that of the international. Lastly, the capability establishment and assessment for energy technology and industrial policy, the main accomplishment was to apply MARKAL-ED model with different scenarios to various electricity demand, accordingly to analyze the cost of electricity generation and CO₂ emissions, and to make suggestions to government in order to achieve the policy goal of renewable energy development and carbon reduction.

1

Development and Applications of Plasma Technologies in the Green Energy-saving Environment

Green energy-saving environmental concept is the main basis to plan in this project. Continuing to promote the environment-friendly core plasma technologies and using them to develop a series of energy-saving films with light weight and flexibility are always conducting, including thermal insulation film with low- emissivity, electrochromic film regulating light transmission, and silicon thin-film photovoltaic powered feasibly by low illumination. In addition, a key component with a rather good thermal conduction developed for transferring the sun heat collected by film focus. Those are effectively used in civilian applications in green energy-saving products, creating the new industries of the next generation. Several feature achievements are as follows:

1-1 Low-emissivity Energy-saving Film with High Visibility

According to the U.S. Department of Energy, 25~35% of energy waste in buildings is due to inefficient windows. So, to improve the existing buildings to save energy, the easiest way is to stick directly a thermal insulation film on the window glass. The general thermal insulation film blocks vision, so one kind of insulation films based on nano-particle properties came into being where there is a better light penetration, but most of the heat is absorbed within the film to make itself temperature rise. Then the heat from high temperature film in the form of radiation released into the room. Those detract performance of thermal insulation. Top high-level thermal insulation film, in addition to maintaining a high clear vision, reflects directly infrared light to the outdoor instead of absorption to avoid the secondary heat radiation. However, all commercial low-emissivity (Low-E) films with high performance currently come from foreign country and very expensive. Institute of Nuclear Energy Research (INER) has developed the roll-to-roll plasma deposition technology for the low-E coatings on flexible substrates with 60 cm in width. At the film transmittance of 70 % for visible light, the reflectance is still as high as 80 % for infrared radiation. This film emissivity is quiet low as 0.15 and the solar heat gain coefficient (SHGC) is 0.35, which indicated that it has a strong capability to reduce solar heat through it.

These films were assembled as two types of energy-saving windows, including 800mm×1200mm glazing with a low-E film and double glasses with suspended low-E film, and both of them exhibit at the Taipei International Invention Show and Trade in 2013. The visitors can touch the great articles personally to sense its insulated heat efficiency and high visibility. In addition, another achievement of promotion is that INER signed a technological pre-research contract to develop high quality Low-E films with Taiwan's largest manufacturer which produces traditional insulated heat films. It means that INER can instantly take a big step forward extending plasma coating technology using industry-scale roll-to-roll system for the high-end flexible energy-saving film.



Optical Spectrum of High Efficiency Low-E Film





1-2 Electrochromic Film Regulating Light transmission

Windows are always the point to the building design. Apparently, they serve as a bridge for visual field, but also open the path of heat penetration accompanied with light transmission. Air condition and lighting are the substantial energy consumption in buildings. Conventionally, curtains, external shades or some special structure systems are considered to employ, which complicate the building design and limit the view area. INER has been adequately applying the core plasma technologies to further develop the energy-saving electrochromic (EC) devices, where transitions between clear and variable tint control the amount of light and heat entering building. The 300mmX300mm EC module equipped with the plasma coated WO₃ and NiO film has been assembled. Its optical variation 40% (visible light transmission from 70% to 30%) under the driving voltage of 2.4 volt was verified. By rough estimation, if EC films are capable of applying in buildings extensively, air-condition of 23% during the period of peak load as well as consumption of 20% are able to be reduced significantly. Hence, the air condition systems of buildings could be scale-down to have the lower costs in years. Therefore, the EC films are likely to be a smart building material suitable for a comfortable as well as energy-saving environment.









1-3 Flexible Thin Film Solar Cells Powered by Low Illumination

In situations where people perform various activities, there is always some form of light. Photovoltaic devices collect the ambient energy (such as lights) that exists around people and convert it into electrical energy to provide with the energy-recycling function. Amorphous silicon solar cells on rigid and heavy glasses are the most common form of photovoltaic device, while INER is further developing flexible photovoltaic device using thin, lightweight, and unbreakable stainless steel substrates. The flexible photovoltaic device is less dependent on the angle of incident lights but higher power generation even from an extremely weak indoor light, which developed at INER by optimizing the combination of materials and the processing conditions. By high-tech roll-to-roll (R2R) plasma coating technology, the 1,500mm x 900mm 21 watt flexible solar module, typically, has been already developed. This solar module under a 50 watt white light-emitting diode (LED) light had successfully driven the electric fan, which provided a concept of energy recycling. Due to lightweight and flexible characteristics, it is good for applications of building materials. Therefore, it is eligible to combine the three elements, energy saving, electric generation, and artistry altogether into energy-saving building materials with the green-living atmosphere.

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▲ The Illustration of Thin, Lightweight and Flexible Thin Film Solar Cells Generating Electricity by LED Light and the Demonstration of 1,500mm x 900mm 21 Watt Flexible Solar Cell Module

1-4 A Novel Two Phase Thermosyphon with Bidirectional Heat Transport Ability

Two-phase thermosyphon is also called gravity heat pipe and with no capillary inside. Because its structure is simple and cost is low, it is usually designed for various applications. It could transfer heat under natural circulations, and hence simplify the complexity of traditional forced circulation with driving pump. Its applications include waste heat recovery, thermal energy system, solar heat collector, air conditioning, cooling for nuclear reactors and electronic devices. For a classical two-phase thermosyphon, the liquid in the evaporator absorbs heat to boiling point and evaporates. Because the density of high temperature gas is low and the induced buoyancy drives the high temperature bubbles flow upward, and natural convection happens. When the high temperature bubbles flow and transfer heat upwardly, the low temperature liquid flows downwardly and supplements the space. However, the traditional two-phase thermosyphon could only transfer heat upward and not downward, so its applications are limited. For the example of thermosyphon solar heat collector, the location of hot water storage tank has to be higher than collector. So, the solar irradiation to the solar heat collector is sheltered by the hot water storage tank and the heating time at day time is shortened. Besides, the highly energy consuming facility such as boiler and furnace, which have exhaust with abound waste heat on the top of bodies. Thus, INER develops a novel two-phase thermosyphon called reverse thermosyphon, which is a bi-directional heat



▲ The Scheme and Prototype Photograph of Reverse Thermosyphon Loop


transfer device and could not only transfer heat upward but also downward. When the liquid working fluid in the heating tube absorbs heat and evaporates, the saturated vapor accumulates in the buffer tank and generates pressure difference for driving the working fluid circulation. So, it could transfer heat downward spontaneously without additional pump, and be suitable for the applications with heat source at top and heat sink at bottom. When the prototype of reverse thermosyphon is filled with methanol and heat input power is 1 kW, the saturated vapor temperature is 106 °C, the thermal resistance is 0.009 °C/W and the downward heat transferring distance is 1.5 m.

1-5 An Innovative Large-Area Plasma Source

VHF (very high frequency) PECVD is an essential equipment for the manufacturing of high efficiency HIT (heterojunction with intrinsic thin layer) and silicon thin film solar cell because it possesses the characteristics of higher deposition rate and better film quality. To reduce the production cost by improving the production throughput, however, it is also necessary to increase the electrode size. Unfortunately, the combination of higher frequency and larger electrode would result in a more substantial standing wave effect, which would impose limitation on deposition uniformity.

An innovative technique, based on the idea of superposing two standing waves that are 90° out of phase both in time and space, is proposed to address the above-mentioned issue. The feasibility of the proposed technique has been successfully verified via numerical simulation and experimental tests. A double-sided discharge reactor schematically illustrated in the left Figure below was adopted for experimental demonstration. A metal rod with diameter of 1 cm and length of 54 cm, serving as the powered electrode, was placed in the middle of two grounded metal plates. The discharge gaps for the upper and lower discharge regions were both 1.7 cm. Two 80 MHz power supplies, synchronized via CEX (common exciter) interface to control the phase difference between their output signals, were designed to generate two specific standing waves that are spatially out of phase by 90°. As can be clearly seen in Figures (a) and (b), the discharge gap is just partially covered by plasma and the non-uniformity is as high as ±100% when only one standing wave is applied. Nevertheless, the non-uniformity of plasma discharge can be effectively improved, once the center-peaked and edge-peaked standing waves are launched at the same time (see Figure (c)). With the proposed technique, VHF plasmas with nonuniformity $<\pm 10\%$, meeting the requirement for thin film silicon solar cell industry, can be achieved over the typical operating windows of pressure (0.1-2 Torr) and power density (0.01-0.08 W/cm²) for the deposition of a-Si:H thin film.



▲ Schematic diagram of experimental setup

 Photos of plasma discharge obtained with (a) the first power source, (b) the second power source and (c) their superposition To meet industry requirements, the high performance plasma reactor with large area, high frequency and high uniformity has been conducting and makes the preliminary breakthrough, and the energysaving films, in the future, the efforts are towards integrating multiple functional films into one unit, such as the silicon photovoltaic film combines electrochromic film as one flexible intelligent energy-saving device, particularly suitable for both comforts and energy-saving at home living. Since a roll to roll plasma coating system is required for flexible multilayer nanometer-film depositions, a rather high technology threshold, and very few company has this capability in the world. INER possesses such a potential and would be to verify shortly to make a contribution to the local industry.

Development of Solar Photovoltaic Technology

"Development of solar photovoltaic technology" project is devoted to the R&D of solar photovoltaic technologies, and its goal is to develop high efficiency, low cost solar cell/solar photovoltaic system, and further assist the establishment of local PV relevant industries with international competitiveness. This project includes (1) technological development of high concentration photovoltaic (HCPV) system, (2) technological development of polymer solar cell, (3) technological development of upgraded metallurgical grade (UMG) silicon solar cell, and (4) technological development of copper zinc tin sulfide (CZTS) solar cell.

2-1 R&D Achievement of HCPV System Technology

2

INER has developed the HCPV system technologies since 2003, including epitaxial and fabricating processes of III-V solar cells, manufacturing process of concentration solar modules, manufacturing of solar trackers, establishment of system monitoring and integration, and qualification of solar modules, etc. The accomplishments are: 91 patents acquired, 14 items of technology transferred, and 46 items of technical services provided till the end of 2013. INER has effectively integrated the upstream, middle-stream, and down-stream of domestic industry to reduce the system cost, and to promote the industrialization of HCPV. The R&D achievements of INER HCPV technologies are listed as follows:

- (1) For the III-V semiconductor solar cell project conducted in year 2013, we have completed the important goals as shown in the following: the establishment of epitaxial growth technique of metamorphic InGaAs material, AlInGaAs material, GaInP material and AlGaInP material; and, the technique development of epitaxial growth and device fabrication for the metamorphic InGaAs/Ge dual-junction solar cells, the metamorphic AlInGaAs/Ge dual-junction solar cells, the metamorphic GaInP/Ge dual-junction solar cells, the metamorphic AlGaInP/Ge dual-junction solar cells, and the metamorphic GaInP/InGaAs/Ge triple-junction solar cells. In addition, an energy conversion efficiency of 40.6% under 131-sun illumination has been obtained from the completed metamorphic GaInP/InGaAs/Ge triple-junction solar cell.
- (2) The height of mainstream HCPV module is larger than 200mm. For HCPV micro-module design and prototype fabrication at INER, we use 0.6mm×0.6mm micro-cell and 20mm×20mm convex lens to reduce module height to 60~80mm. The efficiency of prototype module is 33.9% and 34.43%, respectively, from outdoor and indoor measurements. The associated patents are also applied. (The record of Semprius in 2013 is 35.5% under indoor measurement)



- (3) The developments of solar image tracking technology including a solar image position sensor, an image processing & tracking software, and a tracking controller design are accomplished and mainly used for HCPV solar tracker. By using the solar image position sensor and an image processing technique, the sun position could be precisely located for tracking controller to control the solar tracker as the weather was either sunny or cloudy so as to dramatically improve the sun tracking offset to less than ±0.1 degree. The experimental results show that the tracking bias angle is less than ±0.1 degree even as the direct normal irradiance (DNI) instantly drops to 66 W/m². This achievement is anticipated to raise the HCPV electricity and reach the best performance.
- (4) Through the intranet, virtual private network, firewall, and the internet, the integrated control and monitoring system is established, which integrates the external and internal INER built HCPV systems. Also, database synchronization technique is utilized to integrate the database of Lujhu HCPV system demonstration site, Longtan solar energy application and qualification site, and the 1.2 kW HCPV demonstration system at Pingtong Taipower South Visitors Center. The main goals are to online monitor each system, to reduce the risk of data loss, and to backup system database in different places.
- (5) Based on the requirement of UL, INER is executing technical service of "CPV & PV Outdoor Exposure Project". INER has built the outdoor solar module testing platform in HCPV demonstration Plant at Kaohsiung and National Taitung University to perform long-term outdoor exposure test with CPV and PV modules.



Outdoor Measurement Result of Micro-Module



2-2 R&D Achievement of Polymer Solar Cell Technology

Achievements of this project mainly include two parts: one is the research on high efficiency polymer solar cells (PSCs), and the other is the development of large-area PSCs commercial process.

The PCE of 9.6% of single cell has been achieved in the study of high efficiency PSCs, this performance is comparable with devices reported in previous literature (~9.2%). It reveals that we own advanced manufacturing technology of PSCs.

The other objective of this project is to develop the commercial technology of PSCs, and to promote the PSCs to industry. There are five accomplishments in this section. Firstly, we develop the commercial roll-to-roll process for continuous mass production, and we fabricate the flexible PSCs by using this technology. The flexible inverted PSCs consisting of P3HT and PC61BM was fabricated by slot-die coating process, and the PCE of 2.8% was achieved.

Secondly, we develop a spray technology to fabricate PSCs. An ultrasonic nozzle is used in the spray coating process to atomize the solution into small droplets at micro-scale, and then the droplets are

uniformly deposited on a substrate. The PCE of our sprayed PSCs consisting of P3HT and ICBA was 4%, and the device area can be enlarged to 100 cm².

Thirdly, we develop ITO-free PSCs by using ink-jet printing process. To lower the cost of PSCs, we used a hybrid electrode combining ink-jet printing silver grids with highly conductive PEDOT:PSS as an alternative to ITO electrode. The alternative hybrid electrode exhibits high transparency of 82% and low sheet resistance of 83.9 Ω /square. Moreover, we incorporated the ink-jet printing hybrid electrode with large-area spray process to fabricate ITO-free PSCs with a device area of 4 cm², and the PCE of 2.6% was achieved. This performance is superior to that of devices with the same device area reported in literature (1.54%).

Fourthly, we develop a fully solution-processed transparent PSCs. We replace thermally evaporated metal electrode with highly conductive PEDOT:PSS. PCE of the transparent PSCs is 2.9%, and it is comparable to devices based on thermally evaporated metal electrode. The manufacturing cost could be further reduced by using the printable solution-processed electrode.

Fifthly, we also improve the stability of PSCs by fabricating devices with inverted structure instead of conventional structure. We used ZnO layer to deposit on ITO electrode by replacing the acid PEDOT:PSS to reduce the corrosion of ITO. Moreover, we can improve the air stability of PSCs by using a high work-function metal electrode (silver) to replace the low work-function metal electrode (alumina). Less than 30% PCE reduction of the non-encapsulated inverted devices is obtained after holding in ambient condition for 8000 hours.

We exhibited prototypes of PSC fabricated by our developed commercial technology at PV Taiwan 2013 and NSC Achievements Exhibition. These results attracted broadly attention from the exhibitors including manufacturers and the masses.



▲ J-V Curve of High Efficiency Polymer Solar Cell



▲ Dynamic exhibits of solar house model integrated with the flexible solar cell, translucent awning, saving power windows and sun roof.



▲ Flexible polymer solar cells fabricated by commercial slot-die coating technology incorporated with roll-to-roll and continuous process.

2-3 R&D Achievement of UMG-Si Solar Cell Technology

The R&D of upgraded metallurgical grade (UMG) silicon solar cells aims to exploit thin film epitaxial silicon solar cell technologies that are considered potentially viable alternatives to low-cost, low efficiency amorphous silicon solar cells as well as high-cost, high-efficiency bulk crystalline silicon solar cells.

We have established the critical and related technologies of thin film epitaxial silicon solar cells to date. The main research achievements are as follows:

- (1) The ~20µm thick high quality epitaxial layer was deposited on top of the <5N purity UMG silicon substrate using the atmospheric chemical vapor deposition method. Based on the above technique, we successfully developed large-area (100cm²) thin film epitaxial solar cells with efficiencies up to 13.55%.
- (2) An innovative process of patterning and metallization on solar cells has been developed by INER. The essential point is to use an amorphous silicon layer which is deposited by PECVD on the front surface of n⁺-emitter, and then it is experienced by a laser annealing processing on a specific region to transfer to poly-silicon. The amorphous layer can serve as a mask for plating due to its high resistance even under illumination. In addition, it also provides for passivation function due to its wide band gap. When a high resistive amorphous layer is transferred to a low resist of poly-silicon, nickel film can be selectively plated on the low resistive region by light-induced nickel plating (LINP) process, so that the "patternization" process of front-electrode can be easily achieved. Moreover, we have shown the result of the solar cell in fill factor of 73.8%, which indicates the metallization process is viable.



The I-V Curve of The Thin Film Epitaxial Silicon/ UMG-Si Solar Cell

The OM & SEM images showed with nickel and copper plating (a) OM image on an a-Si layer after laser processing (b) OM image of the nickel film which formed by LINP (c) OM image of the copper electrode (d) SEM image of the Ni-Si interface (e) SEM image of the cross section after copper plating (f) SEM image of Ni-Si interface on a texture structure.



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2-4 R&D Achievement of CZTS Solar Cell Technology

The CZTS solar cell project in 2013 includes two parts. In the first half year, we focused on precursor process development. In the last half year, after the establishment of selenization equipment, we started to study the most important selenization process. The achievements are listed as follows:

- (1) In vacuum processes, devices made by selenization of e-beam evaporated precursors had reached conversion efficiency of 5%, those made by sputtered precursors had reached conversion efficiency of 3%, and those made by co-evaporation process had reached conversion efficiency of 3%
- (2) In non-vacuum process, devices made by selenization of sol-gel precursors had the highest conversion efficiency of 3%.
- (3) In industrial promotion, the Green Technology Research Institute, CPC Corporation entrusted us to develop vacuum CZTS processes.



In the future, we will actively devote to the development of high-efficiency and low-cost HCPV related technologies and cooperate with relevant local manufacturers to enhance their mass production capabilities; meanwhile, further develop the PSC module technology, and integrate the PSCs to create various advanced products. The promotion of UMG-Si solar cell R&D achievement will focus on the application of LINP and patternization of metal electrode processes, while the follow-on work of CZTS solar cell technology development will be directed to the simple, inexpensive and nontoxic processes. It is anticipated that the execution of this and the following related projects will be helpful for the development of domestic solar cell technologies and the establishment of local solar energy industries.

3

Development of High Temperature Fuel Cell Power Generating Technology and System Development and Application

In compliance with the nation's policy on the development and applications of clean energy technology for energy saving and emission reduction, this project specifically devotes to the development and applications of the solid oxide fuel cell (SOFC) power generating technology. In 2013, the targets of the fourth year of the project were: (1) Design, testing and evaluation of the stack and system components for an 1-kW SOFC power system; (2) Performance improvement of the ceramic and metallic SOFC cells; (3) Enhancement of the conversion rate of fuel reformers as well as the durability of reforming catalysts. The achievements are listed as follows:

- An 18-cell stack, where INER's MEA was employed the first time for a long stack, was assembled and tested with a success. The open circuit voltage was 19.23 V (1.07 V/cell). At a stack voltage of 14.39 V, the power output reached 384.3 W.
- The main hot BOP components, burner, reformer, and heat exchangers were innovatively integrated into one and passed the functional tests. The tests indicated that the natural gas reforming conversion efficiency is above 97.5%, and the air in the cathode side can be heated up over 760°C.
- A kilowatt-grade prototype SOFC power system was set up at the China Steel Corporation and fulfilled a 500-hour testing run, while the power output was approximately 730 W and all BOP components functioned normally. The natural gas conversion efficiency in the reformer was above 98%.







Hot-BOP Integration Test Facility.1Image: colspan="2">Image: colspan="2">Image: colspan="2">Image: colspan="2">Image: colspan="2">Image: colspan="2">Image: colspan="2">Image: colspan="2">Image: colspan="2"Image: colspan="2"<

▲ Performance of the 18-Cell Stack with INER's Cells



▲ A kilowatt-grade SOFC system installed at the China Steel Corporation.

750

Fabrication processes for the conventional ceramic cells with nearly 100% production yield were well established. The first 18-cell-stack test was assembled and tested where the average power for each cell was above 21 W. A long-term durability testing has been carried out for over 10,000 hours with a degradation rate less than 1 %/khr. Innovative syntheses were conducted to produce new cathode materials SSC and SBSC for the intermediate temperature solid oxide fuel cell where its power density reached 652 mW/cm² at 800°C. The technical patents on the fabrication process of ceramic substrate membrane electrode assembly were initiated to authorize to Leatec Corp. The Contract for the patent authorization was officially signed on January 16, 2014.

1200



▲The Durability Testing of the Cell





 Technical patent authorization contract to the Leatec corp.

The metal-supported solid oxide fuel cell (MS-SOFC) by the atmospheric plasma spraying (APS) method owns recoverable characteristic after a proper heat treatment, where the cell voltage was able to recover to its initial value. Processing parameters for the induction coupled plasma (ICP) synthesized method were successfully settled to produce nano/micron scale SOFC powders. Compositions of the synthesized SSC and LSCM nano-powders were with high purity. The patent of "Solid Oxide Fuel Cell and Manufacture Method thereof" won the Silver Invention Award in the National Invention and Creation Competition of 2013 by the Ministry of Economic Affairs.



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▲ (a) The XRD Results of the As-synthesized and Heat Treated SSC and LSCM Powders Prepared by ICP Method (b) The High Resolution Image of As-synthesized LSCM Powder



▲(a) The Photograph of Sliver Invention Award of National Invention and Creation Award of 2013 (b) The Ceremony of National Invention and Creation Award

Novel catalysts and optimal operating conditions of experiment to effectively control steam reforming of methane were successfully developed. The high-temperature-resistant material with higher hardness, i.e., α -Al₂O₃, was employed as a support to produce Pt/CeO₂/ α -Al₂O₃ catalyst. The hydrogen concentration from methane reforming is able to reach 68% indicating a remarkable capability for producing hydrogen from the natural gas. The conversion efficiency is higher than 99% with excellent resistance to pulverization and carbon deposition over more than 4,000 hours of operation. Additionally, a new type of natural gas reforming catalyst for use with SOFC is being developed for large-scale power generation. The catalyst prepared using a two-step approach exhibits better catalyst reactivity and coking resistance. The results of XRD and TEM show that Pt particles apparently exist in a crystalline form and are evenly distributed on CeO₂ surfaces.



In this year, improvements have continuously been made for the development of the SOFC core technologies. The performance of the SOFC power system has been validated. A compacter design for substantial volume reduction and increase of the system efficiency is being under way.

In the future, emphasis will be placed on the breakthrough of key technologies, especially on the development of parts, components and materials. Efforts will be paid to the development and refinement for cells, sealants, coating materials, reforming catalysts, etc. Meanwhile, technology transfers and cooperative partnerships with industries will be conducted actively.

Development of Clean Carbon-based Energy Technologies

The guideline for sustainable energy policy has been inaugurated since June 5, 2008, which aims to develop "low-carbon economy," to fulfill the requirements for economic development, environmental protection and social justice. Subsequently, National Science Council (NSC) approved the national energy program (NEP) on June 9, 2009, which is devoted to R&D on energy policy, energy technologies, energy saving and carbon abatement, personnel training and expertise development, etc. The action represents one of the options to implement the said policy above.

This work focuses on the strategic planning of clean carbon-based energy technologies, from the viewpoints of both practical development and advanced research, which covers clean coal, carbon capture and reutilization, advanced gas separation/hydrogen production, etc. The aim is to develop carbon capture-ready processes for the need of sequestration, and advanced clean utilization technologies of carbonaceous fuel for the era of low-carbon economy in the future. The integrated program consists of two projects: (1) Commissioning of an integrated test facility for clean carbon system, which includes System Design and Optimization Technology, Warm/Hot Gas Separation and Clean-Up, and (2) Carbon Capture and Reutilization.

4-1 Development of Gasification Technology

4

The test facility of gasification has been in operation at 900°C, for undertaking performance testing. In addition, the gas analysis system has been built to analyze the outlet syngas from gasifier, and the concentrations of CO, CO₂, H₂, O₂ in syngas were preliminarily analyzed and calibrated. The effect of various operation temperatures on the composition of syngas will be carried out in the further work.

The poly-generation cases based on gasification are evaluated in the project, with methanol and electricity as the products. The effects of different gas turbine types on the system efficiency are discussed in the case studies. The total syngas flow rate from gasification island is kept constant, while the ratio of syngas delivered to power block and methanol synthetic unit is based on the specifications of two commercial gas turbines. The output of MHI M501G is larger, so the syngas flow rate needed for power block in MHI M501G case is higher than that for GE 7FB case. The ratio of syngas delivered to half to half in 7FB case, i.e., the amount of syngas for converting to methanol in the 7FB case is higher than the counterpart in M501 case. The net efficiency of M501G case is 43.5 % (HHV), and CO₂ emission is 366 t/h. Due to the fact that partial amount CO₂ is captured in the methanol synthetic unit, the lower CO₂ emission could be achieved in the 7FB case with the value of 265 t/h.



▲The Test Facility of Gasification

▲ Processes Flow Diagram of Poly-Generation Plant

4-2 Development of Gas Clean-up Technologies

The exhibited technology consists of two categories. The first one is advanced gas filtration technology in moving granular bed filter (MGBF). Development of the moving granular bed filter system was operated under the high-temperature of 500°C. In 2013, commissioning the hot model of threedimensional granular bed filter (GBF) with the sub-systems (filter granule supply device) is was finished to supply the high-temperature environment for experimental study under 500°C.

Secondly, warm-hot gas desulfurization (WHGD) with the porous metal-oxide is one of the pioneer technologies to control gas contaminant emission. In preliminary study, the metal-oxide materials of Fe₂O₃, ZnO, CuO, and Mn₂O₃ were evaluated for sulfur-capturing ability. Among them, Fe₂O₃-based sorbent shows the sulfur-capturing ability superior to others, and has been chosen for further study in WHGD field. In 2013, 10 multi-cycle tests for Fe₂O₃-based sorbent were finished. The results showed that the sulfur capacity was maintained in the range more than 80% of the initial value.

In the future, integrated tests will be executed in warm-hot gas clean-up. By developing two-stage granular filter system, which includes particulates removal in the first stage and sulfide removal in the second stage. When raw syngas passes throw this system, particulates and sulfide will be captured accordingly to obtain clean syngas. The domestic R&D ability on gas clean-up technologies will be improved by developing two-stage filter system, which can convert into multi-contaminant control system. The related technologies could be applied to catalysis, fluidized-bed combustion, oil-refining, semiconductor industry, etc.



▲The Multi-Cycle Desulfurization Performance of Fe₂O₃ Based Sorbent



Filter Granule Supply Device

4-3 Development of Medium-High Temperature Carbon Capture Technology

The aim of this study is to develop CaO-containing CO₂ sorbent in the medium-high temperature range (600~800°C). The CaO sorbent has been caught much more attentions than conventional ones due to its high CO₂ capture capacity, environmental benignity, low costs and wide operation temperature. In our previous work, Ca/Al LDH (layered-double hydroxides) sorbents have been synthesized and it showed better stability than commercial CaO as well as limestone. The goal of this year is to produce it from lab scale to pilot scale and study its performances for the CO₂ capture reaction. The kilogram-scale CO₂ sorbent fabrication system (fabricated by Institute of Nuclear Energy Research) contains heating, mixing, filtration, extruding, evaporation and transport units.

The stability of Ca/Al LDH CO₂ sorbent in 60 hours (40 cycles) fabricated by our fabrication system was compared with the literature. The results demonstrated that the stability of the sorbent fabricated in this study possessed a value of 93%, namely, 93% CO₂ capture capacity still remained as compared to the first cycles. Its stability was obviously superior to that of other synthetic CaO (88% in ~42 hours) and mineral limestone (56~64%) reported in the literature. Various shapes and diameters (100 μ m to 5 mm) of CO₂ sorbents can be produced by this fabrication system. It provides a simple method to massively produce CO₂ sorbents and significantly reduces the manufacturing cost. In the future, various types of CO₂ sorbent fabricated by this technique will be employed to fixed-bed and fluidized-bed reactors, for evaluating the capture capacity and long term stability of these sorbents. The goal is to gradually establish the key technology of CO₂ capture and eventually to commercialization.



▲ Kilogram Scale of CO₂ Sorbent Fabrication System Manufactured by INER



To comply with the domestic technology R&D policy, a feasibility study project on sustainable clean coal technologies has been undertaken at Institute of Nuclear Energy Research (INER) since 2005. This work represents the follow-up efforts for mitigating greenhouse gas emissions from the sustainable development viewpoints. It is expected that this strategic planning will establish the essential foundation for technologies needed to fulfill the policy of energy saving and carbon abatement.

Fossil fuel will remain as major energy supply for human society in this century; hence, clean utilization of carbonaceous fuel will be one of the key options to envisage the issues of carbon mitigation, environmental protection and energy security. This work focuses on the strategic planning of clean carbon-based energy technologies, from the viewpoints of both practical development and advanced research.

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5

Distributed Energy and Wind Power System Technology Development

As compared to traditional and centralized control of power system, the next generation of power system will be small-scale and decentralized control of dispersed generation produced by renewable energy. However, due to intermittent and uncertain characteristics, the high penetration of renewable power generation will cause dramatic impact to the operation stability of regional power system, and result in voltage and frequency fluctuation phenomenon. Dispersed generation (DG) and microgrid (MG) technology provide possible solutions to stabilize regional power system and to control penetration rate of renewable power generation up to 20 %. This technology can not only ensure national energy security but also brings development of national industry. INER is currently developing the low voltage microgrid technology as follows:

5-1 Integration Technology of Power System

We built the first hundred-kW-scale of microgrid test field in Taiwan and developed power monitoring and measurement system, which can display real time information of the power meters and record waveforms into the microgrid data bases. We designed multi-controllers for load banks to synchronously switch a cluster of resistive, inductive, rectified, and motor loads. The load interface software is developed and used to achieve dynamic load adjust. The weighting of each load is given to determine the critical loads so as to execute load shedding scheme via the interface. In addition, the reactive power compensation interface is designed to regulate the reactive power output for the 100 kVA energy storage system. Test results show that the reactive power of energy storage system is well controlled to increase power factor of the microgrid with various loads.





 \blacktriangle Power Monitoring and Measurement System of the Microgrid

▲Load Interface Software



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5-2 Power Electronics Technology

We designed a prototype of inverter hardware with voltage/frequency droop control. By setting voltage/frequency reference and droop coefficient, the output power of the inverters can be dispatched to share the microgrid loads. We developed a three-phase 15 kW grid-connected power converter with CanBus communication and low voltage ride through (LVRT) control. The lithium iron batteries were used as DC source of the converter. The batter management system was designed to maintain voltage balance for each battery. In order to verify the control performance of the converter, we conducted an experiment test in which a microgrid was converted from grid-connected to islanded operation. It is verified that the power converter is capable of ride through low voltage and to provide real and reactive power compensation. In addition, the voltage drop of the microgrid was significantly improved and quickly recovered within 4 cycles.



- ▲ Three-Phase 15 kW Grid-Connected Power Converter with Low Voltage Ride Through Control
- Microgrid Voltage and the Current of Power Converter Response to Transition from Grid Connect to Island Operation

5-3 Intelligent Control and Energy Management Technology

In order to promote microgrid technology to domestic houses, we implemented energy management and control system with a 5 kW bidirectional inverter and 20kWh batteries in a smart house. The energy management system can real time display the trend of power usage for every minutes and forecast renewable power generation in 5 minute ahead. The state of charge (SOC) of the batteries can be estimated by calculating the DC voltage of inverter. Based on the SOC limits, the charge/discharge rate of the inverter can be automatically set to perform peak shaving by the energy management and control system. In the future, the time-of-use electricity pricing will be taken into account in the energy management system, and the smart house microgrid will operate more cost effectiveness.



Energy Management and Control System of a Smart House Microgrid



▲ Peak Shaving Control by the Energy Management and Control System

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The development of microgrid technology allows distribution network to cope with more power generation from renewable energy. The microgrid technology can be widely implemented in the offshore island, remote communities, and small city to enhance the power quality, stability, and reliability of their regional grids. In the short term, the microgrid test field will be connected to an actual Taipower distribution feeder and complete the microgrid demonstration site for stable operation. We will cooperate with the industries, government, academic and research institutions to develop the innovation microgrid products and industries. Regarding the med-term and long-term benefits, the operation of this demo site can create business model for the microgrid industries in Taiwan. We hope that the widespread use of commercial microgrids will have advantage to increase energy independence, provide stable energy supply, and reduce carbon emissions.

5-4 Small Wind Turbine Design Evaluation Laboratory

Governments worldwide have been actively promoting usage of small wind turbine systems these years. Safety standards of small wind turbines have been continuously revised and issued associated with various incentive programs. The Bureau of Standards Metrology and Inspection (BSMI) in Taiwan also revised the design standards for small wind turbines, CNS 15176-2 and CNS 15176-2-1, in 2013. Specifically, CNS 15176-2-1 is for use of the small vertical axis wind turbine system.

The Institute of Nuclear Energy Research (INER) has been dedicated in the development of smalland-medium wind turbine systems since 2005, and the 25 kW and 150 kW wind turbine systems have been successfully developed since then. In 2008, INER initiated the program to develop the technique of design assessment in compliance with IEC 61400-1 & 2 standards and fulfilled the requirements in 2010. Then, the Small Wind Turbine Design Evaluation Laboratory (SWTDEL) was further established in 2012. After 7 months of review process by Taiwan Accreditation Foundation (TAF), the laboratory was accredited to ISO/IEC 17025 in July 2013 by TAF. With the assistance from INER, local companies such as Hi-VAWT Technology corp. and Delta Electronics Inc. also built up the technique of design assessment for small wind turbines in this time period. In particular, INER completed the design evaluation report for the small vertical axis wind turbine system (DS3000) designed by Hi-VAWT and applied for certification in Japan in 2012. A review committee was formed by the Japan Small Wind Turbines Association (JSWTA) and the primary reviewers were from ClassNK in Japan. After the completion of review process, DS3000 was certified by JSWTA in June 2013and this is also the first foreign small wind turbine has been certified in Japan.

In the future, SWTDEL of INER will continuously support BSMI in promoting the certification of small wind turbines. Furthermore, INER will also extend the related techniques to the application of large and offshore wind turbine systems.



▲ Certificate of SWTDEL

▲ Certificate of Hi-VAWT DS3000

6

Research and Development of the Mass Production Technology for Cellulosic Ethanol

The objective of this project is to develop cellulosic ethanol production technology according to national policy for promoting bioethanol, and to assist in developing domestic cellulosic ethanol and derived industries. Owing to the cellulosic ethanol is an emerging biomass energy conversion technology, it is necessary to set up a pilot plant as a large-scale research platform for validating the mass production process and reducing the risk in applying such technology to commercialization. In 2009, INER first completed the construction of a cellulosic ethanol pilot plant with the capacity of processing one ton feedstock per day, and it has been assigned to run the tests since 2010. The pilot plant is now become a major platform for developing cellulosic ethanol technology. It is used to validate the feasibility of production processes, test the bio-resources in scale-up performance, provide staff training and education promotion, and collaborate with industries or international organizations. Through the implementation of this project, it is expected to establish commercially applicable cellulosic ethanol technology for producing ethanol as transportation fuel from agricultural or forestry residues. Further benefits such as the development of low-carbon industries, energy diversification and reduction of carbon dioxide emission would also be achieved.



▲The One Ton Feedstock per Day Cellulosic Ethanol Pilot Plant in INER

Quite a few operating experiences and testing data had been accumulated after operating the one ton feedstock pilot plant in 2010~2013. The major accomplishments are as follow:

- Established steady operating capability of the whole plant. The pilot plant can now be continuously running for 2 weeks. It mainly adopts SSF bio-chemical process, but also can be operated with SSCF process.
- (2) Established featured cellulosic ethanol conversion process with international competitiveness. This project is the few that focused on developing the mass production technology for converting to ethanol from the globally most abundant lignocellulosic biomass – rice straw, and the plentiful residue in subtropical regions – sugar cane bagasse. Through continuous review and improvement of the main system equipment and facilities, one dry ton rice straw can be converted



Ethanol yield improved in each year.

to about 200 L ethanol at present increased from 150 L at the beginning, and one ton dry bagasse can produce about 220~250 L ethanol. The yield is on a par with that of international level.

- (3) Completed the rational layout and 3D model of a metric ton-scale plant based on SSF process. The net energy ratio (NER) of this plant is estimated to be at least 2.0, so that a cellulosic ethanol mass production process with energy benefit can be built.
- (4) Based on the results of the pilot plant's operations and the rational layout, factory equipment arrangement and operating schedules have been planned, so that to establish a basic design plan for a cellulosic ethanol plant with the capacity of processing 30 tons rice straw per day, and complete the plant's energy-benefit analysis and cost estimation. The necessary information about the required land, equipment, facilities, energy and materials for design and building a plant were estimated. They can then be the references for conducting detailed design of a verification plant or basic design of a scaled-up 1000 tons per day commercial plant.

The core technologies of the acid-catalyzed steam explosion pretreatment system developed by this project include:

- (1) Special continuous input-output transporting design for cellulosic raw materials, which can isolate the pressures between inner and outer reactor for feeding at ambient pressure into high-temperature and high-pressure vessel.
- (2) Special screw-blade design for conveying lignocellulosic biomass and mixing with acid solution completely.
- (3) A complete continuous feeding, preheating, metering-injection under high-temperature and highpressure condition, mixing, flash-explosion and discharging, and solid-liquid separating system.

This system has been validated for processing various lignocellulosic biomasses such as: rice straw, sugar cane bagasse, bamboo, and wood chips. The rice straw residues produced from the pilot plant's pretreatment system had been tested on enzymatic hydrolysis performance by a world famous company (Novozymes) and the result showed the efficiency of most residues at different operating conditions is above 80%, which passed the commercial threshold. The pretreatment technologies developed by this project have already been awarded 5 patents (I340192, I346723, I369944, I364427, and I392544) in Republic of China and 1 patent (8,080,128B2) in USA, and 4 patents and 9 patents are being applied in ROC and in south-east Asia, respectively.



Novozymes had evaluated the pretreated rice straw residues of INER.

The features and achievements of the bio-chemical process developed include:

- (1) The bio-chemical process' adaptability can be evaluated based on the composition of raw material. SSF process and SSCF process can both be used for converting lignocelluloses into ethanol, and which process should be chosen depends on the compositional characteristics of the raw material. For example, rice straw or bagasse contains about 20~25% xylose and about 30~40% cellulose. The xylose concentration is about 40~50 g/L in pretreated hydrolyzate and SSCF process is suitable to use. Wood chips contain about only 10~15% xylose and about 50~60% cellulose so that its xylose concentration is limited, and using SSF process should be proposed then.
- (2) With SSF or HSSF bio-chemical process, the mass production process is established, which can convert one dry ton rice straw into about 200 L ethanol. The ethanol yield can be maintained above 65% (i.e., enzymatic hydrolysis efficiency >70%, glucose fermentation efficiency >90%). Enzyme loading is the major factor in choosing hybrid SSF/SSCF, or traditional SSF/SSCF process. It will depend on the enzyme cost at that time. The hybrid process combining with pre-hydrolysis could reduce about 1/3 enzyme loading, but may relatively need more inoculated yeasts and longer reaction time.

The features and achievements of the fermentation strains developed include:

- (1) The developed co-fermentation yeast had been tested in the hydrolyzate from pretreating various lignocellulosic biomasses, and the results showed xylose utilization rates kept above 1.0 g/L/h and ethanol yields were around 0.33~0.4 g/g.
- (2) As an international collaboration, a foreign company had provided its pretreated hydrolyzate for testing the capability of Y15 co-fermentation yeast developed by this project. The test result showed the fermentation capability of Y15 has reached the international leading standard.

 Co-fermentation Test with the Corn Stover Hydrolyzate



(3) In response to the coming SSCF process tests in the pilot plant, scale-up and scale-down experiments had first been carried out alternatively in 5L and 100L fermentors. Experimental results showed the inoculated yeast must be more than 1 g dry cell weight/L and aeration rate is controlled at 0.03~0.05 vvm for overcoming the effect of inhibitors. Scale-up tests of the co-fermentation yeast with actual hydrolyzate were then implemented in 5L, 100L, and ton-scale fermentors, and results showed the total sugar (xylose + glucose) conversion efficiency could be kept steadily at 80~90%, and the utilization rate could be maintained around 2.6~2.9 g/l/h. This means the developed co-fermentation yeast can maintain its capability on the pilot plant's fermentation facility.

Currently, the activity of the on-site produced enzyme has reached 20 FPU/mL, which is also about the international leading level compared with the published data in academic journals. The use of rice straw as induced carbon source to produce enzyme is innovative, and has been awarded an invention patent (I408231) in ROC. A metric ton-scale on-site enzyme production technology with technology-transfer potential was established in 2013; and it increases the enzyme activity of the crude extract and then reduces the enzyme cost for producing cellulosic ethanol. Present assessment shows the cost of the on-site produced enzyme is about NT\$8.4/L, which has already possessed quite competitiveness.



However, the activity of β -glucosidase among enzyme's composition still needs to be increased, and the engineering scale-up technology for on-site production also needs to be improved.

Study of the energy and resources integration is practiced in coordination with the pilot plant's operations and aided with simulation and analysis technologies, so that the basic information created should be quite feasible. Its major accomplishments include:

- (1) Mass and energy balances for SSF and SSCF bio-chemical processes have been completed, and a comprehensive calculation model for a whole cellulosic ethanol plant is then constructed. It has combined the lignin residue with anaerobic treated wastewater for recovering energy by cogeneration. The whole model is built on commercial software and has deleted negligible trace constituents without affecting the accuracy to increase its performance.
- (2) Applied energy conservation measures and heat integration of a cellulosic ethanol verification plant, so that the energy content of the product could be higher than the energy consumed for production (i.e., NER>1). After using waste heat to preheat feedstocks in the pretreatment and distillation systems, steam consumptions have been actually decreased 10% and 8%, respectively. Fed-batch SSF process has been developed, and the reaction time for hydrolysis and fermentation decreased from 60 hours to 48 hours and the electricity consumption reduced 20%. Applying the mass and energy balance calculation platform and the pinch analysis technique to design energy conservation measures such as heat recovery from steam explosion and reboiler equipment may decrease about 20% of the total steam consumptions, using blower for fermentors' aeration could save about 15% of the electricity for compressor, recovering the wastes from manufacturing process for cogeneration, and using absorption chiller. The NER of the rice straw conversion process could be increased from 0.43 if none of the measure was used to 4.61 if applying all the designed energy conservation measures. The NER would be more than 5 if bagasse is used as the raw material.

Raw material	Measure	Consumptions		Generated by CHP		Net input	Output	NED
		electricity(kWh)	steam(kg)	electricity(kWh)	steam(kg)	(MJ)	Ethanol(MJ)	INER
Rice straw	None	902.0	2350.8	0	0	9288.9	3986.1	0.43
	Process integration	902.0	1524	0	0	7164.0	3986.1	0.56
	Lignin for CHP	902.0	1524	-127	-1358	3216. 8	3986.1	1.24
	All wastes for CHP	902.0	1524	-662	-1524	864. 2	398 6.1	4.61
Bagasse	None	902.0	2350.8	0	0	9288.9	4453.3	0.48
	Process integration	902.0	1524	0	0	7164.0	4453.3	0.62
	Lignin for CHP	902.0	1524	-127	-1358	3216. 8	4453.3	1.38
	All wastes for CHP	902.0	1524	-662	-1524	864. 2	4453.3	5.15

NER of the Conversion Process with V	/arious Energy Conservation Measures
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Research and development of cellulosic ethanol technology has come to the pre-commercial stage. To advance to build the cellulosic ethanol plant with an existing relevant factory as a co-construction mode at present is the first priority promoting strategy for developing such industry. Scale-up engineering will subsequently be the bottle-neck for this technology to be commercialized. A pretreatment unit capable of feeding more than 100 tons per day can just be fit for the commercial cellulosic ethanol plant. Engineering design of large hydrolysis reactor and the robustness of the yeast in scale-up fermentation are the important subjects for further study. Thus engineering scale-up technology for cellulosic ethanol conversion should be aggressively developed to help industry walk across the death valley of commercialization, and build the benchmark cellulosic ethanol commercial plant then.

Capability Establishment and Assessment for Energy Technology Policy and Industrial Policy

7

.1 Taiwan Power Planning and CO₂ Mitigation Analysis - Zero Growth in Electricity Demand

Following the global GHGs mitigation trend, Taiwan government has set ambitious CO₂ reduction target. From the aspects of power supply and demand, feasible carbon reduction measures include the reduction of electricity demand, the development of renewable energy, and the adjustment of power generation mix. In this study, we analyze the cost of electricity generation and CO₂ emissions in Taiwan during 2010 to 2050 by MARKAL-ED model with different scenarios based on excluding CCS power plants and zero growth in electricity demand. The feasibility of the government's CO₂ reduction target has also been assessed. It is both important and beneficial to perform power planning analysis in order to make the resources allocation of government as cost-effective as possible and to reach the mitigation target.

The analytic result implicates that the usage of nuclear power can reduce the cost of electricity generation and CO₂ emissions in 2025. Extensive application of renewables makes the cost of electricity generation increase by 13.2% due to the high cost of renewables, but emissions could only be reduced by 6.2%. In 2050, generation costs of renewables are approximate to those of fossil fuels. The massive usage of renewables could reduce emissions by 19.8%, so the cost-effectiveness of emissions reduction becomes obvious in the long term. In consequence, it is feasible to reduce both the generation cost and CO₂ emissions by using low-carbon fuels such as nuclear and natural gas in the mid-term (2025). These low-carbon fuels are suitable for transition to the system of high share renewables. However, compared with the government's CO₂ reduction target, the gap would still exist although the electricity system in Taiwan satisfies the assumptions including zero growth in electricity demand, lifetime extension of existing nuclear power plants, operating the Nuke4 as scheduled, and maximizing the utilization of renewable energy and gas-fired plants.

In summary, based on the scenario assumptions in this study, the ambitious CO₂ reduction target could hardly be achieved. Furthermore, ambitious target might cause unaffordable economic impact. It is recommended that the government might consider adjusting the target. Otherwise, in order to reach the ambitious target, it is necessary to further enlarge renewable policy objectives, to develop CCS power plants or more nuclear plants, or to reduce total electricity demand further.

7-2 Estimation of Price Elasticities for MARKAL-ED Model-Evidence from Taiwan

The price elasticity of energy service demand is a set of critical parameters in MARKAL-ED model. Due to variations of national geographic, socio-economic backgrounds, the principle of the price elasticity setting requires to consider the difference between the region, countries, and various energy service demands. If the price elasticity of energy service demand was overvalued, it may overestimate the effect of government price policies (e.g. energy tax policy), and then it would be too optimistic to look the reduction from of greenhouse gas emissions contributed by the demand side. In contrary, if the price elasticity was undervalued, it may underestimate the energy saving contribution of energy demand side to carbon policy, and then energy policy will be oriented toward energy-supply side, such as CCS, renewables, nuclear power plants. This paper applies the local energy statistic data to estimate the



price elasticities of energy service demand for different sectors in Taiwan. The reasonable parameters are helpful for the localization of MARKAL-ED model; furthermore, it makes the policy evaluation more realistic.

We suggest the elasticity for other appliances should be relatively small, around -0.12, because that top priorities of demand reduction is cooling or lighting rather than other appliances in Taiwan. The price elasticities for commercial sector are lower than that in the UK MARKAL model, which range around -0.32. For transport sector, we observe that the estimated elasticity for motorcycle is 0.09 which is different from the parameter -0.41 assumed by UK MARKAL. The positive elasticity represents the rising price of gasoline could increase the energy service demand of motorcycle. This exactly reflects the unique fact that the citizens in Taiwan are heavy reliance on motorcycle in their daily life. For the industry demands, we find the price elasticities of Taiwan's industry are smaller. If we explore the reasonableness of price elasticities based on the differences of national industry structure, we can interpret that the export value ratio of GDP in UK(32%) is smaller than Taiwan(74.5%). It reflects the export-oriented economic characteristics of Taiwan differ from the domestic demand-oriented economics of United Kingdom.

	202	25	2050			
Scenario*	Generation Cost (2010 USD/kWh)	Emission Level Compared with 2010 Historic Data (%)	Generation Cost (2010 USD/kWh)	Emission Level Compared with 2010 Historic Data (%)		
N ₀ R ₁	0.096	-5.5	0.120	-52.3		
N ₁ R ₁	0.089	-9.8	0.109	-56.5		
N_2R_1	0.077	-16.8	0.108	-56.7		
N_0R_2	0.082	+9.2	0.119	-31.9		
N_1R_2	0.076	+3.5	0.111	-36.9		
N_2R_2	0.068	-10.6	0.110	-36.9		

Costs of Electricity Generation and CO₂ Emissions of All Scenarios

* [1] N0 (No life extension of existing plants & Nuke4 will not operate)

N1 (No life extension of existing plants & Nuke4 will operate as scheduled)

N2 (Life extension of existing plants & Nuke4 will operate as scheduled)

R1 (Renewables capacities meet policy objectives & give priority to nuclear and gas-fired plants & the annual amount of LNG imports is limited)

R2 (Renewables capacities keep in 2010 levels & building new coal-fired plants is prohibited & the annual amount of LNG imports is unlimited)

[2] The existing nuclear plants will have been phased out by 2025. Lifetime extension of existing plants will be ceased by 2045. The Nuke4 is the only concern when we discuss the influence of nuclear power in 2050.

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		Our Study		UCL	UKERC	Suggestion
Sector	Demand/industry	Short Term	Long Term	(2010)	(2009)	Values
	Lighting	-0.33	-0.51	-0.31	-0.31	-0.33
	Space cooling and heating	-0.39	-0.71	-0.31	-0.31	-0.39
Desidential	Refrigeration	-0.30	-0.53	-0.31	-0.31	-0.30
Residential	Cooking	-0.28	-0.45	-0.33	N/A	-0.28
	Water heating	-0.39	-0.53	-0.34	-0.34	-0.39
	Others ¹	-0.12	-0.12	-0.31	-0.31	-0.12
	Space cooling and heating	-0.38	-0.38	-0.32	-0.32	-0.38
Services	Lighting	-0.42	-0.55	-0.32	-0.32	-0.42
	Others ²	-0.42	-0.65	-0.32	-0.32	-0.42
	Car	-0.01	-0.34	-0.54	-0.54	-0.34
	Bus	-0.05	-0.18	-0.38	-0.38	-0.18
	HGV	-0.31	-0.52	-0.61	-0.61	-0.52
Transport	LGV	-0.19	-0.32	-0.61	-0.61	-0.32
Transport	Rail	-0.04	-0.45	-0.24	-0.24	-0.45
	2-wheeler	-0.04	0.09	-0.41	-0.41	0.09
	Air	0.51	-0.36	-0.38	-0.38	-0.36
	Marine/shipping	-0.42	-1.29	-0.18	-0.18	-0.42
	Iron and Steel	0	-0.14	-0.35	-0.44	-0.14
	Non-Ferrous metals	-0.11	-0.15	-0.35	-0.44	-0.15
	Chemical/Chemical-material	-0.20	-0.38	-0.50	-0.49	-0.38
In duate of	Pulp-paper	-0.21	-0.22	-0.15	-0.37	-0.22
and others	Electronics and Electrics	0	-0.14	-0.15	-0.32	-0.14
	Other industry for electricity	0	-0.15			-0.15
	Other industry for heating	-0.19	-0.24			-0.24
	Non-energy sector	-0.25	-0.25	-0.15	N/A	-0.25
	Combined agriculture	-0.12	-0.62	-0.32	-0.32	-0.12

Price Elasticities of Energy Service Demands

Source: (1) William and Neil(UCL) (2010) UK MARKAL Modelling - Examining Decarbonisation Pathways in the 2020s on the Way to Meeting the 2050 Emissions Target - Final Report for the Committee on Climate Change

(2) Anandarajah et al.(UKERC) (2009) Pathways to a Low Carbon Economy: Energy Systems Modelling-UKERC Energy 2050 Research Report 1

(3)INER's Data

¹ Other items of residential sector include "residential computer", "residential television", "other residential electric equipment". residential water use the elasticity of the cooking.

² Other items of service sector include "other service for electricity", "other service for fuel".



III. Radio-biomedical Research

In 2013, Radiation application group of INER focuses on:

- 1. Diagnostic Nuclear Medicine: (1) F-18 FDGalactose: Development of a radiofluorinated method from talose precursor was successful and would achieve the mCi scale. (2) Development of the Positron generator technology: establishment and evaluation of manufacture parameters for automated synthesis of radiopharmaceutical injection is expected to improve radioisotopic labeling techniques. (3) Dual function agent of imaging and therapy for colorectal cancer: application of novel micelles carrier would increase the accumulation of drug on tumor that is to improve effectiveness of image and inhibition of tumor. (4) Development of PLGA biodegradable and multifunctional microspheres: increasing the accumulation of diagnostic or therapeutic drug on interested area. (5) Tumor imaging agent: successful development of I-123 InerTA for imaging tumor cell proliferation. (6) Establishment of molecular modeling virtual screening platform: successfully discover the precursor of radiopharmaceutical imaging agents of central nerve system symptoms.
- 2. Targeted Therapeutic Nuclear Medicine: (1) Passive targeted therapeutic drug: phase 0 clinical trial of Re-188 liposome has been performed at Veteran General Hospital-Taipei. 14 subjects were completed this year. Physiological and biochemical results showed that it is safe in patients. (2) Active targeted therapeutic drug: Re-188 liposome-Fcy-hEGF/5-FC, possessing the bifunction of radiotherapy and chemotherapy, has more therapeutic potential in EGFR over-expressing tumor cells. (3) Radioembolization: the treatment of hepatoma with a new Re-188 MN-16ET/Lipiodol radiopharmaceutical has been confirmed from the biodistribution and therapeutic data in rat tumor model.
- **3. Service of Molecular Imaging Platform:** The main construction of the platform can provid radiation technology and molecular imaging services, more importantly, the platform collaborated with NRPB projects helps local institutes and universities for the development of novel drugs. With the assistance of this platform, the developing speed towards clinical trial could be accelerated.
- 4. Novel in Vitro Diagnostics (IVD): The effectiveness of Co-60 irradiated modification of IVD for EB virus, with features of rapid, easy to use and low detection limits, has been verified by analysis of 50 patient subjects' samples from Mackay Memorial Hospital.
- 5. High-end Medical Equipment and Bone Graft: Light, thin, low energy cost, and anti-interfere radiation diagnosis instrument would be developed to assist local companies with world-wide competitive ability. Furthermore, good biocompatibility of Co-60 irradiated nano-composite hydrogels of bone graft was verified.

In 2013, research achievements including 34 patents, 33 journal papers, 4 international conference papers, and 85 internal reports are very fruitful. The purpose of this research is to establish the commercial technology of nuclear medicine in Taiwan, and to maintain the health welfare of our countrymen.

The strategies of the new drug development for radiation application research are the establishment of precursor synthesis technology for clinical application, the development of key techniques at the various stages and the integration of professional resources from bench-top to bedside to develop potential diagnostic radiopharmaceuticals and valuable new drugs. This year we focused on the development of diagnostic drugs for hepatocellular carcinoma, lung cancer, neuroblastoma cell tumors and neurological diseases. In the future, the research and development is to actively promote not only the clinical application of the drugs, but also extend research directions toward more innovative drugs. For the medical equipment R&D team, a lot of effort was put into developing practical radiation application technologies, such as semiconductor-photosensor-based image detectors, physical models and algorithms of imaging system, and Co-60 irradiated medical devices. With the developed patentable technologies and the established platform for high-end medical device development, the aim is to cooperate with the existing/developing domestic industrial chain and achieve commercialization in the future.

Both the new drugs and medical equipment development of this project not only upgrade the nuclear medicine industry in Taiwan, but also safeguard the health of citizens. More importantly, to let the local biotechnolgy developments in Taiwan keep pace with the world.

Radiation Biomedical Research, Development and the Application

This project includes three sub-projects, which are "The research of isotope production development and application", "The research and development of new radiopharmaceuticals for cancer diagnosis and treatment assistance" and "Development of radiation-related biotechnologies and imaging technologies". The main goal of this project is to comprehensively develop new drugs, high-end medical equipments and other technologies, including the establishment of radioisotopes, generators, precursors, labeling, cell studies, animal studies and clinical trials. In 2013, research achievements were Sub-project I: "New positron molecular imaging agents", "The constructing of positron generator technology", "Manufacture of single photon imaging agent", "New single positron molecular imaging agents for nucleotides"; Sub-project II: "Dual function agent of imaging and therapy for colorectal cancer", "Development of PLGA biodegradable and multifunctional microspheres", "Creation of molecular modeling virtual screening platform", "Synthetic of BANI and DANI for novel hypoxia imaging agent"; Sub-project III: "A high sampling model for the DOI (Depth of interaction) correctionimproving quantitative accuracy in nuclear medicine imaging", "Establishment of the basis of a new imaging detector technology based on silicon photonic devices" and "Verification of biocompatibility of nano-composite hydrogels of artificial aggregates". The main outcomes and achievements in 2013 are described as follows.

1-1 The Research of Isotope Production Development and Application

The goal of the project is to develop radioisotope technologies in biomedical fields in order to be a pioneer of radio-pharmaceutical research and development. This year, the main objectives are (1) to develop and extend the technology of isotopes production via a high energy proton beam accelerator, (2) research on technology of radio-pharmaceutical automated process and modules, and (3) evaluations of cancer efficacy. In 2013, research achievements including, "new positron molecular imaging agents", "constructing the positron generator technology", "manufacture of new single positron molecular imaging agents for nucleotides ".

Development of new PET imaging agent

1

New molecular positron tomography (briefed as "PET molecule" below) produced from a mediumsized cyclotron is an application of nuclear reaction from high energy proton beam. This nuclear reaction produces positron emitting isotopes, which are taken as the key probe elements for the PET molecule



development. Therefore, in this project, the cyclotron proton beam is extended, as well as proton irradiation stations. By increasing proton irradiation stations, they are combined with the already-done target irradiation technology, and the F-18 ion produced is applied on the PET molecule development.

Two PET radiopharmaceutical licenses, INER Sodium Fluoride [F-18] Injection and INER Fludeoxyglucose [F-18] Injection, were achieved in the pastbesides, several F-18 PET molecules which are considerly interacting with phosphorylation of glucose enzyme, calcium ions, galactose phosphorylation, tyrosinase, enzyme thymidine, GST enzyme, galactose receptor and the enzyme TAU, respectively are under development.



A PET molecule research framework

Research achievements in 2013

- (1) Study of PET imaging agent for tumor: recently, [F-18] FDGalactose has attracted attention from both academia and research community nationwide. [F-18] FDGalactose is phosphorylated by galactose enzyme in vivo. This phosphorylation reaction rate could be imaged through PET. In Europe, the clinical trial has obtained a result that, the sensitivity on liver cancer reached 96% and specificity is 100%. As liver cancer has been one of the domestic common cancers, [F-18] FDGalactose could be in a great help with such specificity and sensitivity. The synthesis of precursor for [F-18] FDGalactose begins with tarot sugar, with elimination and addition of leaving group and protecting groups, plus a further replacement mechanism, high purity of the precursor and mCi scale of radioactivity.
- (2) Study of SPECT image agent for tumor: With academic cooperation, this precursor is further developed to produce [I-123] IOFA, a new single photon imaging molecule initiates with COX-2. It is proved to be visceral absorbable in animal model experiments, and the result has been published and discussed. Due to [I-123] IOFA imaging is based on the biochemical effect initiated between [I-123] IOFA and COX-2, it is believed that another new PET molecule is possible to be formed by changing the bonding of I-123 to I-124.

Method for automated formulation process for production of radiopharmaceutical injection medicine and evaluation thereof

To achieve automatic process and high yield of biotech drug of pharmaceutical industry is one of the important key aspects. This project focuses on building suitable parameters of automation system and assessment methods to assess the system for improving the quality and production efficiency of product.

One object of this invention is to provide a method for solving the problem due to uncontrolled pH value and isotonic solution. The other object of the present invention is to provide a method for solving the problem with uncontrolled percentage of impurities contained in radioactive dose.

Description of the Prior Art

In conventional way, an extracted radioactive dose was directly dispensed with saline or injection solvent without considering the pH value or the isotonic of injection dose, as a result, it will cause painful or uncomfortable for human body after receiving the injection.

Also, the radioactive dose is dispensed directly after the measurement of radioactivity without taking consideration of the contribution of impurities in the dose. Due to shorter period of half-life of impurities, the content of radiopharmaceutical injection dose may shift from its normal value. As a result, the insufficiency of the dose will be detected during calibration.



 Automatic Control Interface for Ga-68 Radiopharmaceuticals.



▲ Dispensing Module Ga-68 Radiopharmaceuticals.



Final Products from Automatic Dispensing equipment

▲ Lead Vessel for Radiopharmaceuticals.

Detailed Description of the Preferred Embodiment

For these two objects, a method of automated formulation process for production of radiopharmaceutical injection medicine and evaluation of the present invention comprises the following steps: a) preparation steps of process control and measurements of parameters; b) calculation of parameters for formulation control to obtain the volume of dispensing solvent and the pH value of finished product.

The present invention provides a new evaluation system, a parameter survey system, which can be used to calculate the contents of the radiopharmaceutical injection, such as thallous chloride [TI-201] (6mL). Here takes TICI [TI-201] as an example to present its novelty and productivity in the embodiment of the present invention. The pharmacy will maintain its stability and constant quality, and



in conformance to its physical and chemical property at isotonic state and pH value of 6.5. After the formulation of the pharmaceutical solvent being completed, the relative standard deviation (RSD%) is $\leq 1\%$ at calibration time.

The coefficient X is calculated by:

X=EXP (-(LN (2)/73.5), (Tc-Tm), wherein Tc is calibration time and Tm is measurement time.



Evaluation of radioiodinated InerTA as a proliferation imaging probe in a lung tumor xenografts

Lung cancer is the leading cause of cancer deaths in women and men throughout the world. Many different technologies have been and continue to be developed to image the structure and function of human body, such as computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, positron emission tomography (PET), and single photon emission computed tomography (SPECT). There are advantages and limitations for each with unique applications. The high-resolution CT and MRI are anatomic imaging techniques, but are hard to detect the small lesion in the early stage, due to the limitation in detection sensitivity. This drawback has been overcome through the use of PET and SPECT, which are frequently used in oncology as a functional and molecular imaging routine, both provide the information about the biological behavior of tumor cells such as metabolism, proliferation, and receptor density. One of important characteristics of malignancies is the uncontrolled rate of cell division. Accurate information of proliferation rate would be valuable for reflecting the response of chemotherapy or guiding optimal clinical management. Molecular imaging with a radiotracer that is proliferation specific would be valuable for tumor detection and, especially, in reflecting the tumor response to treatment. Radiolabeled thymidine analogs can be used to image cell proliferation in-vivo. This study aims to evaluate a novel radioiodinated thymidine analog, *InerTA, as a probe for imaging tumor in A549 lung carcinoma-bearing mouse model. *InerTA was labeled with I-123/I-131 and was prepared in high radiochemical yield (85%) and radiochemical purity (95%). Biological characterization studies of *InerTA including serum stability, cellular uptake and SPECT imaging were performed. The results indicated that the percentage of intact *InerTA in mouse serum after 24 h incubation was greater than 90%, demonstrating good in vitro stability of *InerTA. Besides, the accumulations of *InerTA in A549 cells increased with time. The percentage uptake of million cells of *InerTA reached 8.01 \pm 0.02 after 24 h incubation (see Figure). SPECT imaging of *InerTA in A549 lung carcinoma-bearing mouse clearly delineated the tumor lesion with increasing tumor-to-muscle ratio from 2.79 at 1 h post injection (see Figure). In this study, the radioiodinated *InerTA was successfully prepared with high yield and radiochemical purity. In addition, *InerTA was highly accumulated in the tumors and was demonstrated as a potential radio-probe for clinical tumor imaging.

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The SPECT image of mice bearing A549 lung carcinoma (deep blue circle) after injection of ¹²³I-InerTA.

▲ Cellular uptake of ¹²³I-InerTA in A549 lung cancer cells.

1-2 The Research and Development of New Radiopharmaceuticals for Cancer Diagnosis and Therapeutic Assistance

Cancer has been the leading death cause in Taiwan for many years. To develop the new therapeutic and diagnostic drug/method is quite important for improving the life quality of human beings. It's also an important medical application for atomic technology. Due to the characteristics of high permeability and retention effect (EPR), micelle is an attractive nano-carrier for the diagnosis and therapy of cancers. Human epidermal growth factor receptor 2 (HER2) participated in the proliferation of tumor cells. Afatinib, a HER2 inhibitor, was used to mix with DiR and encapsulate into micelle to establish afatinib-and DiR-encapsulated micelles as a dual-functional agent. The preliminary animal study showed the potential for colorectal cancer imaging and therapy.

In this year, we also established a new drug delivery system for cancer radiotherapy using a biodegradable PLGA microspheres consisting of diagnostic/therapeutic radionuclides. From the basic studies of manufacturing method of PLGA-microspheres to ¹¹¹InCl3 labeling methods, we obtained the high radiochemical purity of ¹¹¹In-PLGA-microspheres. The animal data confirmed that ¹¹¹In-PLGA-microspheres stably accumulated in the tumor site and only little radioactivity leaked out to the blood. It was supposed that the highly-uniformed PLGA-microspheres with isotope-labeling have a great potential to be applied in the hepatoma therapy.

BANI and DANI were new designed ligands which have the following characteristics: (1) nitroimidazole moiety shows high affinity to hypoxia area, (2) N2S2 donor: conjugate with technetium or rhenium through carboxylic acid. We suppose that BANI and DANI could be used as novel hypoxia imaging agents for clinical diagnosis. We will evaluate their potential in biological system. In 2013, we also applied molecular modeling virtual screening platform to find the precursor of radiopharmaceutical imaging agents for central nerve system symptoms. Several potential candidate compounds will be tested the pharmacological activity *in vitro*. This model could enhance the probability to find the lead compounds.

Dual function agent for colorectal cancer imaging and therapy: HER2 activation-inhibited afatinib micelles

Recently, polymeric nanoparticles (NPs) such as liposomes, nanogold particles, dendrimers, and micelles, are used as drug carriers in diagnostics and therapeutics of cancers due to the high permeability and retention effect (EPR), leading to increased drug accumulation and spreading into the tumor parenchyma. It has been reported that synthetic biocompatible polymer NPs can also prolong the



half-life of drugs in circulation coupled with reduction in rapid renal clearance of soluble proteins by reticuloendothelial system (RES). Therefore, antitumor drug-or fluorescent- encapsulated micelles can provide tumor-distributed imaging and increase therapeutic efficacy. Human epidermal growth factor receptor 2 (HER2) participated in the proliferation of tumor cells. Studies have indicated that afatinib can block HER2 activation, and hence reduce tumor growth consequently. In addition, it has been reported that the polymeric micelles, which possess the effects of enhanced permeability and retention (EPR), were used as drug carriers to improve the accumulation of drugs in tumor tissues for increasing therapeutic efficacy. First, the cytotoxicity effects of afatinib on HER2-overexpressed CRC cells and tumors were detected. The result revealed that afatinib can inhibit HER2-overexpressed CRC cells and tumors growth. We further used afatinib-encapsulated micelles for CRC tumor therapy. The result showed that afatinibencapsulated micelles significantly reduced tumor growth as compared to afatinib performed alone in HCT-15-induced tumor xenografts. Moreover, DiR-encapsulated micelles were used for CRC tumordistributed detection. The result presented that the fluorescent signaling was higher in tumors site of CRC mice than in control. In conclusion, afatinib can be used for therapy in HER2-overexpressed CRC cells and tumors. The afatinib- and DiR-encapsulated micelles can be used as a dual function agent in CRC imaging and therapy for improving clinical applications.



▲ Afatinib specifically inhibited HER2-overexpressed tumors. (A) Comparing with the cell viability of afatinib in various tumor cells. Colorectal cancer cell line (HCT-15), gastric cancer cell line (AGS) were HER2-overexpressed tumor cells. Gastric cancer cell line (MKN45) was HER2 -low expressed tumor cells. The result showed that afatinib significantly reduced cells growth in HER2-overepressed tumor cells. (B) The tumor growth inhibited effects of afatinib on HER2-overexpressed and -low expressed tumor tissues. The result indicated that afatinib can inhibit HER2-overexpressed tumor growth. **P< 0.05, versus control.



Schematic design of dual function agent for CRC imaging and therapy

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▲ Afatinib- and DiR- encapsulated polymeric mecelles increased the therapeutic efficacy and tumor distributed imaging in HER2 ovevexpressed CRC animals. (A) The cytotoxicity result indicated that afatinib-encapsulated micelles significantly reduced cells growth as compared to afatinib performance alone in HCT-15 cells. (B) The in vivo assay demonstrated that afatinib-encapsulated micelles can decrease tumor growth in HER2-ovexpressed CRC animals. (C) The tumor-distributed imaging of HER2-overexpressed CRC. The result presented that DiR-encapsulated micelles significantly increased tumor accumulation. The arrow indicated the tumor site. *p<0.05.

The development of biodegradable and multifunctional microspheres for the application in hepatocellular carcinomas treatment

PLGA (polylactic acid-glycolic acid) is a nontoxic, biodegradable and biocompatiable polymer. The PLGA microspheres were conjugated with DOTA for the labeling of In-111. SD rat with N1S1 hepatoma cell lines will be used as the animal model for pharmacokinetic and therapeutic evaluation via TAE (transarterial embolization) pathway.

In 2013, we established the manufacturing method for PLGA-microsphere which was in the range between 15±5µm 47±5µm. The surface of microspheres was identified by FTIR with the distribution of NH₂ functional group. The modified PLGA-microspheres were labeled with ¹¹¹In radionuclide. The radiochemical purity (RCP) of ¹¹¹In-PLGA- microspheres was more than 95% and kept stable for one week in serum. SD rat implanted N1S1 hepatoma cell line was used as our animal model to evaluate the targeting potential of ¹¹¹In-PLGA-microspheres via TAE. The Nano-SPECT/CT images and biodistribution data of SD rats obtained at 4, 24, 48 and 72 hr post-injected with ¹¹¹In-PLGA-microspheres demonstrated that most of radioactivity accumulated in the tumor and liver tissues. The data also showed that less than 0.1% (ID %/g) of radioactivity could be detected in blood sampling from tail veins at 24 hour post-injected with ¹¹¹In-PLGA-microspheres via TAE. The animal data confirmed that ¹¹¹In-PLGA-microspheres via TAE. The viame viame viame viame viame v

blood. We suppose that our highlyuniformed PLGA-microspheres with isotope labeling have great potential to be applied in the hepatoma therapy. In the future, we will develop Y-90 microsphere labeling technique and will conduct Y-90 microsphere efficacy evaluation in animal models to assess its biodistribution, pharmacokinetics and anti-tumor effect.



Animal model : N1-S1 induced HCC SD rats ; Injection way : Trans-arterial Embolization

▲ The nanoSPECT/CT images of ¹¹¹In-PLGA-Microspheres in SD rats implanted with N1S1 hepatoma



Molecular modeling virtual screening platform applied to find the precursor of radiopharmaceutical imaging agents for central nerve system symptoms

The Nobel Prize in chemistry 2013 was awarded to the scholars who studied molecular models and simulate chemical reaction processes using computing in silico. Computers are the same important as flasks for understanding chemical reaction nowadays because computer simulation visualizes the progressing of chemical reactions based on microscopic scale and predict the probability.

The population suffers from central nervous system (CNS) diseases including depression, Parkinson's disease, etc. is rising. Those symptoms come from improperly regulating of neurotransmitters such as dopamine, serotonine, and norepinephrine etc.. In order to survey the CNS patients early and accurately, it is necessary to develop imaging agents specifically binding with CNS regulator proteins for single photon emission computed tomography (SPECT) or positron emission tomography (PET). After we had figured out the three- dimensional structures for CNS transporter proteins for dopamine, serotonine, and norepinephrine (the amino acid sequencies were acquired from UniProt website: http://www.uniprot. org) by means of molecular modeling in silico and biomolecule simulating software-- Discovery Studio (DS), we virtually screened the suitability of complexes between ligands structures (from data banks for natural products and synthesis sources) and the key proteins that cause CNS symptoms: calculating free energy, affinity, charge interaction, steric hindrance, hydrogen bonding, $\pi - \pi$ interaction, and Van der Waal's force etc. In this way, we can get the more potential candidate compounds, ThT and BTA-1 to test pharmacal activity in vitro and significantly enhance the opportunity to find the lead compounds.



 Molecular modeling interaction between compounds and target protein in silico on molecular level to predict the bio-effect in vitro



▲ The software and hardware of virtual screening platform in silico to find the precursor of radiopharmaceutical imaging agents

2013 Annual Report



Synthetic research of BANI and DANI for novel hypoxia imaging labelling precursors

modeling between

inhibitors and the

character and space

dimension

BANI and DANI were designed to integrate bioactive amines and radioactive technetium or rhenium through carboxylic acid and N₂S₂ donor set respectively into a molecule. The nitroimidazole moiety they have showed high affinity to hypoxia, and they also can bind to TcO³⁺ for radioactive technetium imaging. The synthesis of BANI was started at the couple of DL-2,3-diamino-propionic acid monohydrochloride and thionyl chloride in methanol, then the formed mixture was proceeded to a series of esterification, amidation and hydrolysis reaction, and collocated with thiol protecting, then deprotecting reaction to yield BANI. The synthesis of DANI was initiated to the mixture of 6-amino-1hexanol and tertbutylcarbonate which was carried through aminoprotection, substitution, amidation, and hydrogenation, followed by deprotection and two fragment connecting reaction to obtain DANI. Both were confirmed with IR and NMR spectrums. The above synthetic routes were run at the condition of full of nitrogen to isolate the moisture, and the desired product could be to avoid hydrolysis, then the overall yield might be improved significantly.

We have established the synthetic pathway for BANI and DANI whose structures have been identified by IR MS, NMR. We suppose BANI and DANI have the potential as novel hypoxia imaging agents for diagnostic or therapeutic radiopharmaceuticals

Development of Radiation-Related Biotechnologies and Imaging 1-3 **Technologies**

The program includes three parts, which are "Medical image processing technologies and applications", "Semiconductor-based radiation image detector development", and "High-energy radiation applications to medical devices and biotechnologies". Based on INER's nuclear energy technologies, this program applies radiation technologies to healthcare use and livelihood use, to meet the national biotechnology policies and the needs of domestic industries. The program develops practical radiation application technologies, such as semiconductor-photosensor-based image detectors, physical models and algorithms of imaging system, and radiation improved medical devices. With the developed patentable technologies and the established platform for high-end medical device development, the aim is to cooperate with the existing/developing domestic industrial chain and achieving commercialization.

The main outputs of three parts of the program in 2013 are as follows.

Improving quantitative accuracy in nuclear medicine imaging: A high sampling model for the DOI (Depth of interaction) correction

Quantitative analysis in nuclear medicine imaging plays an important role for diagnosis and staging, prognosis and response monitoring. Several studies have shown that the correction with physical model can obviously improve the accuracy of nuclear imaging.



For accurate quantitation of nuclear breast imaging, such as positron emission mammography, we modified the model-based iterative DOI (Depth of interaction) correction method with high sampling model, and solved the time-consuming issue. Thus, the method can obtain accurate images in proper correction time without sacrificing accuracy.

The results show that the quantitative accuracy is improved significantly and the relative error is reduced from 10.3% to 1.6% after applying the correction to simulated data. Moreover, the correction time is also significantly shortened.

eg ea	Activity Ratio A/B (ideal =1)	Relative Error (B-A)/A	Correction time (iteration=1)
w/o DOI correction	1.264	-20.9%	
w/ the old-version DOI correction	0.906	10.3%	553sec
w/ the accelerated high- sampling DOI correction	1.016	-1.6%	50sec



▲ The test results show that the relative error between two tumors with the same radioactivity which placed at center and margin of field of view respectively is reduced from 10.3% to 1.6%. And the correction time is also significantly reduced.

The example mentioned above is one of our researches to improve quantitative accuracy. Further researches for physical models and high performance computing are still going on for providing a reasonable image quality and processing time in clinical use.

Establishment of the basis of a new imaging detector technology based on silicon photonic devices

Nuclear imaging devices have shown their market potential recently. To make the latest product well competitive, a new imaging detector core is necessary. The advantages of compact, low-power consumption, and magnetic-insensitive make the semiconductor-photonics-basedimaging detector technology an essential key for developing the new-generation nuclear imaging devices. In this project, the mature PMT-based technology was integrating with basic researches on semiconductor photonic elements, and our own tech-ability basis of the semiconductor-photonics-based imaging detector was established.

The most important technical progress this year (2013) is successfully integrating the small-scaleextended imaging detector and the dedicated front-end analogue processor. With the technology development and integration, a semiconductor-photonics-based imaging detector with an effective area larger than 1.5×1.5-square inch was successfully developed. Through this output, a world-wide comparable tech level was exhibited [Kim et al., 2013]. The technical outputs this year were contributed to the semiconductor-photonics-based imaging detector development, which are essential and basic abilities for developing imaging scanner of a new-generation nuclear imaging device.

Through the results, the establishment of signal manipulation technology for the semiconductorphotonics elementswas presented. To achieve the tech-necessaries for developing practical and valuable scanners, i.e. large detecting area, dead-gap-less packagesand high-performance electronics, further improvements on the optical assembling techniques and research on parallel multi-channel electronics are required. It is expected that the complete semiconductor-photonics-based imaging detector technology makes us capable of developing the world-wide competitive, new-generation molecular imaging devices.



Study for biocompatibility and animal experiment of nano-composite hydrogel as bone graft

In recent years due to increasing patients with severe bone defects or acute osteomyelitis and other bone damage, making the demand of medical bone graft significantly increased. In this study, we used a biocompatible nano-composite hydrogel aggregated by γ -rays and UV light irradiation as bone graft. This hydrogel has high mechanical strength and good viscoelasticity, can be applied to bone repair as a stent and drug delivery system. Besides, with this radiation production method, the process of product is much more simplified and also energy frugal. We've previously proved that it has no cytotoxicity, but good biocompatibility; this study will continue to discuss its effects of bone repair and osteogenesis.

This continued for a skin sensitivity animal experiment test with guinea pigs, and a acute toxicity animal experiment with mice. The results showed that this hydrogel won't cause animal allergic and toxic reactions, and suitable as a bone filling material. The bone damage animal experiment model has been established with experimental mice by surgery to open a gap on the skull bone, to simulate bone injury in human situation. The hydrogel was mixed with platelet-rich plasma (PRP) to fill the bone injury wound. Four months after surgery, the mice were sacrificed and take out the part of bone injury for histopathological analysis. Results showed that hydrogel could significantly ameliorate bone injury, and accelerate osteogenesis by allowing osteoblast adhesion. In addition, we executed another paranasal sinuses bone proliferation experiment with New Zealand white rabbit. Hydrogel was also mixed with PRP, filled in the bone cavity of paranasal sinuses. One and three months after the hydrogel implantation, the rabbits were sacrificed and take out the part of paranasal sinuses for CT scanning. Results showed that hydrogel could also promote osteogenesis by generating bone osteoblasts in the cavity. This might have a favor for the treatment of sinus bone augmentation in cosmetology.

Summing up the results, indicated that this hydrogel is more effective for bone repair or osteogenesis, both in bone injury animal model or paranasal sinuses bone augmentation model. Moreover, it is low-cost, simply and fast to manufacture without any catalytic agent. This hydrogel bone material has high medical application value and potential in the future. We hope this might have opportunity to cooperate with enterprises, to save more patients.





- Hydrogel applied on guinea pigs for skin sensitivity test, showed no response
- A Results of hydrogel implanted into mice skull bone injury



2

Development of Nano Diagnostic and Therapeutic Radiopharmaceutical Technology and Their Applications

The Project, entitled "development of nano diagnostic and therapeutic radiopharmaceutical technology and their applications", covers three main topics, including (1) nano diagnostic radiopharmaceuticals (2) nano therapeutic radiopharmaceutical (3) carbon nano tubes as early phase NPC diagnostics. The main purpose of this project is to integrate radiopharmaceutical and nanotechnology for medical diagnostics and therapy.

2-1 Preparation and bioactivity evaluation of radio-nano-targeted novel drug of ¹⁸⁸Re-liposome-Fcy-hEGF.

Human epithelial cancers cause approximately 50% of all cancer deaths and are characterized by excessive activation and expression of the epidermal growth factor receptor (EGFR). The EGF-EGFR signaling pathway is critical for cancer cell proliferation, survival, metastasis and angiogenesis. Hence, it has been validated as an important anticancer drug target. Increasing numbers of targeted therapies against this pathway have been either approved or are currently under development. The prodrug system

(Fcy-EGF/5-FC) using 5-fluorocytosine (5-FC) and human EGF (hEGF) fused with yeast cytosine deaminase (Fcy) can inhibit the growth of EGFR-overexpressing cancer by Fcy converting 5-FC to a 1000-fold more toxic chemodrug, 5-fluorouracil (5-FU).

The purpose of this study is evaluating a novel combined drug for radiotherapy and chemotherapy. The novel drug, ¹⁸⁸Re-liposome-Fcy-hEGF, provides an internal β -emittor and the prodrug system (Fcy-EGF/5-FC) for EGFR-overexpressing cancer therapy.

We conjugated the Fcy-hEGF on the surface of liposome successfully. In addition, cytotoxicity study demonstrates that the liposome-Fcy-hEGF converts 5-FC to 5-FU efficiently. Hence, liposome-Fcy-hEGF/5-FC can preferentially suppress the viability of EGFR-overexpressing cancer cells, A431. Furthermore, the ¹⁸⁸Re-liposome-Fcy-hEGF/5-FC reveals a better cytotoxic effect for EGFR-overexpressing cancer cells than the treatment of liposome-Fcy-hEGF/5-FC or ¹⁸⁸Re-liposome-Fcy-hEGF alone. Therefore, we have selected a potential EGFR-overexpressing cancer therapeutic drug successfully and the further pre-clinical animal studies will be performed recently.



▲ Preparation of ¹⁸⁸Re-liposome-Fcy-hEGF. (A) Schematic diagram of cytosine deaminase (Fcy) converts the prodrug 5-fluorocytosine (5-FC) to 5-fluorouracil (5-FU), a cytotoxic compound for cells by inhibition of DNA and protein synthesis. (B) Schematic diagram of preparation of ¹⁸⁸Re-liposome-Fcy-hEGF. The reaction of Fcy-hEGF with Traut⋅s reagent and the thiol-conjugate of Fcy-hEGF-SH to maleimide-PEG₂₀₀₀-DSPE were performed firstly. The monomer of Fcy-hEGF-PEG₂₀₀₀ was then inserted on the liposome surface. Finally, The BMEDA-conjugated ¹⁸⁸Re was incorporated into the liposome.



Cytotoxicity of liposome-Fcy-hEGF and ¹⁸⁸Re-liposome-Fcy-hEGF. (A) Liposome-Fcy-hEGF/5-FC (1 mg/ml) displays a significant inhibitory effect on EGFR-overexpressing A431 cells. (B) ¹⁸⁸Re-liposome-Fcy-hEGF (100 μCi)/5-FC (10 μg/ml) (line 4) displays a better inhibitory effect than treatment of ¹⁸⁸Re-liposome-Fcy-hEGF (100 μCi) (line 3) alone or Liposome-Fcy-hEGF/5-FC (10 μg/ml) (line 2) alone on MDA-MB-231 cells.
2-2 Preclinical and clinical studies of ¹⁸⁸Re-liposomes in cancer therapy.

Nanoliposomes are designed as carriers capable of packaging drugs through passive targeting tumor sites by enhanced permeability and retention effects. Preclinical studies of therapeutic efficacy, biodistribution, pharmacokinetics, and dosimetry of ¹⁸⁸Re-labeled nanoliposomes (¹⁸⁸Re-liposomes) in C26 colon carcinoma peritoneal metastasis mice model have been published in our previous reports. In this study, we combined the clinical first-line drug Fluorouracil (5-FU) and ¹⁸⁸Re-liposomes in the same animal model. 5-FU has been considered having not only the antineoplastic property but also as a radiosensitizer. Thus, we proposed that the combination of 5-FU and ¹⁸⁸Re-liposomes will enhance the therapeutic effect. Colon carcinoma peritoneal metastatic BALB/c mice were intraperitoneal (i.p) administrated with ¹⁸⁸Re-liposomes and 5-FU. For the combination therapy, 5-FU was administrated two days before the treatment of ¹⁸⁸Re-liposomes. The survival time of mice after respectively treating with ¹⁸⁸Re-liposomes, fluorouracil (5-FU), and ¹⁸⁸Re-liposomes combined with 5-FU were evaluated and compared. The results showed that ¹⁸⁸Re-liposomes combined with 5-FU attained a longer life span in tumor-bearing mice than only chemotherapeutics of 5-FU and radiotherapeutics of ¹⁸⁸Re-liposomes did. These preclinical results first demonstrated that the combination of 5-FU will enhance the therapeutic effect of ¹⁸⁸Re-liposomes. This information will provide the ideal therapeutic strategy of the ¹⁸⁸Reliposomes in clinical application. In additions, Phase 0 clinical study of ¹⁸⁸Re-liposome was performed in Veteran General Hospital-Taipei, the aim of study is to investigate the safety of microdose ¹⁸⁸Re-liposome in patients with metastatic cancers and who are refractory to current standard/available therapies. Each subject will receive a microdose of less than 3 mCi ¹⁸⁸Re-liposome by intravenous drip at day 1. The SPECT/CT scan, which provides information for biodistribution and dosimetry, will be conducted one hour after drug administration, as well as at 4 h, 8 h, 24 h and 48 h a post-injection. Similarly, blood and urine sample will be taken at the mentioned time point right before SPECT/CT scan for radioactivity analysis. From June 2012 to December 2013, 14 metastasis subjects have completed Phase 0 clinical study. All of subjects didn't induce any serious adverse effect after ¹⁸⁸Re-liposome injection, and no

clinically significant abnormalities in physical exams or laboratory exams were judged. Clinical studies have proved the safety of ¹⁸⁸Re-liposome in patients. This information will provide a suitable therapeutic strategy of the ¹⁸⁸Re-liposomes in further clinical application.

 Survival curves for mice bearing C26 peritoneal metastatic tumor after administering of drugs by i.p. injection



2-3 Development and application of IVD for EBV clinical diagnosis

As the changing of biomedical technology, modern IVD has been early detection of the disease or asymptomatic disease to predict and assess the condition or prognosis of the effectiveness of drug therapy, such as the development direction of functionality. The development of *In Vitro Diagnostics* (IVD) improves enormously with advanced modern medicine. By With the help of nonivasive test noninvasive test, doctors can receive the measured data shortly and decrease the related risks. Over the years, Institute of Nuclear Energy Research (INER) developed the IVD which can detect the Epstein-Barr virus (EBV)

or Nasopharyngeal Carcinoma (NPC) by improving the new nano-materials modified with irradiation. We combine the Carbon nanotubes (CNTs) modified with Co-60 irradiation used as the sudstrate and diagnosis techniques to make a IVD kit. This kit is different from commercially available kit used the 96-well plate as the substrate. It has the rapid, convenient and low detection limit characteristics. The achievement this year not only obtained the product patent and related reports but also cooperated with Mackay Memorial Hospital of Otolaryngology, Pathology and Hematology departments. We collected the clinical specimen of healthy person and patient for examination and the test result would be published in 2014. Moreover, General Biologicals Corporation (GBC) was invited to attend 2013 Taipei Int'l Invention Show & Technomart by INER. And GBC executed a MOU (Memorandum of Understanding) with INER. This project is expected for developing more diverse product with the purpose to promot the qualities of life.



 GBC executed a MOU (Memorandum of Understanding) with INER in 2013 Taipei Int'l Invention Show & Technomart.

The purpose of this project is to develop nano-radiopharmaceutical from bench to bedside. Currently, the clinical trials of "¹⁸⁸Re-Liposome for internal radiotherapy drug" and "EBV IgA detection kit" are proceeding. ¹⁸⁸Re-Liposome is the first nanotargeted radiotherapeutic drug for cancer translated into human clinical trials in the world. We have finished 14 patients in Phase 0 trial in 2013 and proved the safety of ¹⁸⁸Re-liposome in metastatic cancer patients. We expect the development of "INER Rhenium-188-liposome injection" will have contributions in enhancing the health quality of people in Taiwan.

3

Radiation Applications and Molecular Imaging Technical Platforms for Domestic Highly Epidemic Diseases

The overall objective of this project is to construct and provide technology platform for radiation applications and molecular imaging. By collaborating with National Research Program for Biopharmaceuticals (NRPB), this project develops drugs for early diagnosis and treatment of domestic highly epidemic diseases. The tasks of this project include isotopes production, radiation irradiation, drug production, liver- and cancer- targeting technology, molecular imaging platform, neurological assessment technology platform, cGMP/GLP pharmaceutical analysis and quality control, small molecules and chelating agent technology platform.

Important achievements during the year included: (1) the completion of procurement of an animal MRI scanner (1.5 Tesla), including the peripheral power systems and cooling devices, the 3Q validation and verification reports and nanoSPECT/PET/CT/MRI fusion system. MRI can be used with existing SPECT/PET/CT for image fusion, and has the potential of replacement of the traditional technique of



Comparison of nanoMRI, nanoPET/MRI and nanoPET/CT. MRI images with high soft tissue contrast enables more accurate quantitative

analysis of PET scans

autoradiography. This imaging system allows repetitive imaging of live animals in short time, saving costs and time, and improves the accuracy and precision of experiments. (2) 6 SCI papers were obtained; awarded in the 2013 Annual Meeting of Nuclear Medicine and International Symposium, including one oral paper and two poster awards. (3) 7 ROC patents and 3 U.S. patents were obtained; 4 patent applications were completed. (4) Gold medal was obtained in the 2013 Taipei International Invention Show & Technomart by the patent "Method of radiolabelling multivalent glycoside for using as hepatic receptor imaging agent". (5) R & D results, entitled "a quantitative residual liver function test methods test its novel liver receptor imaging agents", won the 10th National Innovation Award. (6) 20 nuclear medicine applications and molecular imaging services commissioned by the industry and academia were completed (including 6 NRPB users); in the service case from ITRI, the completion of pharmacokinetic and biodistribution studies of bone morphogenetic protein helps the application of the drug move into clinical trials stage. In addition, completion of biodistribution studies of anticancer peptide from NARL NDL provided evidences of lung tumor targeting of the modified peptide, and this study also won the 10th National Innovation Award. (7) Evaluation of cell proliferation imaging agent InerTA2. The use of nanoPET/CT in experimental animals can detect orthotopic liver tumors with volume of 0.7mm³ and lung tumors with diameter of 5 mm, this imaging probe helps the development of drugs for cancer treatment and screening. A variety of RGD imaging derivatives were used in orthotopic and EGFR-mutated lung cancer animal model for evaluation of angiogenesis imaging and detection of lung cancer.

This molecular imaging platform will actively collaborate with NRPB projects to strengthen international competitiveness, and will help potential lead compounds to pass TFDA regulation and enter clinical trial in the shortest period. Furthermore, we will focus on Asian highly epidemic diseases to become the world's leader of molecular imaging technology and drug development.



nanoPET/CT

Biodistribution and SPECT/CT Imaging of I-131-BMP-2/ACS in Rat

Objective: Recombinant human Bone Morphogenetic Protein-2 (rhBMP-2) plays an important role in the development of bone and cartilage. The absordable collagen sponge (ACS) is an absorbent implantable matrix for rhBMP-2. This study aims to evaluate the retention and pharmacokenetics of radiolabeled rhBMP-2 following implantation of rhBMP-2/ACS at orthotopic sites in rats by using nanoSPECT/CT.

Methods: rhBMP-2 was radioabeled with iodine-131 by standard lodogen method. A section of right radius of male SD rat was removed and replaced with I-131-rhBMP-2/ACS. NanoSPECT/CT imaging of implanted rats were performed with 16 scans in 1 month. ROIs at imlpanted site and other major organs were selected and the radioactivities of the ROIs were calibrated and decay corrected.

Results: I-131-rhBMP-2 was prepared in high radiochemical purity (\geq 95%). NanoSPECT/CT studies showed that almost entire radioactivity was accumulated at implanted site and no obvious radioactivity was observed in any organ and tissue. On 29 days after implatation, about 43% of original radioactivity was still retained at the implanted site.

Conclusion: The release/retention profile of I-131-rhBMP-2 could be monitored by using nanoSPECT/ CT for more than one month. Most I-131-rhBMP-2 was accumulated at the implanted site and could be slowly released from the ACS with desirable half-life.



▲ Left: SPECT/CT images of SD rats at 4h and 29d after implantation of I-131-BMP-2/ACS (111 MBq/rat). The red crosses indicated the location of the implant. Right: radioactivties of the implants and normal tissues after implantation of I-131-BMP-2/ACS in SD Rats.

4

Current Status of INER¹⁸⁸Re-MN-16ET/Lipiodol Radiopharmaceutical for Hepatoma Treatment

Hepatocellular carcinoma (HCC) is extremely common in South-East Asia and in South Africa. HCC has been the major ones among ten leading death causes in Taiwan for more than 25 years. Although the new therapeutic methods were introduced into the clinic, the mortality rate of HCC is still increasing in the world.

Radiolabeled Lipiodol has been used in hepatoma therapy. We have engaged in the development of the new ¹⁸⁸Re-MN-16ET/Lipiodol radiopharmaceutical in which the chelating agent, H3MN-16ET, was designed chemical by INER. The biodistribution and therapeutic data in rat tumor model showed the potential for hepatoma treatment. In 2013, we established the semi-automatic process for manufacturing 188Re-MN-16ET/Lipiodol injection. The pharmacokinetic data was transformed into the medical internal radiation dosimetry via OLINDA/EXM software. The absorbed dose is the needed information for clinical trial application in the future. The relationships between exposure rate (mR/hr) and dose rate (mSv/ hr) of 188Re isotope and distance of ¹⁸⁸Re point source were estimated by the Health Physics Division. The data can be applied to the patient release issue for clinical trial. We also setup the mass production capacity for the raw material H3MN-16ET. The related SOPs for manufacturing and quality-analyzing of H3MN-16ET were gradually established by Chemical division at INER. We devoted to meet the working standard of GMP for bio-active ingredients. In this year, we also developed the radio and tandem mass spectrometry multi-detection HPLC system for radiopharmaceuticals analysis in bio-matrices. This system and analytical technique could help us to identify the metabolic pathway for the radiopharmaceutical in the animal or human body. All the efforts were devoted to the compilation of the necessary materials for promoting the clinical trial application of ¹⁸⁸Re-MN-16ET/Lipiodol in the future.



Radiopharmaceuticals have been used for the treatment of hepatocellular carcinoma (HCC) for years. In our research, rhenium-188 has several merits to be chosen as the radionuclide, included:(1)theranostic radionuclide: emitting beta particle (2.12 MeV) and gamma ray (155 keV) at the same time; (2) suitable half-life (16.9 hours) for management and dose control; (3) easily obtained from tungsten-188(W-188)/ Re-188 generator which could be used for up to six months or more. Rhenium-188, a cost-effectively theranostic radionuclides, was used to label with H3MN-16ET and extract from Lipiodol phase to obtain the final product, ¹⁸⁸Re-MN-16ET/Lipiodol.

¹⁸⁸Re-MN-16ET/Lipiodol was proven to stably accumulate in the tumor site and show the therapeutic potential in N1-S1 rat hepatoma model. The main mechanisms used in the treatment of liver cancer include beta-emitting brachytherapy and gamma-ray diagnostic. As well as the embolization effect of lipiodol can prolong the radiopharmaceutical retention in the tumor site. Because of the brand-new designed radiopharmaceuticals by INER, 188Re-MN-16ET/Lipiodol shall be tested in lots of detailed studies to prove its safety and efficacy. We engaged in the preclinical tests and manufacturing design for ¹⁸⁸Re-MN-16ET/Lipiodol. In 2013, we have established the column-extracted methods in order to improve its efficiency of ¹⁸⁸Re-MN-16ET/Lipiodol. The derived semi-automated manufacturing procedure that could improve product stability and reduce the radiation exposure of researchers was also setup as shown in Figure. The HPLC method for radiochemical purity analysis was designed and performed stably. The standard operation procedures for quality control and manufacture have been written and evaluated. The model of chemical-induced hepatocellular carcinoma in Wistar rats has been established. This disease model will be simulated the more in line with the clinical pharmacology assessment. We have established the rat hepatic arterial embolization technology and evaluate the efficiencies of radiopharmaceuticals used in HCC treatment. In cooperation with Taipei Veterans General Hospital research team, the internal dose assessment has been done, and the result could be used in safety assessment and as a reference for clinical dosage adjustment. The National Taiwan University Hospital research team was invited to assist INER in preclinical trial planning. We have made a SWOT analysis between ¹⁸⁸Re-MN-16ET/Lipiodol and other existing liver cancer therapeutic radiopharmaceuticals. According to this report, our preclinical research data will recently be complemented and strengthened.



▲ The HPLC method for ¹⁸⁸Re-MN-16ET/ Lipiodol injection radiochemical purity analysis was established



 Semi-automatic radiopharmaceutical labeling module was designed



 (Left) Liver nodules induced by feeding 0.3%TAA for 4 months (Right) Single tumor induced by N1-S1 cell line orthotopically implanted into liver

4-2 Dosimetric Studies of a New Radiopharmaceutical ¹⁸⁸Re-MN-16ET/ Lipiodol for Hepatocellular Carcinoma Treatment

Hepatocellular carcinoma (HCC) is one of the most common malignant tumors in Taiwan. Our team has developed a new HCC embolic agent: ¹⁸⁸Re-MN-16ET/Lipiodol for the purpose of HCC embolization. This study would be mainly focused on the estimation of dosimetric characteristics and the evaluation of internal dose distribution of ¹⁸⁸Re-MN-16ET/Lipiodol. For the evaluation of internal dose distribution, the ¹⁸⁸Re-MN-16ET/Lipiodol. For the evaluation of internal dose distribution of 0.1 ml (0.1 Ci) lipiodol. These data were later extrapolated to obtain time-activity curves of human, and imported as the input of OLINDA/EXM. Equivalent doses (mSv/MBq) of both beta and photon emission, and effective dose (mSv/MBq) would then be calculated by OLINDA/EXM using Medical Internal Radiation Dose (MIRD) methodology.

For the estimation of dosimetric characteristics, relationship between exposure rate (mR/hr) and distance and relationship between dose rate (mSv/hr) and distance of ¹⁸⁸Re point source were calculated. Moreover, the relationship between cumulative dose (mSv) and distance (from 30 cm to 200 cm) was also calculated for patient release issue. The results were compared to ¹²³I, ¹³¹I, and ^{99m}Tc, which are widely used in nuclear medicine applications.

Target Organ	Beta(mSv/MBq)	Photon(mSv/MBq)	Total(mSv/MBq)	Ratio
A dren als	0.00E+00	6.78E-03	6.78E-03	0.19%
Brain	0.00E+00	1.79E-04	1.79E-04	0.01%
Breasts	0.00E+00	1.76E-03	1.76E-03	0.05%
Gallbladder Wall	0.00E+00	1.16E-02	1.16E-02	0.33%
LLI Wall	0.00E+00	1.17E-03	1.17E-03	0.03%
Small Intestine	1.31E-01	2.63E-03	1.33E-01	3.75%
Stomach Wall	0.00E+00	2.99E-03	2.99E-03	0.08%
ULI Wall	0.00E+00	3.54E-03	3.54E-03	0.10%
Heart Wall	0.00E+00	4.40E-03	4.40E-03	0.12%
Kidneys	1.78E-01	5.49E-03	1.83E-01	5.16%
Liver	1.93E+00	2.46E-02	1.96E+00	55.24%
Lungs	6.88E-01	5.63E-03	6.94E-01	19.56%
Muscle	5.45E-02	1.85E-03	5.63E-02	1.59%
Ovaries	0.00E+00	1.64E-03	1.64E-03	0.05%
Pancreas	0.00E+00	6.03E-03	6.03E-03	0.17%
Red Marrow	0.00E+00	2.00E-03	2.00E-03	0.06%
Osteogenic Cells	0.00E+00	2.34E-03	2.34E-03	0.07%
Skin	0.00E+00	9.94E-04	9.94E-04	0.03%
Spleen	3.61E-01	4.15E-03	3.65E-01	10.29%
Testes	1.95E-02	6.71E-04	2.02E-02	0.57%
Thymus	0.00E+00	2.03E-03	2.03E-03	0.06%
Thyroid	0.00E+00	9.70E-04	9.70E-04	0.03%
Urinary Bladder Wall	0.00E+00	1.03E-03	1.03E-03	0.03%
Uterus	0.00E+00	1.53E-03	1.53E-03	0.04%

▲ The internal dose results for ¹⁸⁸Re-MN-16ET/Lipiodol for hepatocellular carcinoma treatment



▲ The calculated cumulative dose (mSv) of ¹³¹I, ¹²³I, ¹⁸⁸Re, and ^{99m}Tc (at a distance of 30 cm to 200 cm)

4-3 Synthetic Research of Imaging Precursor MN-16ET for the Therapy of Hepatocellular Carcinoma

Lipiodol, an iodinated and esterified lipid of poppy seed oil, was initially developed as a radiocontrast agent. Due to its high-viscosity character, Lipiodol has been found to be retained selectively in liver tumors after infusion via the hepatic artery. Among several β emitters, ¹⁸⁸Re has become the most probable candidate for labeling Lipiodol because of its convenient, economical and energy characteristics. Since ¹⁸⁸Re is obtained as an aqueous solution and Lipiodol is available as an oily solution, many chelating agents were developed to link Lipiodol and chelate with ¹⁸⁸Re.

The research work was aimed to the synthesis of long chain alkyl substituted diamine-dithiol compound, MN-16 ET. The long chain alkyl derivative was furnished by the esterification of 16-bromohexadecanoic acid to ethyl 16-bromohexadecanate; the part of diamine-dithiol moiety was initiated to the protection reaction of 2-mercaptoethyl hydrochloride, followed by the reaction with acyl chloride, then the coupling reaction to give the diamine-dithiol derivative, N-[2-((triphenylmethyl)thio)ethyl] [2-((triphenylmethyl)thio) ethyl amino]acetamide. Both were coupled, then deprotected to yield the final



product, MN-16 ET, which was complexed with ¹⁸⁸Re to produce stable chealating agent easily dissolved in Lipiodol, available for a therapeutic radiopharmaceutical for hepatoma treatment.



[▲] The synthetic process of MN-16ET

4-4 Development of Radio and Tandem Mass Spectrometry Multidetection HPLC System for Radiopharmaceuticals Analysis in Biomatrices

In the progress of research and development of radiopharmaceuticals, it is necessary to set up the analytical methods to check the quality of product and trace the residual compound and its metabolites after the biotransformation in animal tissues. The biospecimen (liver tissue, blood, urine and feces) were pretreated to separate and concentrate the radiopharmaceutical ¹⁸⁸Re-MN-16ET, and then the sample was injected into a high performance liquid chromatography (HPLC) system which couples with radio detector and tandem mass spectrometry with T-type splitter (see Figure). In this way, we could determine the amount and structures for ¹⁸⁸Re-MN-16ET in animal model and to study the fate of the ligand. The results showed that the sensitivity for Re-MN-16ET in biospecimen is 1 ppb by LC-tandem MS and the recoveries for the ligand in biomatrices (liver, blood, and feces) are in the range of 72~98%. The study of liver tissue ex-vivo metabolism rate for Re-MN-16ET showed that the ligand amount was reduced to 50% after 2 hours enzyme reaction. On the other hand, ¹⁸⁸Re-MN-16ET/lipiodol, the agent solution was injected into hepatoma tissue, was separated from its precursor and analysed by HPLC-radio detection, the sensitive is 1 μ Ci. The multi-detection HPLC system was expected to be widely applied to R&D of other radiopharmaceutical.



▲ The scheme of LC-UV-radio-MS/MS multi-detection system



▲ The LC-MS/MS chromatograph and calibration curve for Re-MN-16ET



▲ Ex-vivo metabolism rate study for Re-MN-16ET in rat liver tissue



▲ The LC-radio detection chromatograph and calibration curve for ¹⁸⁸Re-MN-16ET/lipiodol





In order to avoid subjective judgments and self-complacency, the INER encourages all divisions to participate external evaluation to establish the progressing organization culture. The award-winning records of INER at superior authorities or external organizations are outlined as following.

1 Organization performance re-affirmed:

The INER is the only government agency for ten consecutive years to get the Defense Industrial Training storage system awards and 'blue chip' employers of Ministry of Interior alternative R & D.



Quality system certification

- 2.1 The concentrating solar modules were given IEC 62108:2007 certificate of products and UL8703 certificate of product safety in October 11, 2012 and October 16, 2013, respectively. It is the first product internationally to be certified by the UL system, receiving two kinds of certificates of products at the same time. Such recognition greatly helps manufacturers of related industries to enter the international market.
- 2.2 The INER was included in the list of Small Wind Design Consultants by North American Small Wind Certification Council (SWCC), in January 2013. Small wind turbine design evaluation laboratory passed in TAF certification in July, 2013.





3 Help industries to expand the markets

- 3.1 Help Hi-VAWT Technology Corp. DS3000 to get verification of small fan in Japan. Currently, there are only three models of small fan received validation. DS3000, counseled by INER, is the first product to receive validation of the vertical axis wind turbine and is the first one made by the foreign manufacturer.
- 3.2 Licensing technology to Malaysian's Timber Company to build fiber chemical production plant, and has significant implications to National Science and Technology Program for Energy in promoting biomass energy industry.
- 3.3 Licensing technology to China Steel Corporation to build the first set of kW-class SOFC power generation system. The new technology has attracted more than ten manufacturers to involve in SOFC industry alliance to promote new energy.
- 3.4 Mr. Charbel Bou Maroun (advanced Medical Support) from Middle East ordered TRODAT-1Kit and ECD Kit, two products of INER. We successfully expanded the international market again.

4 Awards and active promotion of technology development

4.1 The proposal of the "Private Cloud Storage Systems on the Application of Coordination and Cooperation" won the Honorable Award in the "Innovation Economy and Technology Development" group by Executive Yuan for establishment of the proposed system and recommendation in 2012.



4.2 Won Technology Invention Award and Signed Technology Transfer Contracts in 2013 Taipei International Invention Show & Technomart: The INER got seven gold, one silver and four bronze medals, total of 12 medals in 2013 Taipei International Invention Show & Technomart. During the exhibition, signed with 21 companies for "Contract of Technology Licensing and Co-development" and "Intent Letter of Cooperation and Joint Research Contracts", total of 22 copies.

10 Appendices

Award numbers in Taipei International Invention Show & Technomart during three years (2011-2013)

YEAR	Total	Platinum	Gold	Silver	Bronze
2011	5	-	2	0	3
2012	12	1	4	2	5
2013	12	0	7	1	4

Awards list in 2013 Taipei International Invention Show & Technomart

Type of Award	Patent title		
Gold Award	• The integrated design of burner, reformer and heat exchangers for the solid oxide fuel cell		
	 High-Power Pulse Magnetron Sputtering Apparatus and Surface Treatment Apparatus Using The Same 		
	 Multi-gas mixer and device for supplying gas mixture to plasma torch 		
	 Image reconstruction method for structuring two-dimensional planar imaging into three-dimension imaging 		
	 Circuit of reducing power loss of switching device 		
	 Method of radiolabelling multivalent glycoside for using as hepatic receptor imaging agent 		
	ullet Process and apparatus of CO ₂ energy source adopted in solid oxide fuel cell		
Silver Award	 Innovation process for anode treatment of solid oxide fuel cell-membrane electrode assembly to upgrade power density in performance test 		
Bronze Award	Manufacturing method for electro chromic thin films		
	 Decontamination method of metal surface contaminated by radioactive element 		
	 Method for automated formulation process for production of radiopharmaceutical injection medicine and evaluation thereof 		
	 A new kit formulation for the preparation of immunoliposome drug in combined bimodality radiochemotherapy 		



Affairs, in 2013 Technology Trade Show.



Contract manufacturers list in 2013 Taipei International Invention Show & Technomart

ltem	Company	Signing Title	Class
1	Sanmaw Wood Co., Ltd.	The key technology research and development program for non-food biomass materials solution glycation	Technology Licensing
2	Lucky Seven Industrial Co., Ltd.	The key technology research and development program for non-food biomass materials solution glycation	Early participation
3	Far Eastern New Century Corporation	The key technology research and development program for non-food biomass materials solution glycation	Early participation
4	Far Eastern New Century Corporation	Biomass ethanol production technology research and development	Technical Services
5	United Oriental Glass Ind. Co., Ltd.	Arrayed lens of miniaturized concentrator solar cell module	Early participation and Willingness to cooperatebook
6	Regatech Corporation	Arrayed silicone glass lens of miniaturized concentrator solar cell module	Early participation
7	Yue Xin BiotechnologyPharmaceutical Co., Ltd.	Biodegradable and multifunctional microspheres for transcatheter arterial embolization/chemoembolization (TAE/ TACE) therapy in hepatocellular carcinomas	Joint Development
8	Show Chwan Health Care System	Integrated research project of lodine -123 MIBG uses in heart failure disease	Joint Development
9	Han Tai Technology Co., Ltd.	The preparation and characterization of protective LSM coatings produced by atmospheric plasma spraying technique for solid oxide fuel cells	Joint Development
10	Taiwan CareTech Corporation	Three-dimensional cone-beam CT image reconstruction technique	Joint Development
11	TAIWAN OSTOR Corp.	PET imaging of local major organ systems of semiconduc- tor optoelectronic detectors core	Joint Development
12	Jia Xie Metal Co., Ltd.	Aluminum smelting slag for advanced refractory materials	Joint Development
13	REGA Biotechnology Inc.	Rapid test reagent development plan	Joint Development
14	3D Cell Culture Company	Three-dimensional cell scaffold technology development of vitro cell pharmacokinetic analysis	Joint Development
15	General Biologicals Corporation (GBC)	Development of external diagnostic reagents	Joint Development
16	HITEKCORPS Co., Ltd	Electrochromic module development	Joint Development
17	TOPCO Scientific Co., Ltd.	Technology development and application promotion of water floating solar power system	Joint Development
18	Lee Chang Yung Group wholly Energy Industry Corp.	Technology development and application promotion of water floating solar power system	Joint Development
19	EVERSOL Company	Technological development and application promotion of mono-like silicon solar cells using the plasma immersion ion implantation method	Joint Development
20	Green Source Technology Co., Ltd.	Licensing and cooperative development of the sun position sensing technology	Joint Development
21	Yulon Energy Service Co., Ltd.	Deployment and technology management of micro-grid energy systems for electric vehicles	Joint Development
22	LEATEC Fine Ceramics Co., Ltd.	Production technology for support unit cell of the ceramic substrate of solid oxide fuel cell	Joint Developmen

4.3 The Tenth National Innovation Award: "A quantitative residual liver function test methods and its novel imaging pharmacy to liver receptor" and "Higher Order Medical Imaging Equipment - Dedicated Breast Positron Emission Tomography Instrument Development" won "The 10th National Innovation Award sponsored by National Biotechnology Industry Promotion Committee.





4.4 National Invention and Creation Award: "Solid oxide fuel cell and its production method" won the silver award and a NTD 200,000 prize of the National Invention and Creation Competition sponsored by the Ministry of Economics.



- 4.5 Radioactive Material Safety Operating merit award and Outstanding Contribution Award for Research and Development.
 - Radioactive Material Safety Operating merit award (Group Award): Micro-power reactor (ZPRL) decommissioning planning team.
 - Outstanding Contribution Award for Research and Development (Individual Award): Associate Professor Zhang Guoyuan.
 - Outstanding Contribution Award for Research and Development (Group Award): Wet storage facilities within high-activity radioactive contamination removal technology R & D team.



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