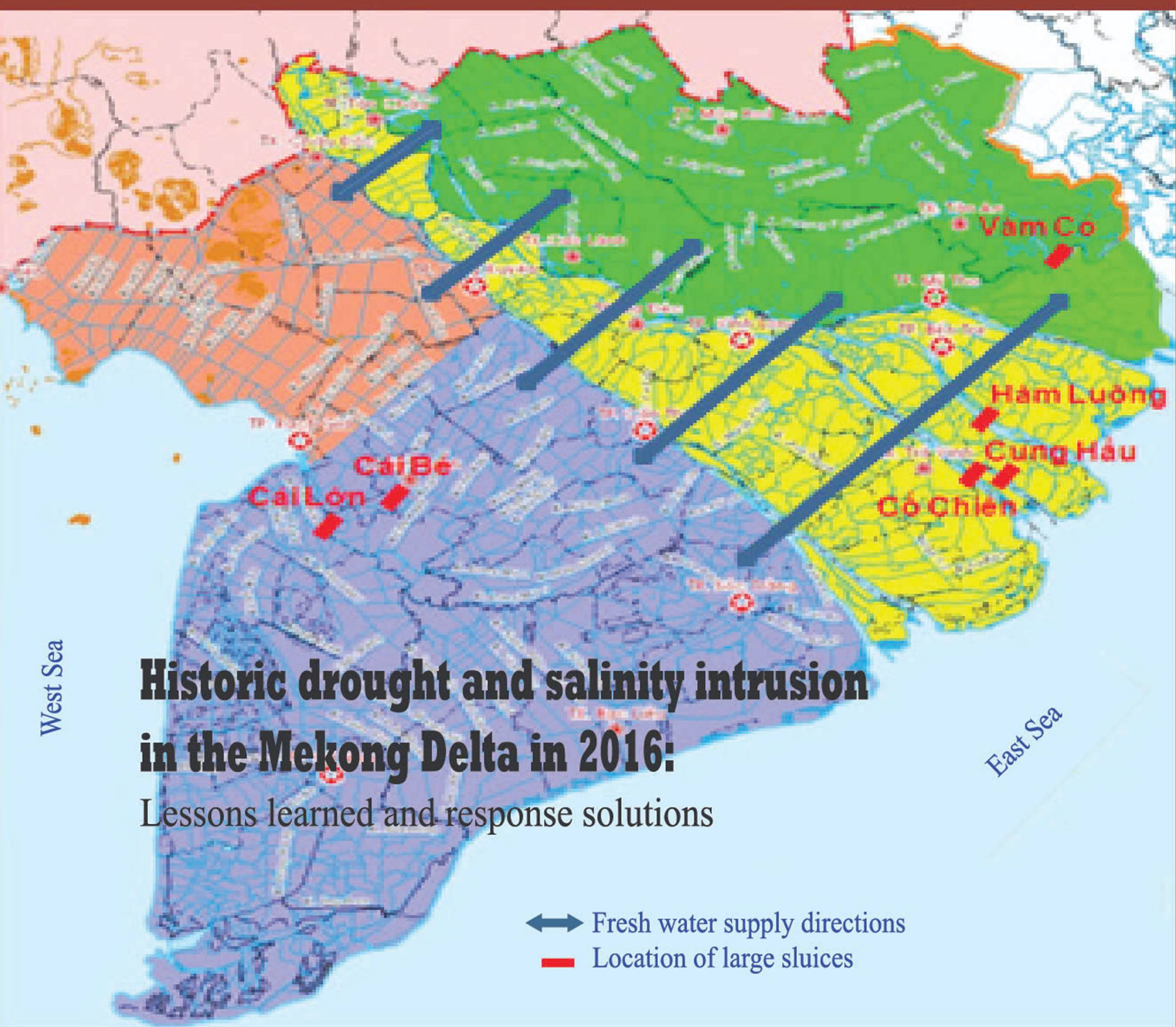




CLASSIFICATION SCHEME

1. Mathematics and Computer Science

- 1.1. Mathematics
 - 1.2. Computer Science
 - 1.3. Computational Science
-

2. Physical Sciences

- 2.1. Physics
 - 2.2. Chemistry
 - 2.3. Engineering
-

3. Life Sciences

- 3.1. Agriculture
 - 3.2. Medicine
 - 3.3. Pharmacology
 - 3.4. Biology
 - 3.5. Biotechnology
-

4. Geosciences

- 4.1. Geography
 - 4.2. Geology
 - 4.3. Geophysics
 - 4.4. Oceanography
-

5. Nanoscience and Nanotechnology

- 5.1. Nanophysics
 - 5.2. Nanochemistry
 - 5.3. Nanobiotechnology
 - 5.4. Nanomedicine
 - 5.5. Nanoengineering
-

6. Environmental Sciences

- 6.1. Ecology
- 6.2. Climatology

Vietnam roadmap to master satellite technology

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Abstract:

Vietnam has spent a considerable amount of money to install a satellite exploration program. This article presents the most important achievements of the implementation of this program in Vietnam and gives recommendations for supportive policies that will allow for the development of space exploration in the future.

Keywords: satellite technology, space technology, Vietnam National Satellite Center.

Classification number: 2.3

Introduction

Space technology is considered by many as one of the key symbols of a country's technological power and competitiveness in advancing technologies, and acts as an important motivator for the development of further science and technology in a country. That is to say, space technology is the culmination of many different technologies with an ultimate goal of benefitting the economy and boosting the development of other technologies. As a developing country, Vietnam can certainly benefit from space exploration technology - both the economy and society would benefit through science and technology advancing activities that lead to programs that prevent and mitigate the effects of natural disasters and climate change; manage and grow natural resources, especially marine resources; develop agriculture; configure telecommunications and television infrastructures via satellites; and navigation applications of satellites. Moreover, through space exploration technology, a country can not only secure protection of the territory, the territorial waters, and the territorial airspace, but also protection of the national outer space achievements.

Policy of satellite technology development in Vietnam

With an understanding of the importance of space technology in the development of Vietnam, the government, in 2006, approved the "Strategy for Research and Application of Space Technology until 2020" [1] consisting of some major

standpoints, which are:

- To widely popularize knowledge about aerospace technology through mass media, especially among pupils and students; to organize programs and textbooks for graduate and postgraduate subjects on aerospace technology; to formulate and apply on a trial basis, a mechanism for the recruitment, training, and use of talented professionals at home and abroad in association for research and market development; to send talented people to developed countries for training in aerospace technology funded by the state budget, so as to meet immediate demands and achieve the strategy's objectives; and to update achievements and retrain Vietnamese specialists on aerospace technology with cooperation from foreign countries.

- To continue participating in aerospace technology activities organized by the United Nations (UN) agencies, such as OOSA (Office for Outer Space Affairs), UN-ESCAP, UNESCO, etc., or by organizations in the ASEAN community; to consider and conclude projects on aerospace technology R&D with some countries which have favorable conditions.

- To build partner with countries that have compatible needs and offerings, especially those in Southeast Asia and Asia-Pacific. To research and form bilateral and multilateral agreements to support building and exploitation of infrastructures (ground stations, communication systems, and remote sensing satellites) and share remote sensing databases, especially in the warning of natural calamities and management of the environment.

- To create favorable conditions for overseas Vietnamese aerospace professionals to participate in research, work, and training activities for domestic professional personnel.

It is necessary to mobilize all economic sectors to invest in the implementation of the strategy for aerospace technology research and application. Budget and ODA loan capital shall be invested in the performance of research and testing, construction of key laboratories, overseas personnel training, and other necessary tasks. The State shall create favorable conditions to promote investment, support the results of aerospace technology research and application into

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commodities, and introduce them into market.

The primary goal of the “Strategy for Research and Application of Space Technology until 2020” is to bring Vietnam to an above-average level in the region, with of the key objectives set as: constituting and completing the legal policies to support space technology research and application; constructing the space technology infrastructure; studying space exploration science and technology; and applying the resulting space technologies. To promote the actualization of this strategy, the Vietnamese government established Vietnam National Satellite Center (VNSC), operating under Vietnam Academy of Science and Technology (VAST), in 2011, to concentrate on the professional development and synchronization of infrastructure, technology skill, and human resources for satellite technology. After five years, VNSC has achieved the first recognizable steps towards mastering Vietnamese Earth observation small satellite technology.

Infrastructure construction

VNSC, which belongs to the VAST, was established pursuant to Decision No. 1611/QĐ-TTg dated on September 16th, 2011, by the Prime Minister of the Vietnamese government. Over five years, VNSC has been successfully implementing its programs: developing the infrastructure for manufacturing small Earth observation satellites, technological research and development, satellite application, and human resource development for space exploration. A professional investment into the proposed roadmap is set to achieve the target of lifting VNSC to become an organization for the research and application of space technology, that can be comparable in the region, especially in satellite technology following the “Strategy for Research and Application of Space Technology until 2020” approved by the Prime Minister of Vietnam.

Currently as being executed by VNSC, the Vietnam Space Center project, is one of the biggest science and technology projects that has ever been organized and funded by the Vietnamese government and assisted with an ODA loan from Japan. The project focuses on three synchronous parts, which are:

- Constructing the infrastructure and facilities in the center to set the example as the top level in the South East Asia region, to be able to adapt with the rising demands of researching, implementing and applying space technology in Vietnam.

- Transferring technology used to observe Earth, specifically through small satellites using the Synthetic Aperture Radar (SAR) technique, which provides high resolution images and can operate in all weather conditions. These satellites are utilized to prevent and mitigate the influences from natural disaster and climate change.

- Developing human resources and modern technology skills being transferred from Japan, with the goal of being

able to construct small earth observation satellites in Vietnam (Fig. 1).



Fig. 1. Three main parts of Vietnam Space Center project.

The Vietnam Space Center, located in Hoa Lac High Tech Park (HHTP) in Hanoi City, will begin operations at the end of 2018, with an infrastructure that supports the design, implementation, integration, and operation of Earth observing small satellites. Besides, VNSC also simultaneously builds other supplements, such as the Space Application Center in Ho Chi Minh City (2019), the Center of Human Resource Development in Space Technology in Hanoi (2016), and the Nha Trang Observatory (2016) (Fig. 2).



Fig. 2. Four headquarters of VNSC.

Gradually master satellite technology

Though VNSC has been established not long ago, its key members and young scientists have been continuously

progressing to master satellite technology. After the success of developing PicoDragon satellites, VNSC has been doing other projects including NanoDragon, MicroDragon, and LOTUSat satellites following the designated satellite development plan (Fig. 3).

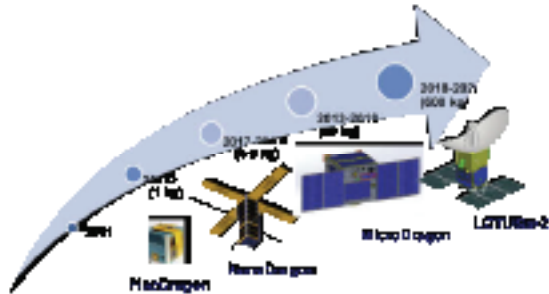


Fig. 3. VNSC's "Made in Vietnam" satellite development plan.

On October 19, 2013, the Pico satellite "Made in Vietnam" named PicoDragon, with a mass of 1 kg and developed by young Vietnamese researchers and engineers from VNSC, was successfully deployed into orbit from the International Space Station (ISS). Afterward, VNSC's ground segment and other ground stations around the world were able to record the signals from the satellite. This was an important milestone showcasing PicoDragon as the first Vietnamese satellite that successfully operated in space. Based on the success of the PicoDragon project, another satellite development project named NanoDragon satellite, was proposed to launch during the three years of 2017 and 2019, with a mass of 4 to 6 kg, and the purpose is to navigate ship locations using the Automatically Identification System (AIS) for ships.

Additionally, VNSC has collaborated with Japanese universities to develop the MicroDragon satellite project [2], a satellite with a mass of 50 kg, in Japan as an essential part of the overall Vietnam Space Center project. Through this collaboration, 36 engineers from VNSC have been sent to five universities in Japan to study masters level space technology courses, whilst simultaneously participating in the designing, manufacturing, and testing of the MicroDragon satellite with instruction from their Japanese professors. As a result from this breakthrough project, Vietnamese engineers not only have opportunities to grasp the basic knowledge about satellite technology, but also have the chance to be involved in the practical implementation of a micro-satellite and gain experience through the satellite development project. The main mission of the MicroDragon satellite is to observe the coastline of Vietnam in order to determine seawater's quality in order to determine the most suitable area for aquaculture. Currently, the satellite is in the design and integration phase, and will be completed in September, 2017 aligned with the schedule. The satellite is expected to be launched into orbit in the beginning of 2018 by the Japanese Epsilon rocket.

Finally, two satellites masses of approximately 600 kg, which employ the modern technique SAR (Synthetic Aperture Radar) in order to provide high resolution images and operate in all weather conditions, the LOTUSat-1&2, will be developed as part of the Vietnam Space Center project. The development plan of LOTUSat-1&2 is divided into 2 phases. To be specific, LOTUSat-1 will be manufactured in Japan with the participation of Vietnamese engineers, and LOTUSat-2 will be implemented and tested by VNSC's engineers at the Satellite Assembly, Integration and Test Department (AIT) in Hoa Lac. The second phase will be the achievement that shows the local development of the Earth observational small satellites from Vietnam. In present-time, the LOTUSat-1 satellite is in progress of contractor selecting and is expected to start manufacturing in the beginning of 2017.

In order to master satellite technology in 2020, simultaneously with the satellite projects, VNSC has deployed other important research and applications via the "National Programs for Earth Observation Satellite Development in Vietnam Until 2020". For example, VNSC proposed and successfully implemented the project of "Research and development of a high accurate attitude determination and control system simulator for Earth observation satellite" and participated in a national level branchy topic about designing, manufacturing and launching rocket models (Fig. 4).

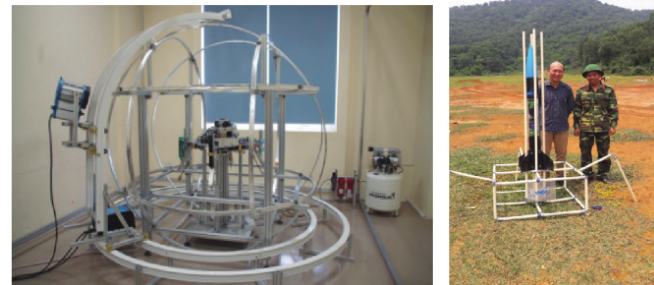


Fig. 4. Outcomes of satellite development researches in VNSC.

Concurrently with the process of moving forward to master satellite technology, the investment in the application of satellite technology is carefully focused. The goal is to bring the application and the benefit from satellites to help boost the development of the country through practical contributions: forest and agriculture management, climate change and environment analysis, natural disaster prevention and mitigation, and marine economics development. As indicated on the plan, there will be 32 officials from VNSC, appointed to participate in the educational program about satellite imagery application and satellite operation of the LOTUSat satellites, starting in 2017.

On the other hand, VNSC has actively encouraged activities and fundamental research of space science and astrophysics. An excellent research team, which includes researchers who hold doctoral degrees and is led and consulted by Prof. Pierre

Darriulat, has been developed. In the upcoming time, VNSC will continue activating the observatories in Nha Trang and Hoa Lac with the modern equipment from Vietnam Space Center, aiming to strengthen the activities of space science researching.

Human resource development and International collaboration

In the short term, with the aim of being able to train young researchers in space technology, in 2012, VNSC and the University of Science and Technology of Hanoi (USTH) signed an MOU to develop a space technology bachelor, master, and doctoral program for students. In 2013, VNSC and the University of Engineering and Technology - The Vietnam National University in Hanoi, signed the collaboration agreement, supporting the training of bachelor students specialized in space technology. In 2015, VNSC also collaborated with the International University - The Vietnam National University in Ho Chi Minh City, in an educational program for human resource in Space Science and Technology, and support internship environment to students. Besides, VNSC has signed the Memorandum of Understanding with five universities in Japan (the University of Tokyo, Tohoku University, Hokkaido University, Keio University, and Kyushu Institute of Technology) followed by the trainings for 36 VNSC's master degree students for the Vietnam Space Center project.

Considering Vietnamese society, education is an absolutely essential element in the dissemination of space technology to the population. In 2013, the Asia Pacific CanSat contest was organized for the first time in Hanoi by VNSC. The contest attracted many students with electronic engineering backgrounds from both Vietnam and Japan. In 2016, within the events to celebrate the fifth year anniversary of VNSC, a CanSat competition "Hanoi, beauty from the air" was launched to create a new, innovative approach, a new space for Vietnamese youth in studying about satellite technology, as well as to arouse the unlimited creativeness of the young engineers focused on a huge applicability of this technology sector in life. Furthermore, VNSC organizes an annual "Space Day" festival to promote space technology and youth application. Activities were especially held at the Space museum in Hoa Lac High-Tech park, along with the Planetariums under the Vietnam Space Center project, will be put into service at the end of 2017 to universalize the knowledge and to evoke and develop the passion of the youth, the pupils and the students about space technology (Fig. 5).

Regarding international collaboration, VNSC has actively participated in international cooperation activities with NASA (The United States), JAXA (Japan), ESA (Europe), CNES (France), KARI (Korea). Moreover, being authorized by VAST, VNSC has become involved and is now an official member of several space organizations, including the International Astronautical Federation - IAF (since 2012), the Committee on Earth Observation Satellites - CEOS (since 2012), the



Fig. 5. CanSat teams 2016.

Group of Earth Observations - GEO (since 2014), the Asia-Pacific Regional Space Agency Forum - APRSAF. These collaborations have contributed in ranking up Vietnam on the world space technology map.

After five years of operation, with many inclusive, synchronized and active solutions, starting with 31 members at the beginning, VNSC has developed a robust team with the total number of 125 members including 13 PhDs, 47 masters, and with 87% of members under 40-year-old. Investing in the modern, synchronistic infrastructure, through the Vietnam Space Center project, in 2020, VNSC is striving to become a modern center of science and technology for the nation, specifically: possesses the space technology infrastructure which is on top in the South East Asia region; masters technology in order to be able to manufacture "made in Vietnam" earth observation satellites; up to 300 young researchers and staffs who are professionally well educated both inside the country or abroad. This will ensure the high quality human resource, which is fundamental to space technology development in the future.

In the near future, two SAR satellites under the Vietnam Space Center project are expected to ensure that the whole territory of Vietnam and the region around its coastal line are carefully observed throughout various weather conditions with high resolution images showing occurrences. The earth observation satellites and the infrastructure, the facilities, the equipment on the ground segment shall contribute in: decreasing 10% of the damage influence Vietnam from natural disasters and climate change, seemingly equal to 0.15% of the annual GDP of Vietnam (approximate 200 mil. USD); supporting to marine rescue activities as well as marine resource economics developing; participating in protecting the society - economy benefit, marine and space environments.

Based on the adaptive convergent investment and the adequate attention from the Government, as well as the orientation and support from VAST, VNSC is believed to complete the aligned plans, involve in achieving the target of the "Strategy for Research and Application of Space Technology until 2020".

REFERENCES

- [1] Decision No. 137/2006/QĐ-TTg of the Prime Minister on approving the strategy for research and application of cosmopolitan space by 2020.
- [2] <https://vnsc.org.vn/en/projects/vnsc-training-project-in-japan/>.

A new approach for landslide mitigation for sustainable development of the transport sector

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Abstract:

The phenomenon of landslides is a strong example of natural disasters that directly affect the development of mountainous areas in general, and the traffic and transportation sectors in particular. By observing the damages caused by typical landslides in Vietnam, it can be recognized that the response to this dangerous phenomenon is often quite passive. This paper proposes a new strategy to proactively prevent and mitigate the occurrence of this natural disaster for sake of new design and management of roads, especially in mountainous terrain areas. The core of the new strategy is to identify an area's vulnerability to landslide using a landslide hazard map (LHM), created through a combined use of the landslide risk assessment map (LRAM) and the landslide susceptibility map (LSM). LRAM is outlined based on landslide inventory maps and is used for evaluation of an area's re-activeness to land sliding. LSM is created using landslide manifestation data collected about landslide causative factors such as topography, geomorphology, geology, climate and human impact as a basis for predicting the future of a particular area. The establishment and use of LHM will contribute to landslide mitigation.

Keywords: *landslide, risk assessment, susceptibility, transport, Vietnam.*

Classification number: 2.3

Introduction

Landslides are considered as a persistent problem in mountainous regions, especially along transportation corridors. Landslides not only cause damages to property (houses, buildings, vehicles, etc.) and large numbers of casualties, but also disrupt utility services and economic activities. Located on the Eastern Indochina Peninsula, Vietnam has an expanse of mountainous terrain up to 3/4 area of its territory covered by steeply sloped terrain as created from the earth's crust's powerful tectonics. Moreover, it also

has a complex geological structure and a tropical monsoon climate with an average annual rainfall of as much as 3,000 to 4,500 mm/year in some regions. Consequently, Vietnam is a typical tropical country with serious landslide disasters in both Southeast Asia and the Mekong sub region.

The vulnerability of landslide hazards is referred to as the portability of slopes by land sliding. There are many causes of landslide-vulnerability, including the conditions of topography, geomorphology, geology, climate and artificial activities. Landslide-

vulnerability assessment is a major component of a risk assessment of re-active landslides and landslide susceptibility [1]. In order to mitigate the affect that landslides have on human life, landslide risk assessment is an absolute requirement.

Recent strategies for reducing the affect of landslides

As can be seen from the recent bouts of damage from landslides in Vietnam, specifically on Highway No. 37 (at Chen Pass), Son La Province; Nam Non Bridge on the Western Route, Nghe An Province; Hai Van Pass Station; on Highway No. 6; and along the Ho Chi Minh Highway in the central region; the response to this dangerous phenomenon is quite passive.

The preparation efforts for new mountainous road projects, specifically with the selection of road alignment designed to prevent landslides and landslide-damage has not been effective due to a significant lack of necessary tools, including landslide inventory, risk assessment maps, and landslide susceptibility maps. As well, the landslide identification conducted by site surveyors is insufficient and uncredible. Due to these issues, new roads are susceptible to problems with landslides. Regarding existing road management, the most recent strategies seem too passive. This can be seen in the large number of landslides that have occurred along Vietnam's traffic arteries, especially in the raining season, including National Highway No. 2, No. 3, and Ho Chi Minh Highway; landslides that damage the roads cause havoc with traffic and hurt the economy. Often, the biggest effort of landslide risk mitigation is to recover those roads after landslides have occurred. Fig. 1 presents some pictures of landslides that have occurred along Vietnamese roads.

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Fig. 1. Some pictures of landslides along Vietnamese roads.

The vulnerability of landslide hazard

Landslides are a natural phenomenon strongly tied to the topography and slope formation processes. These processes are affected by climatic and crustal movement occurring over a very long time. However, looking at a slightly shorter time-scale, the earth's topography is essentially formed by a combination of rock strength, weathering processes, and erosion stress [2].

The natural formation of slopes depends on both internal impacts and external factors. These Internal factors are also often changes by actions occurring on the outside such as weather, metamorphosis, organization and other geological and morphological phenomenon. External factors include rain, earthquakes, and steam, and contribute to the increased strain and decreased shearing strength of the crust's surface. As a result, balance is thrown off and landslides are created. Slopes can be made unstable by both internal and external factors, but not always at the same levels of contribution.

A country's vulnerability of landslide hazard is caused by the portability of

slopes by landslides. Slope portability includes the pitch of the original slope (the slope that during the period of creation was only affect by erosion) and the slope has caused landslide in the past. Slopes that have experienced previous landslides may be susceptible to more future landslides. So when discussing the vulnerability of landslide hazard this paper will mention two scientific concepts: landslide risk assessment to re-active landslides and landslide-susceptibility due to slope pitch.

The principles of research methodology

1) The primary conditions that cause landslides are identified, and most can be shown on a map. There are many causative factors affecting landslides and those factors usually can be divided into four groups: topo-morphologic, geologic, climatic and artificial actions. However, ten factors that usually directly relate to landslides include slope angle, weathering, land use, geomorphology, fault density, drainage distance, elevation, precipitation and human actions. For each landslide, the weight of distribution contributing to the landslide may be different. The main

causes that trigger landslides can be identified. Landslide position, boundary and micro feature can be realized mostly through aerial photographs through stereoscopic projection, or based on field surveys [3, 4].

2) For landslides, "the past and the present are the keys to the future" [5, 6]. The causation of landslides is a changing processes affected by morphological factors over time, which are impacted by many other natural morphologic, geologic and climatic factors. On the other hand, human capacity of landslide recognition is limited. So when considering the natural rule of landslides, landslide occurrences will be recognized as often as possible. Per region, landslides in the future may occur in the same geologic, geomorphologic and hydrogeologic conditions as it happened before. From studying identified landslides and the causes of landslides, predictions of future landslides can be made. Therefore, to understand clearly about the movement of landslides in the past is very importance to assess landslide causes.

3) Each region is at risk for landslides at different probabilities. In an ideal situation, landslide risk would be considered according to all causative factors. Sorted by different probabilities can be gathered and used to build predictive models for landslides using different landslides phenomena controlled by the laws of mechanics, by which we can determine empirically, and statistical probability of occurrences. However, depending on the availability of relevant data, individual causative factors may be used for evaluation. From landslide occurrence data, there are many method for evaluation, including AHP, fuzzy, and a combination of both.

Proposing a flow chart for approach and discussions

The research methodology that was applied is outlined in a flowchart in Fig. 2. The chart is based on the idea that "for landslides, the past and the present are the keys to the future" [7]. By this notion, landslide occurrences can be recognized as often as possible,

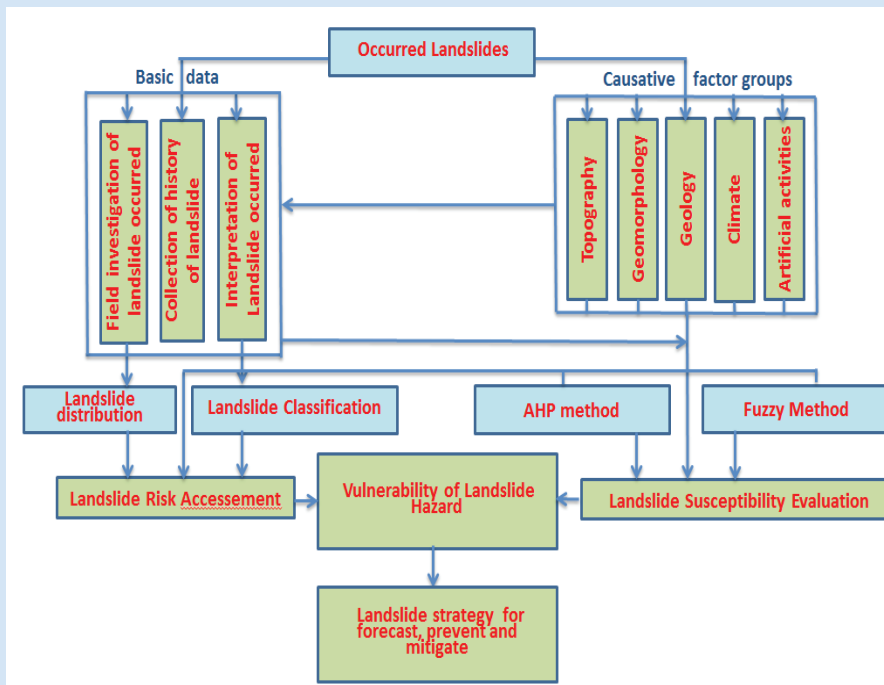


Fig. 2. Flow chart for vulnerability of landslide hazard research.

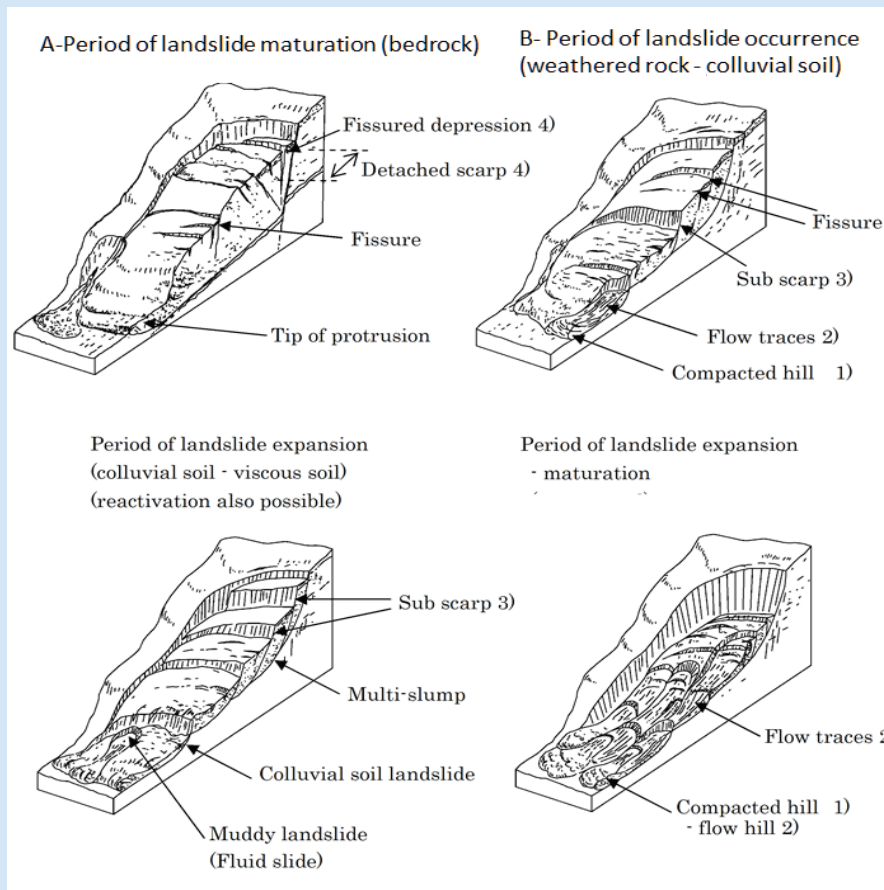


Fig. 3. Landslide micro topography [8].

depending on the test's ability to identify the influencing factors and basic data about landslides (because landslides are a phenomenon affected by time, and the capacity to recognize landslides is limited, along with other topography and slope formation phenomena, vegetation from tropical forests often cover and hide valuable signals used for landslide recognition).

To gather basic data about landslides, three basic methods used to create landslide inventory maps should be employed: field recognition methods to investigate landslide occurrences, evaluation of historical records of landslides, and study of landslide occurrences from aerial photographs. From investigations of prior landslides, the relationship between causative factors such as topography, geomorphology, geology, climate and artificial activities and landslide distribution, micro-topography can be studied. Rules regarding landslide distribution can be used for landslide classification, risk assessment and landslide susceptibility.

The conventional method of classifying landslides is based on evaluating the characteristics of the area's makeup and movement type. A recent method of classification also evaluates other factors including the affect of weather on the ground, geological features, and landslide scale. The fuzzy nature method can also be applied for this classification.

Landslide risk assessment evaluates the sensitivity of an area to re-activate landslides from previously investigated landslides. Landslide micro-topography is the interior of the landslide body, head, side, and toe. For each landslide, the internal micro-topography of landslide bodies include compacted hill, flow traces/flow hills, sub scarp, and detached scarp/fissured depression, which is very useful information used to understand the landslide phenomenon history of an area. Fig. 3 presents landslide micro topography (A) for a period of landslide maturation (bedrock) and (B) for a period of landslide occurrence on weathered rock - colluvial soil. The information observed through basic data concerning

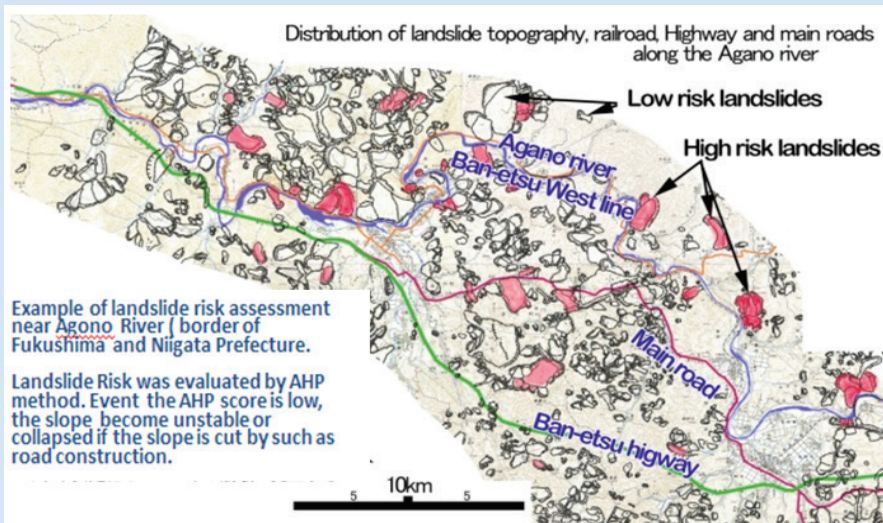


Fig. 4. Design of highways Ban-Etsu, Japan which was designed to avoid sensitive landslides.

to position, micro features and causative factors is very important for landslide assessment. For comparison and evaluation, the analytical hierarchical process approach or the fuzzy relation approach are applied. Depend on the results of the assessment; the sensitivity of an area to reactive landslides can be divided into groups of low, moderate or high classes.

To assess landslide susceptibility, the identification of causative factors, which are classified as dynamic factors (e.g. pore-water pressure) and passive factors (e.g. rock structure), might also be considered in terms of their roles as pre-conditioning factors (e.g. slope angle), preparatory factors (e.g. deforestation), and triggering factors (e.g. rain fall), which are usually targets of studies. Actually, the landslide process depends on many causative factors, such as topography and geomorphology, geology, climate, and human impact. However, depending on a full research study of the area, the relevance, availability and scale of a map [9] with necessary factors should be used. Therefore, as objects of analysis were used for this research, minor and indirect factors were ignored in favour of ones such as elevation, slope angle, land use, rock type, total annual average precipitation, fault density, and distance to the road.

For landslide susceptibility mapping, causative factors must be prepared by causative-factor maps, in which each factor map of the study area is classified into many different class groups. The weight of each factor is studied based on the results of the analytical relation between landslide occurrences with each class' factor map using GIS. Methods of analytical hierarchical process approach or fuzzy relation are applied for evaluating the contribution weight of each factor, then overlay causative maps with calculation weights. The result of this is landslide susceptibility mapping is created. The landslide susceptibility map, in which its indicator will be divided into four classes from low to very high landslide sensitivity will be used for forecast, prevent and mitigation for a region.

Conclusions

To best assess the vulnerability of landslide hazard, the LRAM and LSM are the most effective tools for forecast, prevention and mitigation of negative impacts caused by landslides and used for planning, land use, and construction of infrastructure. The combination of LRAM and LSM will give us a full picture of landslide risk regarding the sensitivity of reactive landslides and the landslide susceptibility of a given slope. The application of LRAM has been

found in the transport sector of developed countries. Fig. 4 shows an example of the application LRAM in Japan. In the scope of the technical cooperation project named "Development of landslides risk assessment technology along transport arteries in Vietnam", the LRAM and LSM was developed and announced [10]. The application of LHM as discussed above is feasible.

REFERENCES

- [1] D.V. Tien, Toyohiko Miyagi, Eisaku Hamasaki, Shinro Abe, Nguyen Xuan Khang (2014), "Landslide prevention and mitigation for road in humid tropical region", *The 4th volume of World Landslide Forum 3 (WLF3)*, Beijing.
- [2] M. Toyohiko (2012), "TXT-tool 1.081-2.1. Landslide topography mapping through aerial photo interpretation", *In ICL, Landslide teaching tools*, pp.1-10, Tokyo: ICL.
- [3] D.J. Varnes (1978), "Slope Movement Types and Process", *In Transport research board, Landslides, Analysis and Control, Special report 176*, pp.11-33, Washington, D.C.: National Academy of Sciences.
- [4] A. Hansen (1984), "Landslide Hazard Analysis", *In D.B. (editors), Slope Instability*, pp.523-602, New York: John Wiley & Sons.
- [5] D. Vaners (1984), *Landslide hazard zonation: a review of principles and practice*, Paris: UNESCO.
- [6] Carrara, et al. (1991), "GIS Techniques and Statistical Models in Evaluating Landslide Hazard", *In Earth Surface Processes and Landforms*, **5(16)**, pp.427-445, New York: John Wiley & Sons.
- [7] D.V. Tien, Toyohiko Miyagi, Shinro Abe, Eisaku Hamasaki, Hiroyuki Yoshimatsu (2016), "Landslide susceptibility mapping along the Ho Chi Minh route in central Vietnam - an application of an AHP approach to humid tropical area", *Transactions, Japanese Geomorphological Union*, **37-1**.
- [8] Kyoji Sassa, Hirotaka Ochiai, Toyohiko Miyagi, D.V. Tien, N.X. Khang (2015), "Development of Landslide Risk Assessment Technology along Transport Arteries in Vietnam", *Abstracts of the 54th annual meeting of the Japan landslide society*.
- [9] Sassa, Toyohiko Miyagi, Hirotaka Ochiai (2016), *Project report for final evaluation*.
- [10] Le Hong Luong, Toyohiko Miyagi, Shinro Abe, Eisaku Hamasaki, D.V. Tien (2014), "Detection of active landslide zone from aerial photograph interpretation and field survey in central provinces of Vietnam", *Proceedings of World Landslide Forum 3*, Beijing.

A design of the universal color-space converter IP-cores based on field - programmable gate array

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Received 1 December 2016; accepted 22 January 2017

Abstract:

This paper presents the implementation of RGB $\leftrightarrow$ YCbCr color space conversion circuits (IP-cores) necessary for many video designs. These IP-cores offer simplified 3x3 matrix multipliers used to convert three input color samples (RGB or YCbCr) to three output samples (YCbCr or RGB). The optimized structure of IP-cores uses only four multipliers (or XtremeDSP slices) to implement the RGB $\leftrightarrow$ YCbCr transformation by taking advantage of the dependencies between coefficients in the conversion matrix. Parameterizable IP-cores are used to confirm compliance to multi-standards and optimize hardware implementation. IP-cores have been verified successfully using xilinx vivado system generator 2016.2 for visually inspected output results and for verification against known models in the MATLAB/Simulink software environment.

Keywords: color space conversion, field-programmable gate array, IP-Core, RGB, Vivado System Generator, YCbCr.

Classification number: 2.3

Introduction

A “color space” is a mathematical representation of a set of colors. There are two popular color models: (1) RGB (red, green, and blue) or R’G’B’ (gamma corrected RGB) which is often used in computer graphics, and (2) YCrCb (Y - luminance or brightness, Cr - chrominance of red and Cb - chrominance of blue) which is often used in video systems. These color spaces are directly related to the intuitive notions of hue, saturation and brightness. The convergence of computers, the Internet, and a wide variety of video devices, all using different color representations, is forcing the digital designers of today to convert between the two. Converters are useful for a number of purposes, including video image compression and transmission, such as with video/image compression JPEG and MPEG [1, 2] and in NTSC/PAL/SECAM television standards.

As far as we know, there are currently no publications about color space converters with multi-standard and adjustable parameters. There are, however, several methods for YCbCr $\leftrightarrow$ RGB color space conversion [3-6]. There are also methods in the works [3, 4] implemented with the fixed ITU-R standard. In practice, image and video processing systems require the integration of many color space conversion standards and adjustable parameters which can be set by users, such as H.264 and H.265 encoders [1, 2]. Xilinx IP-cores [5, 6] provide four common format conversions as well as a custom mode for entering user-defined conversion matrices. Users can configure these using the GUI (Graphical user interface) and instantiate the core from the Vivado design tool. However, after configuring the cores and downloading bit files on the target device, the field-programmable gate array (FPGA) operates with a fixed set of parameters, including a fixed ITU-R standard. This work aims at developing the universal color-space conversion IP-cores based on FPGA for a product with selectable parameters.

Color Spaces

RGB color space is used by computer displays. RGB corresponds most closely to the behavior of the human eye. RGB uses three numerical components to represent a color. This color space can be thought of as a three-dimensional coordinate system whose axes correspond to the three components, R (red), G (green), and B (blue). RGB is an additive color system. The three primary colors (red, green, and blue) are added together to form the desired color. Each component has a range of values from 0 to 255, with three ‘0’ values producing black and three ‘255’ values producing white.

Since all three components are highly correlated, RGB is not very efficient when dealing with real-world images. Therefore, compression standards employ the YCbCr color space, because human eyes are more sensitive to differences in brightness than differences in color, the reduction in bandwidth requirement seemed a valid trade for little or no visual difference.

The most frequently used color transform is defined by ITU-R recommendation BT.601 [7], BT.709 [8] and BT.2020

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[9] for SD, HD and UHD standards, respectively. Conversion between the YCbCr and RGB formats can be accomplished using the following equations [7-9]:

$$\begin{bmatrix} EY \\ ECr \\ ECb \end{bmatrix} = \begin{bmatrix} k_a & 1-k_a-k_b & k_b \\ k_c(1-k_a) & k_c(k_a+k_b-1) & -k_c k_b \\ -k_d k_a & k_d(k_a+k_b-1) & k_d(1-k_b) \end{bmatrix} \begin{bmatrix} ER \\ EG \\ EB \end{bmatrix} \quad (1)$$

$$\begin{bmatrix} ER \\ EG \\ EB \end{bmatrix} = \begin{bmatrix} 1 & 1/k_c & 0 \\ -k_a & -k_b & -k_c \\ 1 & 0 & 1/k_d \end{bmatrix} \begin{bmatrix} EY \\ ECr \\ ECb \end{bmatrix} \quad (2)$$

where, the signal values ER , EG and EB are normalized signals R , G , and B in the $[0,1]$ range; coefficients k_a and k_b are chosen between 0 and 1, actual values for them differ slightly in different standards, as shown in Table 1; constants $k_c = 1/2(1-k_a)$ and $k_d = 1/2(1-k_b)$ allow dynamic range compression of chroma-components (Cb and Cr).

Both RGB and YCrCb color space are represented by a three dimensional, Cartesian coordinate system, as shown in Fig. 1.

Table 1. Parameterization Values for ITU-R Standards.

Standards	ITU-R BT.601	ITU-R BT.709	ITU-R BT.2020
k_a	0.299	0.2126	0.2627
k_b	0.114	0.0722	0.0593

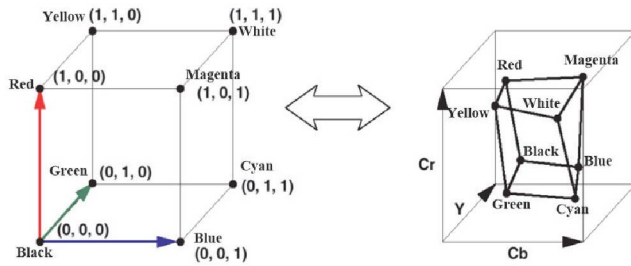


Fig. 1. RGB and YCbCr color representations.

Hardware Implementation

To map the hardware architecture, the color space transformation equations (1) and (2) can be expressed as:

$$\begin{cases} EY = k_a(ER - EG) + EG + k_b(EB - EG) \\ ECr = k_c(ER - EY) \\ ECb = k_d(EB - EY) \end{cases} \quad (3)$$

$$\begin{cases} ER = EY + 1/k_c * ECr \\ EG = EY + \frac{-k_a ECr}{k_c(1-k_a-k_b)} + \frac{-k_b ECb}{k_d(1-k_a-k_b)} \\ EB = EY + 1/k_d ECb \end{cases} \quad (4)$$

The decimal value of the quantized Y, Cr and Cb signals is:

$$\begin{cases} Y = \text{int} \left[(219EY + 16) \cdot 2^{n-8} \right] \\ Cr = \text{int} \left[(224ECr + 128) \cdot 2^{n-8} \right] \\ Cb = \text{int} \left[(224ECb + 128) \cdot 2^{n-8} \right] \end{cases} \quad (5)$$

$$\begin{cases} ER = \frac{Y - 16 \cdot 2^{n-8}}{219 \cdot 2^{n-8}} \\ EG = \frac{Cr - 128 \cdot 2^{n-8}}{224 \cdot 2^{n-8}} \\ EB = \frac{Cb - 128 \cdot 2^{n-8}}{224 \cdot 2^{n-8}} \end{cases} \quad (6)$$

where, “ n ” denotes the bit length of the quantized signal. The operator $\text{int}(\cdot)$ returns the value of 0 for fractional parts in the range of 0 to 0.4999 and +1 for fractional parts in the range 0.5 to 0.999, i.e. it rounds to nearest integer.

In the case of a uniformly-quantized 8-bit binary encoding, Y is defined to have a nominal range of 16-235; Cb and Cr are defined to have a nominal range of 16-240.

The decimal value of the quantized R, G and B signals is:

$$R | G | B = \text{int} \left[(2^n - 1) * ER | EG | EB \right] \quad (7)$$

Architecture of the color-space converters shows in Fig. 2. ROM memory stores coefficients k_a and k_b in different ITU-R BT standards. Signal “stand” selects stored coefficients k_a and k_b in ROM memory or user-defined coefficients. This architecture allows users to substitute values from any previous standard and new standard, which usually specify k_a and k_b values. This solution only requires four multipliers to replace the prior 3x3 matrix multiplier.

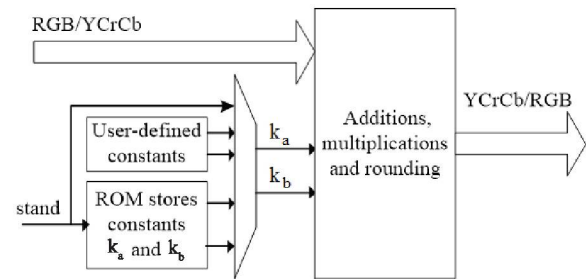


Fig. 2. Architecture of color-space conversion IP-cores.

Error Analysis

Errors are expected to occur from these calculations because of the nature of the quantification, rounding and fixed-point operators used. Thus, the results must be further analyzed to verify correct implementation for the conversion processes. The error analysis [10] allows for mean-square-error (MSE) calculations for the conversion from RGB to YCbCr and back to RGB. We assume that RGB data width is n_{RGB} bits, YCrCb data width is n_{YCC} bits, and coefficient precision is n_{Const} bits.

Practically, the YCbCr sample values are computed using the same number of bits ($n_{RGB} = n_{YCC} = n_b$) of precision with fixed-point RGB data.

IP-cores architecture contains three possible operators that might introduce noise.

1. The outputs of multipliers are truncated down to n_M bits to reduce the size and the carry-chain length of adders. Noise attributed to this truncation is inserted.
2. Word-length is further reduced to n_b bits at the output. The quantization noise is introduced.
3. Since the quantification, Cb and Cr may over - or under-flow, clipping noise gets inserted to the signal flow.

The first rounding noise source can be practically eliminated by the careful choice of n_M . Approximating SQNR by $6.02 \cdot n_M$ [dB], intuitively the rounding noise can be reduced by increasing n_M . However, n_M affects the resource usage and carry chain length in the design, thereby, affecting maximum speed.

Coefficients k_c and k_d in above equations allow designers to trade-off output quantization and clipping noise. Actual noise inserted depends on the probability statistics of the Cb and Cr variables, but in general if k_c and k_d are larger than the actual values in the standard, Cr and Cb output values may get larger (overflow) than the maximum or smaller (underflow) than the minimum values, which result in corrupted output values. If overflow occurs and the design does not have clipping, binary values wrap around and insert substantial noise into the output. Similarly, clamping is included in the design for underflow. If clamping/clipping is used, output values saturate and less noise is introduced, as shown in Fig. 3.

However, the lower k_c and k_d values are chosen, the worse the Cb and Cr values will use for the available dynamic range, thus introducing more quantization noise. Therefore, the designer's task is to equalize output quantization and clipping noise insertion by carefully choosing k_c and k_d values knowing the statistics of Cb and Cr values.

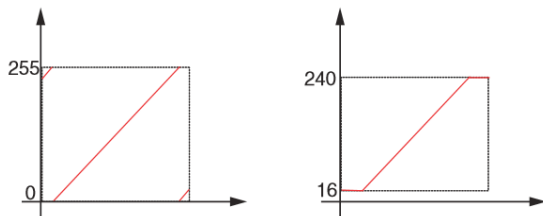


Fig. 3. Wraparound and Saturation.

The rounding operations at the output of converters introduce an approximate MSE of 1/12 due to uniform rounding quantization error [10]. When RGB values are in the (0, 255) range. For sake of simplicity, choose $n_b = 8$. For the cascade of the two conversion processes, MSEs for red (MSEr), green (MSEg) and blue (MSEb) signals are defined as:

$$\begin{cases} MSE_r = \frac{1}{12} \left[1 + \left(\frac{2 \cdot 255(1-k_a)}{224} \right)^2 + \left(\frac{255}{219} \right)^2 \right] \\ MSE_b = \frac{1}{12} \left[1 + \left(\frac{2 \cdot 255(1-k_b)}{224} \right)^2 + \left(\frac{255}{219} \right)^2 \right] \\ MSE_g = \frac{1}{12} \left[1 + \left(\frac{2 \cdot 255k_a(1-k_a)}{224(1-k_a-k_b)} \right)^2 + \left(\frac{2 \cdot 255k_b(1-k_b)}{224(1-k_a-k_b)} \right)^2 + \left(\frac{255}{219} \right)^2 \right] \end{cases} \quad (8)$$

Peak signal-to-noise ratio (PSNR) is defined via MSE as:

$$PSNR = 10 \log_{10} \left(\frac{(2^{n_b} - 1)^2}{MSE} \right) \quad (9)$$

Using the ITU-R Rec. BT.709 standard, $k_a = 0.2126$, $k_b = 0.0722$. We obtain:

$$\begin{cases} MSE_r = 0.464, PSNR_r = 51.4 \text{ dB} \\ MSE_b = 0.568, PSNR_b = 50.6 \text{ dB} \\ MSE_g = 0.223, PSNR_g = 54.6 \text{ dB} \end{cases}$$

Note that the Green component, which is the most perceptually important component, the PSNR, is significantly higher than for the Red and Green components. Also note that all three PSNRs exceed 50 dB. Value of the error of Blue signal is the most maximum.

Experimental results

FPGA Implementation of the color-space conversion IP-cores presented in Fig. 4 is composed of two IP-cores: RGB2YCrCb IP-core converts the RGB inputs to YCrCb, and YCrCb2RGB IP-core converts YCbCr signals back to RGB. The original and converted images and resulting conversion errors are plotted based on MATLAB/Simulink tools.

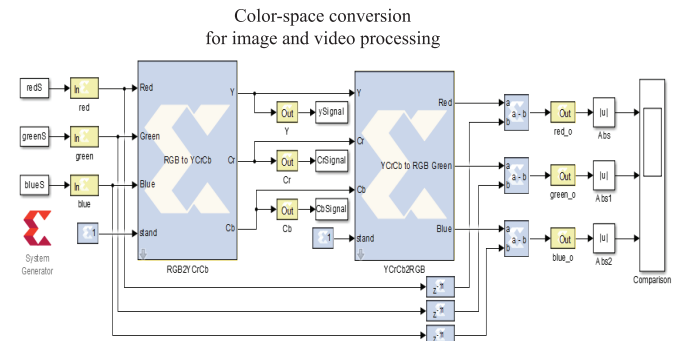


Fig. 4. System Generator Test bench of color-space conversion IP-cores.

The system generator instance can be parameterized through a Graphical User Interface (GUI) activated by double clicking the IP-cores as illustrated in Fig. 5. The designer sets the required input/output precision, enters parameters for k_a and k_b to implement a custom designed converter standard and sets the value for "stand" port to select between a predefined standard and custom.

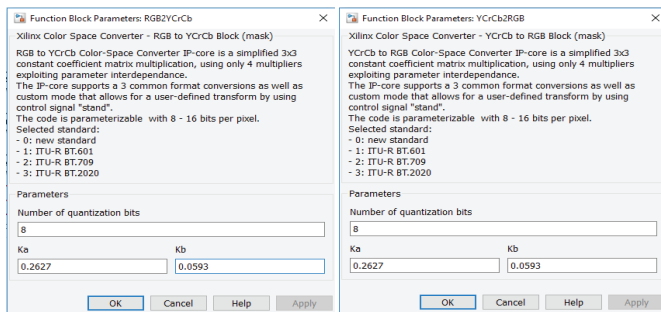


Fig. 5. Setting the configuration parameters for IP-cores.

Original RGB images Lena and Xilinx Logo are used for the inputs to test and evaluate the efficiency of the IP-cores. A digital image consists of a two-dimensional array of color pixels. Each pixel is a sample in time composed of R, G, and B components. RGB data of the original images and YCrCb samples after converting are displayed by using MATLAB/Simulink tools as plotted in Fig. 6. Total errors of the two conversion processes for R, G, B samples are also calculated, as seen on Fig. 7.

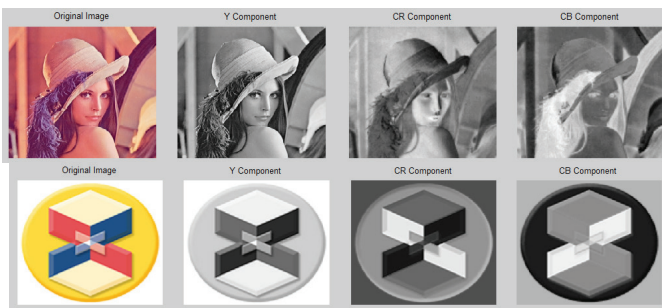


Fig. 6. Original images and Y, Cr, Cb outputs.

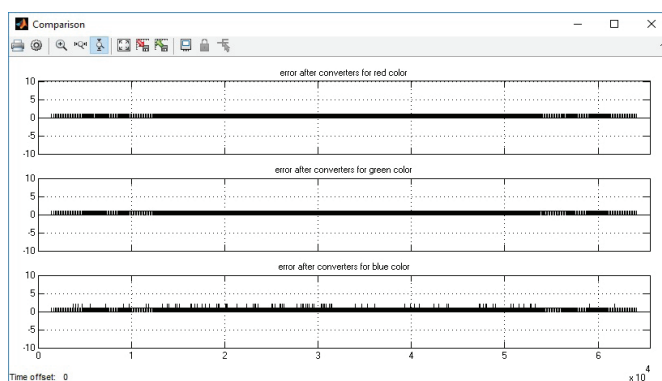


Fig. 7. Error statistics of the R, G, B samples.

According to the experimental results, the maximal error of both conversion processes for the Red and Green samples is only 1 ($2 * MSE_r = 2 * 0.464 < 1$ and $2 * MSE_g = 2 * 0.223 < 1$), and for the Blue samples is 2 ($2 * MSE_b = 2 * 0.568 < 2$). These results are correct in the according to the above error analysis.

Therefore, the conversion precision of the proposed IP-cores is high enough for the video/imaging applications.

Conclusions

FPGA is widely used in video image processing applications, and it's important to speed up the RGB $\leftrightarrow$ YCrCb color space conversion on FPGA. In this paper, the novel color space conversion IP-cores were presented and demonstrated by using the Vivado System Generator. FPGA hardware with these parameterizable IP-cores can allow users to change the parameters and can adapt between a predefined standard and a custom designed converter standard. Experimental results show that the conversion precision of the proposed IP-cores is high enough for the video/imaging applications.

In future work, we intend to consider a conversion between chroma sub-sampling formats (Y:Cr:Cb) of 4:4:4, 4:2:2, and 4:2:0. Since the human visual system is more sensitive to the luminance component than chrominance ones, we can subsample Cr and Cb to reduce the data amount without sacrificing video quality to provide a simple and effective video compression to reduce storage and transmission costs.

REFERENCES

- [1] ITU (2016), *Advanced video coding for generic audiovisual services*, Recommendation ITU-T H.264.
- [2] ITU (2016), *High efficiency video coding*, Recommendation ITU-T H.265.
- [3] Juan Xue, Xudong Cao (2012), "Color Space Conversion Based on FPGA", *IEEE International Conference on Computer Science and Automation Engineering*, 2, pp.422-425.
- [4] Hongxu Jiang, Hanqing Li, Tingshan Liu, Ping zhang, Jinyuan Lu (2013), "A Fast Method for RGB to YCrCb Conversion Based on FPGA", *IEEE International Conference on Computer Science and Network Technology*, 2, pp.588-591.
- [5] Xilinx (2015), *RGB to YCrCb Color-Space Converter v7.1*, LogiCORE IP Product Guide.
- [6] Xilinx (2015), *YCrCb to RGB Color-Space Converter v7.1*, LogiCORE IP Product Guide.
- [7] ITU (2011), *Studio encoding parameters of digital television for standard 4:3 and wide-screen 16:9 aspect ratios*, Recommendation ITU-R BT.601-7.
- [8] ITU (2015), *Parameter values for the HDTV standards for production and international program exchange*, Recommendation ITU-R BT.709-6.
- [9] ITU (2015), *Parameter values for ultra-high definition television systems for production and international program exchange*, Recommendation ITU-R BT.2020-2.
- [10] Gary Sullivan (2005), *Approximate theoretical analysis of RGB to YCbCr to RGB conversion error*, in Joint Video Team (JVT) of ISO/IEC MPEG & ITU-T VCEG (ISO/IEC JTC1/SC29/WG11 and ITU-T SG16 Q.6).

Rice development in the context of climate change in Vietnam

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Abstract:

Rice is the most important crop of Vietnam with a harvested area of 7,835 ha, production of 45.2 million tons of paddies, and export volume of 6,997 thousand tons of milled rice for an export value of USD 2,852 million in 2015. However, if purely considering its economic aspects, rice contributes only 5.45% of national GDP¹ and rice farmer's net income is only USD 419/ha compared to USD 1,128/ha earnings of Thailand farmers. Moreover, it is projected that up to 16.8% of the Red River Delta and 38.9% of the Mekong River Delta will be submerged after sea level rises by 100 cm. If this happens, a reduction in rice production would be more than 30-35%, based on the 2016 climate change scenarios. Therefore, it is necessary to thoughtfully consider rice production and rice export through different perspectives including economic, societal and environmental with a focus on ensuring food security and social stability.

Keywords: climate change, rice development, rice production.

Classification number: 3.1

Main challenges in rice production

Rice production is facing many challenges including climate change, population pressure, production efficiency, free market access, diminishing rice cultivation areas, and a low investment in agriculture; however, within the framework of this article, we only address the two most significant challenges: climate change and sea level rise, and low efficiency in rice production.

¹With rice annual production of 31.5 million tons, export price of 353 USD/ton (source: FAO Rice Market Monitor, 2016) for rice with 5% broken total rice value is only USD 11.12 billion compared with USD 204 billion of national GDP, according to Vietnam Development Partner Forum (VDPF) on the 5th December, 2015 in Hanoi.

Climate change and sea level rise

The impact of climate change on Vietnam's agricultural production is increasingly challenging. According to the Ministry of Agriculture and Rural Development (MARD), for the first time in many years, GDP growth from agriculture, forestry and fishery activities for the first six months of 2016 was negative (-0.18%)². The agriculture growth rate was -0.78%, forestry and fishery increased 5.75% and 1.25% respectively. The main causes leading to the reduction of agricultural production values are due to impacts from climate change and

²GDP same period in 2015 increased 2.36%; 2014 increased 2.96% and 2013 increased 2.14%, 6/2016.

unusually extreme weather conditions. As of the 24th of June, 2016, long term drought and saltwater intrusion damaged 249,620 ha of rice, 19,203 ha of other cash crops, 37,369 ha of fruit trees, and 163,768 ha of perennial industrial crops, altogether valued at VND 142,144 billion³. In the North, during the last ten days of January 2016, a deep cold spell in which the temperature fell sharply and even reached the lowest in weather monitoring history in some regions damaged 69,865 ha of rice and cash crops [1].

Climate change mainly relates to temperature increase, drought and sea level rise. According to a notice from the World Meteorological Organization (WMO, 2016), 2015 was the warmest year on record with a global annual average temperature increase of about 0.76°C. According to IPCC (Report 4, 2007), during the past 100 years, global average temperatures increased by 0.5-0.7°C and will continue to increase by 1.5-4.5°C more by 2050.

In Vietnam, the climate change scenario (Draft version 2016) [2] shows that annual average temperatures increased by about 0.62°C during 1958-2014 and continues to trend upward. Compared with 1981-1990, annual average temperature during 20 years from 1995-2014 increased by about 0.38°C, in the recent ten years (2005-2014), it increased by 0.42°C. Note that, when temperatures increase by 1°C, rice yield decreases by 10%, maize

³1 USD = 22,300 VND.

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Table 1. Sea level rise scenarios in Vietnam, cm.

Scenarios	Timeline							
	2030	2040	2050	2060	2070	2080	2090	2100
RCP2.6	13 (8-19)	18 (11-26)	22 (14-34)	27 (17-41)	32 (20-49)	37 (22-56)	42 (25-63)	46 (28-60)
RCP4.5	13 (8-19)	18 (11-26)	23 (14-34)	29 (18-43)	36 (22-53)	42 (26-62)	49 (30-72)	55 (34-81)
RCP6.0	13 (8-19)	18 (11-26)	23 (15-34)	29 (19-42)	36 (23-51)	43 (28-61)	50 (33-72)	59 (38-84)
RCP8.5	13 (9-19)	19 (13-27)	26 (17-36)	34 (23-47)	43 (28-59)	52 (35-72)	13 (42-88)	77 (51-106)

(Source: Vietnam Institute of Meteorology, Hydrology and Climate Change, 2016).

Table 2. Submergence with sea level rise in the key rice production provinces.

Province/City	Natural areas, ha	Percentage (%) to be submerged by sea level rises					
		50 cm	60 cm	70 cm	80 cm	90 cm	100 cm
Red River Delta	1,492,739	6.93	8.55	10.4	12.5	14.7	16.8
Hai Phong	154,052	5.14	7.61	11.7	17.4	24.0	30.2
Thai Binh	158,131	27.0	31.2	35.4	39.9	45.1	50.9
Nam Dinh	159,394	26.0	32.5	39.1	45.8	52.3	58.0
Ninh Binh	134,700	8.29	11.0	14.0	17.1	20.5	23.4
Mekong River Delta	3,969,550	4.48	8.58	14.7	21.0	28.2	38.9
Tien Giang	239,470	1.56	2.92	4.54	7.08	12.0	29.7
Ben Tre	235,950	6.21	7.58	9.87	12.8	17.0	22.2
Tra Vinh	234,120	0.80	1.02	1.33	2.38	4.93	21.3
Hau Giang	160,240	3.41	10.3	20.6	32.1	42.7	80.6
Soc Trang	322,330	2.46	5.88	10.8	16.7	25.8	50.7
Bac Lieu	252,600	3.65	7.65	14.5	23.4	33.8	48.6
Ca Mau	528,870	8.47	13.7	21.9	30.3	40.9	57.7
Kien Giang	573,690	7.77	19.8	36.3	50.8	65.9	76.9

(Source: Vietnam Institute of Meteorology, Hydrology and Climate Change, 2016).

productivity decreases by 5-20%, and food crop production goes down by 15% on average.

The forecast using RCP4.5⁴ low-

⁴According to assessment report number 5 (AR5) by IPCC, greenhouse gas emission scenarios SRES (Special Report on Emission Scenarios) replaced by scenarios RCP (Representative Concentration Pathways) describing 4 different greenhouse gas emission scenarios, atmosphere composition, emission of pollutants and land use in the 21st century. RCP2.6 is low emission scenarios, RCP4.5 and RCP6.0 are middle and stable emission scenarios and RCP8.5 is high emission scenarios. In Vietnam, the forecasts are based on two scenarios on low middle greenhouse gas emission (RCP4.5) and high emission scenarios (RCP8.5).

middle scenario shows that by the middle of this century, national annual average temperature would increase by 1.3-1.7°C. More specifically, it would increase by 1.6-1.7°C in the Northern Region (the Northwest, Northeast and Northern Delta); by 1.5-1.6°C in the North Central Region, and by 1.3-1.4°C in the Southern Region (South Central Region, Central Highland and Southern). By the end of the century, temperatures in the North would increase by 1.9-2.4°C and in the South temperatures would increase by 1.7-1.9°C. According to the high emission scenario, RCP8.5, by the middle of the century, annual average

temperatures would increase by 1.8-2.3°C, in the North, it would increase by 2.0-2.3°C and by 1.8-1.9°C in the South. By the end of the century, temperatures would increase by 3.3-4.0°C in Northern and by 3.0-3.5°C in Southern Vietnam.

Climate change not only increases the average temperature, but also increases daily maximum and minimum temperatures. According to monitoring data from 1961-2014, daily maximum temperatures (T_{max}) and daily minimum temperatures (T_{min}) increased by 1°C/10 years. The number of hot days (the days with $T_x \geq 35^\circ\text{C}$) tends to increase in most

regions of the country with common increments of 2-3 days/decade.

Average maximum yearly temperatures would increase as well having significant impacts on crop and rice production in particular. According to RCP4.5, in the middle of this century, the average T_{max} over the country would increase by 1.4-1.8°C and in the end of the century the increment is from 1.7-2.7°C. According to scenario RCP8.5, in the middle of the century, the average T_{max} temperature would increase by 1.6-2.4°C and in the end of the century, it would increase by 3.0-4.8°C, with highs that could reach 5.0°C [2].

Sea level rise is a serious challenge to agricultural production, in particular to rice production and aquaculture. According to the 2016 climate change scenario, national average sea level rise during 1993-2014 was 3.34 mm/year, of which the highest level was found in the South Central Coastal Region with more than 5.6 mm/year, it was lower in the North Central Coastal at about 2.5 mm/year (Table 1 and Table 2).

The forecast for sea level rise in the East Sea for the end of the 21st century are seen in Table 1 as: 46 cm; 55 cm; 59 cm and 77 cm according to RCP2.6; RCP4.5, RCP6.0 and RCP8.5 respectively.

With a sea level rise of 100 cm, key rice production provinces (Table 2) would be submerged, particularly the most vulnerable provinces are Hau Giang and Kien Giang (80.6 and 77% of total areas), while in other key rice producing provinces the percent of area submerged would be as follows: Thai Binh (58.0%), Nam Dinh (50.8%), Soc Trang (50.7%), Bac Lieu (48.6%), and Ca Mau (57.7%). In general, sea level rise in the Southern provinces is higher than that in the Northern provinces. Looking at the regional level with 16.8% for the Red River Delta and 38.9% for the Mekong River Delta would be submerged. These

are the rice bowls of the country and overall rice production would decrease 30-35% under that scenario.

Low rice production efficiency

Vietnam is a large rice production and export country with a harvested area in 2015 of 7,835 thousand ha, production of 45.2 million tons, export of 6,997 thousand tons of milled rice, and a turnover of USD 2,852 million [3]. This accounted for more than 17% of the global rice trade (Table 9). However, for many years, Vietnam has had its focus on increasing the quantity of production. In comparison with key rice production countries over the past 35 years, Vietnam's average rice productivity increased by 3.68 tons/ha, which is equivalent to 169.6%, which is triple the world's average. At the same time, other rice production countries targeted production on mainly high quality rice. In the case of India, after 35 years, rice yield increased by only 80 kg/ha, Pakistan increased by 0.9 tons/ha, and Thailand increased by 0.64 tons/ha (Table 3).

With respect to efficiency, research shows that farmer's income from rice cultivation is very low. According to Vietnam - Household living standard survey (2010), income from rice cultivation is only 19% of total income generated if rice areas per household are less than 1 ha. Income generated from rice cultivation increases to 26%; 36% and 68% when rice areas per household are from 1-2 ha; 2-3 ha and more than 4 ha, respectively. Most importantly, more than 90% of farming households in Vietnam own less than 1 ha of rice cultivation area.

Value made from rice production is low and furthermore the real income which rice farmers earned is the lowest portion of the value chain. Based on research by Can Tho University, farmers' profits earned were only USD 240 per year, while collectors could earn USD 25,000; rice milling actors could get USD 48,400 and exporters could get USD 2.22 million per year (Table 4).

Table 3. Vietnam and World rice productivity.

Country/ Region	Yield, tons/ha		2015 vs. 1980		
	1980	2015	Yield increase		Average yearly increase, %
			ton/ha	%	
World	2.75	4.43	1.68	61.1	1.75
Asia	2.79	4.57	1.78	63.8	1.82
USA	4.95	8.37	3.42	69.1	1.97
China	4.13	6.89	2.76	66.8	1.91
India	3.49	3.57	0.08	2.29	0.07
Pakistan	2.43	3.33	0.90	37.0	1.06
Japan	5.13	6.63	1.50	29.2	0.83
South Korea	4.85	7.22	2.37	48.9	1.40
Thailand	1.89	2.53	0.64	33.9	0.97
Vietnam	2.17	5.85	3.68	169.6	4.85

(Source: <http://ricestat.irri.org:8080/wrsv3/entrypoint.htm>).

Table 4. Rice value chain in Mekong River Delta.

Actors	Profits, VND/kg	%	Volume, tons/ years	Total profits, USD1,000
Rice farmers	507	34	8.4	0.24
Collectors	280	19	1,700	25.0
Milling	186	13	4,949	48.4
Polishing	50	3	74,400	195.8
Transporters	29	2	8,550	13.0
Exporters	422	29	100,000	2,221.0

(Sources: Vo Thi Thanh Loc, Nguyen Phu Son, 2011) [4].

cost and selling price. Selling price of 1 kg of paddy rice in Can Tho is the lowest, compared with that in other surveyed sites at USD 0.195/kg or VND 4,290/kg in equivalent, while this parameter is VND 5,192 in India; VND 8,404 in Indonesia, VND 8,889 in Thailand and VND 7,700 in the Philippines. This is the one key factor that makes net income from rice production in Vietnam the lowest, at only USD 419/1 ha (VND 9.2 million), which is only

Table 5. Rice production efficiency in some countries.

Criteria	Surveyed regions					
	Zhejiang, China	Tamil Nadu, India	West Java, Indonesia	Suphan Buri, Thailand	Can Tho, Vietnam	Nueva Ecija, Philippines
Production cost USD/ha/crop	1,621	689	1,591	1,136	910	1,588
Breakdown: USD/ha						
- Seeds	87.19	50.51	20.70	141.51	68.33	69.77
- Fertilizer	149.33	94.91	153.07	205.30	250.81	216.07
- Pesticide	61.44	22.21	185.37	133.93	145.98	39.44
- Labor	1,231.26	299.91	1,001.98	207.65	161.02	765.74
Production price, USD/kg paddy rice	0.244	0.147	0.235	0.206	0.134	0.249
Selling price, USD/kg	0.490	0.236	0.382	0.409	0.195	0.350
Profits, USD/ha	1,633	420	993	1128	419	645

(Source: S. Mohanty, 2014).

IPSARD (2014) also showed that profits (and risks) were not fairly distributed amongst rice actors participating in the rice supply chain. Per export unit, farmers' shares are 52% of total profits, but the cost of goods for farmers is 83%, while the share of rice exporters is 30% total profit with only 4% total costs spent⁵. This is one of the reasons why farmers abandon their farms and choose not to adopt advanced seeds and technology, because it is not worth it for the absolute value earned from their farms, despite impacts from the adoption of science and technology would be

relatively high⁶.

Research on rice production efficiency in some countries by the International Rice Research Institute (Table 5) also reveals that production efficiency is mainly linked to production

37.1% of Thailand's profits, 65.0% of the Philippines and 42.2% of Indonesia profits.

Rice production orientation in the context of climate change and international integration

Rice production makes a significant contribution to Vietnam's economy and society, ensuring political stability and social security. It is, however, necessary to holistically review many issues on the production efficiency and exportation. It is time for us to re-evaluate the production of rice in particular and agricultural products by return per unit area instead of a focus on volume.

⁵Rice subsector restructure proposal, 5/2016.

⁶According to General Statistical Office in 2011, over the whole country, 85% rice farming households have less than 0.5 ha rice (in Red River Delta, 98% rice farming households have less than 0.5 ha). In Mekong River Delta, in particular, production scale is larger at 1 ha/household in average but there are still 38.4% households cultivate less than 0.5 ha; 48.2% households cultivate from 0.5-2 ha and 13.4% households have more than 2 ha. Rice field ownership limits at 3 ha in Mekong River Delta, 2 ha in other regions are one of the barriers that hinder households when scaling up their production.

High level direction for the improvement of rice production efficiency has been depicted in the national product development framework proposal - “Vietnam’s high quality, high productivity rice products”, that is, “the development of competitive and high added-value rice production and commercialization through systematic adoption of improved varieties, advanced cultivation and post-harvest technologies in association with the mechanization, re-organization of production, brand development, and market development to improve productivity, quality and efficiency of rice enterprises to strongly ensure the food nation’s food security, rice cultivation farmers’ income, and rice traders’ income improvements, climate change adaptation, greenhouse gas emission reductions, environment protection”. Moreover, specific objectives towards 2030 are clearly stated in “restructuring Vietnam’s rice sub-sector towards 2020, vision to 2030” include (i) Adopting certified seeds in 100% intensive farming areas in the Mekong River Delta; (ii) Applying IPM in 90% total areas; more than 75% apply sustainable cultivation practices (such as three reduction three gains, one must do and six reductions, alternate wetting and drying techniques, etc.); (iii) Reducing post-harvest loss to less than 6%; (iv) Reducing greenhouse gas emissions by 20%; (v) Producing rice for commercialized use, more than 50% of total areas are integrated and linked between production and marketing or aggregated into large production fields and (vi) Branding 50% of total export rice, out of which 30% is fragrance and special rice.

Vietnam is always ranked in the top 2-3 rice export countries with a market share of approximate 17-20%. Although having abundant rice for export, Vietnam’s food security index is ranked 65th globally and 5th among the ASEAN countries, after Singapore, Brunei, Malaysia and Thailand where rice is mostly imported (Table 6 and Table 7). This shows that food security of Vietnam is only at the national

level (per capita), but not yet at the household level, because there are still many people who do not have access to sufficient food or do not hold disposable cash to buy food. Addressing food security, high index countries are built on their comparative advantages; they invest in the production of higher income generating commodities that carry less risk, and are willing to import rice. The pride of being a world leading rice exporting country, while its rice cultivating farmers are one of the poorest in the world, is no glory for Vietnam or its farmers.

Table 6. Global Food Security Index 2015.

Country	Score/100	Rank
United States	89.0	1
Singapore	88.2	2
Japan	77.4	21
South Korea	74.8	26
Malaysia	69.0	34
China	64.2	42
Thailand	60.0	52
Vietnam	53.4	65

(Source: Global Food Security Index 2015).

Richard Silbergliitt has further identified that while Vietnam’s food

security index is ranked 5th, its water security index is one of the lowest in the ten ASEAN countries, ranked at 9th place. This is really a great challenge because 3,000-5,000 liters of water is required to produce 1 kg of rice and a rice crop consumes more than 40% fresh water volume used for agriculture [6]. Furthermore Vietnam is at the downstream end of a big river with two major deltas (Red River and Mekong River), therefore, Vietnam is often in shortage of fresh water flows and is vulnerable to serious inland saltwater intrusion. According to research from the Cuu Long Rice Research Institute, water volume required for Spring - Summer rice crop is 4,038 m³/ha for each m³ of water can only produce 0.94-1.45 kg of paddy rice. Therefore, in order to spare about 5-7% area in Mekong River Delta, it may require Vietnam to build reservoirs to reserve fresh water for irrigation and increase aquaculture production areas instead of expecting water from upstream.

The Government and MARD also have an intention to re-structure the rice production sub-sector by shifting to the production of other crops or aquaculture on inefficient rice cultivation areas. In the Mekong River Delta, there are programs to encourage farmers to shift

Table 7. Water and food security index of ASEAN countries (scale 1-5).

No.	Nations	Food		Water	
		Index	Ranks	Index	Ranks
1	Singapore	4.0	1	3.4	1
2	Brunei	3.5	2	3.0	3
3	Malaysia	3.2	3	3.4	1
4	Thailand	3.0	4	2.2	6
5	Vietnam	2.4	5	1.8	9
6	Indonesia	2.3	6	2.6	4
7	Philippines	2.3	6	2.2	6
8	Myanmar	2.0	8	2.2	6
9	Laos	1.8	9	2.6	4
10	Cambodia	1.6	10	1.6	10

(Sources: Richard Silbergliitt, 2013) [5].

Table 8. Rice farmer's income in An Giang (2012).

	At scale of 0.75 ha/household	At scale of 1.5 ha/ household
Profit (traditional farming), 1,000 VND/household		
- Summer - Autumn crop	1,263	8,711
- Winter - Spring crop	4,171	16,784
Profit (3G-3T), 1,000 VND/household		
- Summer - Autumn crop	4,229	14,385
- Winter - Spring crop	8,080	24,005
Average income from rice, 1,000 VND/person/month		
- Traditional farming household	103	483
- Farming household adopted 3G-3T	233	727
Average income from rice, 1,000 VND/person/month		
- Traditional farming household	643	1,857
- Farming household adopted 3G-3T	1,457	2,796

(Source: Nguyen Do Anh Tuan, 2014) [7].

to cultivating maize, fruit trees, and other crops. There was a plan to shift 112 thousand ha in 2015 in Mekong River Delta out of rice production, however, the target was not achieved due to challenges, including the mechanisation of the production processes and irrigation system adjustment required to shift from rice to maize cultivation; marketing, value added processing and moreover, economic efficiency achieved from the shift is not yet attractive.

One institutional reason, which is rarely discussed, is land accumulation, and issues resulting from changes of land use right to land ownership, in order to ensure efficiency of land accumulation. Recent research (Table 8) points out that at a larger rice production scale, higher efficiency is a result of diminished costs, high advanced technology adoptability, and better quality, particularly with more consistent quality.

Together with land accumulation policy, an enabling environment for private sector to invest into agriculture plays a decisive role. Even in a developed country, such as Australia, a policy for international support can shift from "traditional diplomacy

Table 9. The world rice export and key rice export countries, 1,000 tons (USDA).

Nations	2010	2011	2012	2013	2014	2015
Thailand	10,647	6,945	6,722	10,969	9,779	9,800
India	4,637	10,250	10,480	11,588	11,046	9,000
Vietnam	7,000	7,717	6,700	6,325	6,606	7,000
Pakistan	3,414	3,339	4,126	3,600	4,000	4,400
USA	3,246	3,298	3,295	2,998	3,472	3,350
Cambodia	860	900	1,075	1,000	1,150	900
World	36,486	39,967	49,493	44,115	42,799	41,353

(Source: <http://ricestat.irri.org:8080/wrsv3/entrypoint.htm>).

for peace to economic diplomacy for prosperity", and private sector's roles are considered vital during the policy shifting process.

In Vietnam, there are very limited enterprises investing into rice production because of its high risks, but low efficiency. It is clear that state-owned enterprises only concentrate on government contracts (currently accounting for 53% total rice export volume); therefore they are only slightly concerned about rice quality, as well as market development and branding. They are mostly granted privileges of

having access to low-interest capital and markets, so it is required that Vietnam implement a policy for enterprises to be accountable for activities from rice production to rice trading, while farmers contribute with land use rights as the enterprise's shareholders. If that is the case, various varieties would be eliminated, mixed varieties would be collected, and recognized rice brands would gradually develop. During this process, a support role from the government in capital and land access is very important (Table 9 and Table 10).

Currently, Vietnam exports about seven million tons of rice per year. However, the real costs and benefits resulting from this activity have not been determined yet. How much water is used

for irrigation, and how much fertilizer and pesticides are applied for that rice exported volume is still not understood⁷. According to a survey by IRRI (Table 5), fertilizer costs for rice production in Vietnam is 1.21 times higher than in Thailand; 1.63 times higher than in Indonesia; 1.68 times higher than in China, and 2.73 times higher than in India. As consequence of using too many

⁷As per our calculation, about 70% of 11 million tons fertilizer all kinds (about 3.0-3.5 billion USD) and 130,000 tons pesticide (about 750 million USD) are used for rice crop.

inputs, fertilizer and pesticide costs per ha of rice in Vietnam is also higher than in Thailand 1.1 times, 3.7 times higher than in the Philippines, 2.38 times higher than in China. Furthermore, analysis has not yet been taken into account of how much greenhouse gas is emitted into the environment, how many cubic meters of water (surface and ground water) are affected by eutrophication, and how aquaculture and human health are affected. Vietnam must ask itself, is it sufficient to make a material trade-off and accept environmental costs for annual rice export earnings of approximate USD 3 billion? And are there other alternatives?

According to FAO statistics, the world rice trade is stable at 40-42 million tons and it is unlikely to grow. Looking at the export countries (Table 9) it is evident that they all prioritize production of high quality rice, and the price for the same rice type from Vietnam is always lower than that from those countries. Table 10 shows that for the case of 5% broken rice, price for Vietnam rice is lower than Thailand rice by USD 44; 141; 127; 13 and 33 per ton in 2011, 2012, 2013, 2014 and 2015, respectively. On average it is USD 44/ton lower in the first six months of 2016. Similarly, to 25% broken rice, Vietnam rice price is lower than that from Thailand by USD 44; 163; 1475 and 39 per ton in 2011, 2012, 2013, 2014 and 2015, respectively diminished price trends are evident in the first six months of 2016 (Table 10). Re-structure of rice sub-sector stated that price of Thailand 100% grade B rice during 2009-2014 was higher than Vietnam 5% broken rice 26%, and price of 25% broken rice of Thailand is 22% higher than that of Vietnam (Table 11).

There is obviously a problem in Vietnam's rice development strategy. It is necessary to change from a mindset focused on quantity to a mindset focused on quality and efficiency. We cannot

Table 10. Rice export price from some countries, USD/ton, FOB.

Year	Thailand 5%	Vietnam 5%	Thailand 25%	Vietnam 25%	USA, #1.4%	Pakistan Basmati	Thai Hom Mali, grade A
2011	549	505	511	467	821	1,060	1,054
2012	573	432	560	397	718	1,137	1,091
2013	518	391	504	363	692	1,372	1,180
2014	423	410	382	377	1007	1,324	1,150
2015	386	353	373	334	857	849	1,008
2016							
- January	369	353	361	340	775	734	783
- February	384	344	374	330	770	745	795
- March	384	357	375	341	745	681	793
- April	393	364	383	345	691	679	797
- May	433	365	415	346	658	750	802
- June	441	358	422	337	610	825	830
2015 (Jan. - June)	402	359	385	339	885	931	1,072
2016 (Jan.-June)	401	357	388	340	708	736	800
Increase/decrease, %	- 0.3	-0.6	0.7	0.3	-19.9	-21.0	-25.4

(Source: <http://www.fao.org/economic/est/publications/rice-publications/the-fao-rice-price-update/en/>).

Table 11. The world rice price index.

Year	Common	Indica group		Japonica group	Fragrant rice
		High quality	Low quality		
	2002 - 2004 = 100				
2012	231	225	241	235	222
2013	233	219	226	230	268
2014	235	207	201	266	255
2015	211	184	184	263	176
2016					
- January	195	179	181	240	149
- February	197	180	181	244	148
- March	196	180	184	242	142
- April	195	181	187	236	145
- May	199	191	195	230	151
- June	198	191	198	223	159
2015 (Jan. - June)	218	189	188	271	190
2016 (Jan. - June)	197	184	187	236	149
Increase/decrease, %	-9.7	-2.4	-0.4	-13.1	-21.3

(Source: <http://www.fao.org/economic/est/publications/rice-publications/the-fao-rice-price-update/en/>).

Table 12. Rice balance in Vietnam (2015)*.

Products/Usage channel	Based on USDA/FAO (2013)		Based on calculation (2015)	
	1,000 tons	% compared to total	1,000 tons	% compared to total
Paddy rice production	45,058	-	45,215	-
Rice production	29,374	100.00	29,389	100.00
Consumed price (for eating)	13,252	45.11	13,325	45.34
Seeds (as rice)	881	3.00	404	1.37
For animal feeds	2,711	9.23	0	0
Loss/waste	2,702	9.20	3,526	12.00
Used for other purposes	1,480	5.04	1,480	5.04
Store	1,259	4.29	1,259	4.29
Balance	764	2.60	2,389	8.15
Export	6,325	21.53	6,997	23.81
Consumption, kg/capita/year	144.6		145.0	

*Remarks: Calculation basis: Population: 91.9 million people (2015), milled rice/paddy conversion rate: 65%; Rice seeds used in Mekong River Delta, South Eastern, South Coastal Region and Central Highland are 100 kg/ha; in Red River Delta, North Mountainous Region and North Coastal Region are 40 kg/ha. Post-harvest loss: 12%; other information sourced from FAO/USDA (<http://ricestat.irri.org:8080/wrsv3/entrypoint.htm>).

and we should not compare ourselves with Thailand, which has much more experience in exporting rice, but compare Vietnam with Cambodia, a country which has lately begun participating in the export markets, and is immediately giving priority to producing rice for diverse markets, with 44% volume of high quality rice. Although Vietnam has participated in the rice export markets for more than 30 years, while Cambodia has only five years, but Cambodian rice has been present in 53 countries and access to high-demanding markets including USA and EU. Vietnam is still limited at exporting to ten middle and low rice quality markets in Asia, Africa and Latin America⁸. Cambodia also has special rice as Phka Malis or Phka Romdoul that are selected as the best rice in the world with price at more than one thousand US dollars.

So, which direction should we develop our rice towards?

First of all, a long-term strategy

towards quality, efficiency, and ensuring food security in any situation is required. Rice export, then, is no less a first priority. Rice cultivation land (not only inefficient rice land) is encouraged to be used for other crops and livestock on the principle that converted rice paddy land can be re-converted again for rice cultivation when required. The coastal flooded areas should shift to aquaculture. Products from livestock, aquaculture, fruits and vegetables are not just for export but for improvement of meals in a way of gradually transforming from food security to nutrition security. Rice consumption per capita of Vietnam then can be reduced 30%, from 145 kg currently to 100 kg and catch up with the consumption of South Korea, Japan with 57-67 kg of rice/capita/year. It is helpful in decreasing pressure on rice production.

Table 12 shows that it is possible to export an additional 2.3 million tons of rice in 2015 and obviously can export 10 million tons rice per year, equivalent to the production made from approximate

3 million ha (about 40% current total rice land areas). The surplus of areas and production completely ensure for breakthrough solutions in transforming rice production models.

First of all, production planning is the most decisive stage. The government at the ministries/sectors and provinces should organize enterprise conferences suitable to current orientation with a facilitative government, instead of organizing regional production meetings, with the suggestion of variety structure, and production technology. The government must provide supportive policies, and be adept to respond to market signals, at the same time receive suggestions and feedbacks on mechanisms and institutions in order to be able to advise the provincial government and local authorities of solutions and improvements.

Second, research should be conducted to judge the affect of converting certain rice areas to plant other crops, also for aquaculture. A recent study by Crawford School of Public Policy, Australian National University (2016), shows that if Vietnam can convert 19% of its rice land (about 1.46 million ha) to other crops, there exists the potential to increase GDP by USD 5.5 billion in the next 20 years. The conversion rate in the Red River Delta is at 6.35-9.71% and 8.58-11.75% in Mekong River Delta [8]. It is possible to reduce rice areas by decreasing cropping, cultivating long-day photoperiod sensitive rice cultivars, and perhaps it is required to produce only 1-2 crops per year instead of three crops in Mekong River Delta. However, plans need to take into account how to create employment for farmers.

Third, the enabling environments for the private sector to fully participate in rice value chain including land, capital for development of infrastructure, mechanization, post-harvest management, brand development and market promotion. The government needs to promote realization of agricultural insurance policies soon, which have been developed but are not yet feasible.

Fourth, in regards to technology,

⁸Dat Viet Paper dated 3 September 2015.

it is necessary to review the roles and efficiency of each stage along the production value chain. Currently, production cost is at its very highest, accounting for about 70% total cost, and it should take action immediately to minimize it. There are many technologies that can be applied to reduce materials and labor costs, in particular, advances in fertilization, water savings, and certified seeds production. According to the Chinese Academy of Agricultural Sciences (CAAS), in 1949, contribution from science and technology was only 19.9% into agricultural growth but in 1979 and 2009 it was 27% and 51%, and the impact made by fertilizer was up to 40% of this (Dongxin FENG, 2012).

Post-harvest loss is a significant issue with rice production, and to date, there has not been any systematic and efficient solution available. According to the national post-harvest strategy by MARD, rice post-harvest loss in Mekong River Delta is about 13.7%; in Red River Delta and other regions is 11.6%; particularly in Summer - Autumn crop in Mekong River Delta, sometimes it is up to 30% (it is 10% in ASEAN country, 3,9-5,6% in Japan). Thus, from 45 million tons of paddy, there is a loss of 5 million tons per year which is equivalent to production of almost 1 million ha of rice (FAO provided lower figures at about 9.2% or 2.7 million tons rice or 4.15 tons paddy rice loss in Vietnam). There are significant constraints in rice drying and storage that need to be quickly addressed to minimize loss in quantity and quality as well.

Fifth, we now have a large number of rice cultivars. According to a survey by the Crop Department [9], in Vietnam farmers are planting 379 cultivars, out of them 270 are open pollinated (OP) cultivars and 88 hybrids, with 21 sticky rice varieties. There is a reduction in the number of cultivars in comparison with five years ago (more than 500 cultivars) but it is still high that is easily leading to a loss in homogeneity in rice quality. The rate of areas cultivated with high quality cultivars is increasing (8/10 leading cultivars have good quality in Red River Delta but cultivated in only 30% areas).

In Mekong River Delta, the top ten rice cultivars cultivated in 91.7% areas are OP, good quality but not yet have brands developed. Therefore, it is required to divide rice cultivar development into two directions: i) Prioritize improving good quality rice cultivars (including special rice, sticky rice) that are in relatively large scale production and have market access to develop an intensive production zone. This is the popular direction of Thailand and India therefore their rice brands are always maintained with cultivars well-known by the markets; ii) the second direction is research on rice breeding meeting market demands.

Coupled with cultivars, an improvement of certified seed percentage is very important. Only replacement by certified seed can increase productivity by 10-15%. Currently, over the country, the usage of certified seed is only 25-30%.

Sixth, improving productivity evenness of every cultivar in each region and in the country and it is required to review them through applying systematic technical packages. This is one of prioritized direction of IRRI with the program "Closing rice yield gaps in Asia with reduced environmental footprints - CORIGAP". Currently, yield gaps on a single cultivar can be very large, reaching up to 7 tons/ha on average, but in other places, it is only 3-4 tons/ha that make the average yield of the country low. If 50% of this gap is filled we would be able to increase at least 3.5-4 million tons paddy rice. Evenness improvement solutions that can be adopted right now include irrigation system upgrading, seed quality improvement, balanced fertiliser application, efficient crop protection and reduction in post-harvest loss.

Conclusion

Rice development is facing significant challenges caused by climate change, land competition against industrialization, urbanization and road development. Over-farming by intensive farming is increasingly diminishing soil productivity, polluting the environment, and increasing greenhouse gas emission. Moreover, rice production brings in low

profits, thus few enterprises choose to invest in rice production. Increasing cost coupled with market fluctuations make farmers uneasy with rice cultivation. It is the time for us to treat rice grains and rice farmers in a fairer way. Rice production must not only be considered as economic object but also social security and macro-economic stability. Converting a part of land for rice or reasonable reductions in cropping patterns together with land accumulation required serious consideration. It is also necessary to develop feasible solutions with effective support from the government for agricultural insurance in general and in rice production in particular. Rice export need to be re-considered in respect of rice farmer's income centered long-term strategy.

REFERENCES

- [1] Crop Department (2016), *Preliminary report on Winter-Spring crops 2015-2016 and deployment of Summer-Autumn, main crop plan of 2016 in the north provinces for restructure of cropping sector*, The report presented in the conference in Ha Nam on 24th May.
- [2] Vietnam Institute of Meteorology, Hydrology and Climate Change (2016), *Climate change and sea level rise scenarios version 2016 (draft)*.
- [3] Ministry of Agriculture and Rural Development (2016), *Agricultural and rural development progress report for the first six month and missions for the last half of 2016* (Attached with official letter number 5505/BNN-KH, dated 19th June, 2016 to the Government Office).
- [4] Vo Thi Thanh Loc, Nguyen Phu Son (2011), "Mekong River Delta rice value chain analysis", *Science Journals of Can Tho University*, **19a**, pp.96-108.
- [5] Richard Silbergliitt (2013), *Scenarios for a Sustainable ASEAN Energy Future*, Presentation at the Workshop on APEC Energy-Food-Water policy and possible strategies, Bangkok.
- [6] To Phuc Tuong (2012), *Water-wise management in rice production*, International Workshop on Trends in Rice Research to Overcome Stresses in a Changing Climate, Hanoi.
- [7] Nguyen Do Anh Tuan (2014), *Vietnam rice markets and policies*, Workshop: Restructure rice sub-sector in Mekong River Delta, Can Tho.
- [8] Tom Kompas, Hoa Nguyen and Long Chu (2016), *Protecting rice land in Vietnam: What's optimal*, Outlook Agro 2016, Hanoi.
- [9] Tran Xuan Dinh, et al. (2015), *National rice cultivar survey results in 2015 for restructure of rice sub-sector*, Report of Crop Department.

Study on the formation and development of aromatic rice spikelets

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Abstract:

In order to detect some of the determinants of rice flavor, an experiment was carried out that studied panicle primordia at the initial panicles of three aromatic varieties: Nang Thom Cho Dao mutation (NTCDm), Thom Bay Nui (TBN), and Jasmine-85, and IR28 was used as the control variety (non-aroma). The samples were dyed from the primordium stage to the ripe-pollen stage. Results showed that there were two key differences between the aromatic rices and the control. The first point of difference was at the primordium stage, and the second was after, as a consideration of the number of bivalents (pairs of homologous chromosomes). As for the three aromatic rice varieties, there appeared a lobe division at the branch primordium; at the diplotene stage of meiosis, and seven to eight stained bivalents appeared while the control had no lobe division and the number of stained bivalents achieved 11 to 12.

Keywords: meiosis, primordia stage, rabl configuration, rice flavor.

Classification number: 3.1

Introduction

In recent years, the production of some famous aromatic rice varieties have been increasing, including Jasmine 85 and NTCDm. Their yields have been ranging from three to five tonnes/ha [1]. In addition to this, the quality of aromatic rice varieties have been distinguished as cooking rice and rice grain that is shiny, fragrant [2], delicious and is many consumers first choice for daily meals; while Vietnam's fragrant rice is not stable and the smell does not keep long.

Twelve consecutive photoinductive cycles have established the full shape of the panicle along with the differentiation of the lodicules, anthers and the pistil primordium in the individual spikelets borne at the apical region (Misra and Khan, 1969). In the P4 leaf primordium, strong OSHB3 expression was evident in

the adaxial cells of the ligule primordium (Itoh, *et al.*, 2008). Spikelet lengths varied significantly among the genotypes. Minimum spikelet length was recorded in Kalijira (White type), while the maximum length was observed in Kaloshailla (P.S. Saha, *et al.*, 2015).

Research of the formation and development of aromatic rice flowers rarely is published. Rice breeding on aromatic rices is very difficult for rice breeder. Thus, finding an indicator to study aroma was important in order to select new aromatic rices. The objective of the study was to detect the formation and development of aromatic rice spikelets at the initial primordium stage.

Material and method

Material

Seeds: seeds of three aromatic rices: NTCDm, Jasmine 85, and TBN; and the non-aromatic rice, IR28, were studied (Table 1). The seeds were provided by the Department of Genetics and Plant Breeding, at the College of Agriculture and Applied Biology, at Can Tho University.

Methods

Sample soil preparation: seeds were soaked in water for 24 hours, then allowed to germinate for 48 hours. When seedlings grew to 2-3 cm, they were transplanted directly into a ceramic pot (30x26x16 cm). Soil in the pot was prepared as follows: 120 g of compost (manure), 0.72 g P_2O_5 , 0.36 g K_2O (100N-60P₂O₅-60K₂O), and water.

Layout: the experiment was arranged as a randomized complete block, four treatments with three replications.

Methods of staining samples

Prepare materials: the meiosis was

Table 1. Some agronomical characteristics of rice varieties used in this experiment.

Characteristic	NTCDm	Jasmine 85	TBN	IR28
Growth duration (days)	110-115	105-110	120-160	90-95
Plant height (cm)	115-145	110-115	120-150	95-100
Yield (t/ha)	3.5	4-6	3-4	7-8
Amylose content (%)	21.26	18-22	14.8	16.03
Chalkiness (%)	0	0	0	0.3
Grain length (mm)	6.3	6.9	7.8-8.0	6.9
Weight of 1,000 grains (g)	27	26	27.2-27.8	27.15

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Table 2. Developmental stages and morphological characteristics^a.

Developmental stages	Morphological characteristics		
	Leaf index (%)	Exertion of n^{th} leaf counted from the top	Panicle length (mm)
1. Necknode differentiation stage	76-78	4 th leaf	
2. Branch differentiation stage	80-86	3 rd leaf	
3. Spikelet differentiation stage	87-92	2 nd leaf	1-15
4. Pollen mother cell differentiation stage	95	Flag-leaf	15-50
5. Reduction division stage of pollen mother cell	97		50-200
6. Extine formation stage	100		Full length
7. Ripe pollen stage	100		Full length

^aModified from Matsushima (1970)

observed when the flower buds were very young (around 50 days after sowing), and panicle length was about 7-8 cm. After cutting the buds from the plant, they were fixed within Carnoy's solution [3].

Staining: the samples were stained with Aceto-Carmine, or the chromosome or cell nuclei would become red, while the rest was pale pink.

Working method: stained specimens were placed in microscope slides covered with lamella, then heated lightly over an alcohol lamp, and pressed lightly by thumb. Chromosomes (if present in the cells) were clearly visible in the microscope.

Methods to identify the stages of spikelet formation and development: to identify the stages of spikelet formation and development, the method of [4] was applied (Table 2).

Results and discussion

Morphological variation of rice spikelet primordium of IR28 and NTCDm

The initiation of the panicle primordium of IR28 began about 25 days before heading, and the remaining experiment lasted for about 30 days. The method was suitable for the time, until the fourth leaf from the top began to elongate. The major elements of the panicle were the base, axis, primary, and secondary branches, pedicels, rudimentary glumes, and spikelets (Fig. 1). The spikelet was borne on the pedicel, and a short stalk was developed as an extension of the panicle axis at the primary or secondary branch. There were two short rudimentary glumes

at the upper end of the pedicel. A pair of sterile lemmas and the rachilla were located between the rudimentary glumes and the spikelet. The flower was enclosed in the lemma and palea. The flower consisted of the pistil, stamens, and lodicules. The components of the pistil were the stigmas, styles, and ovary. The stigma had plumose, on to which pollen grains were stored for germination.

There were six well-developed stamens composed of anther and filament. Two small, oval, thick, and fleshy bodies, called the lodicules, were situated at the base of the ovary. The lodicules became distended with water and assisted in separating the lemma and palea when it flowered, this

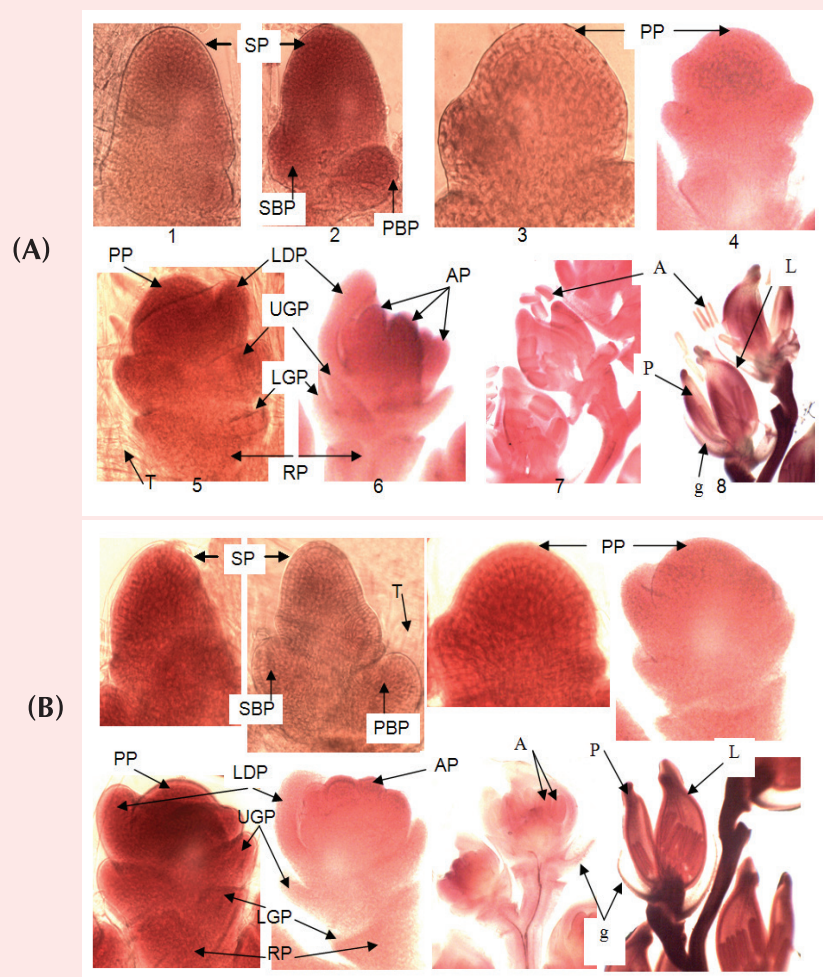


Fig. 1. The development of rice spikelets. (A) IR28; (B) NTCDm.

A, Anther; AP, Anther primordium; g, sterile lemmas; L, Lemma; LDP, Lodicule primordium; LGP, Lower glume primordium; P, Palea; PBP, Primary branch primordium; PP, Pistil primordium; RP, Rachilla primordium; SBP, Secondary branch primordium; SP, Spikelet primordium; T, Trichomes; UGP, Upper glume primordium.

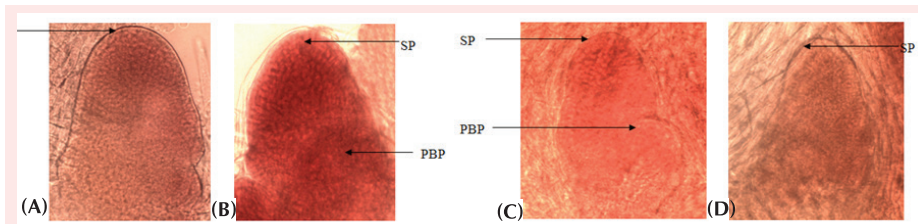


Fig. 2. Necknode differentiation stage (X100). (A) IR28; (B) NTCDm; (C) TBN; (D) Jasmine. PBP, Primary branch primordium; SP, Spikelet primordium.

was consistent with the results of other studies [5].

Panicle development of aromatic and non-aromatic rice

The formation and development of aromatic rice spikelets were observed through seven stages as Matsushima's research (1970) presented.

Necknode differentiation stage:

In the necknode differentiation stage, the spikelet primordium was formed. As for the non-aromatic rice (IR28), this stage appeared from 42-44 days after sowing (DAS), but for aromatic rices, it was 50-53 DAS for NTCDm; 45-48 DAS for TBN, and 40-43 DAS for Jasmine 85, respectively. Panicle development and growth started with the neck-node differentiation and end when the pollen was fully matured.

In this phase, the part at the top bud was called the spikelet primordium, below this part was the position of the primary branch primordium (Fig. 2). The young panicle was a very small size and had protruding blocks that were not visible to the naked eye, and surrounded by trichomes. Therefore, the samples in necknode differentiation stage were very difficult to subject and difficult to be clearly visible under an optical microscope.

Branch differentiation stage:

In the branch differentiation stage, spikelet primordium continued to grow and sprout, while primary branch and secondary branch sprouts began forming. As for the non-aromatic rice (IR28), this stage occurred from 44-49 DAS, and for the aromatic rice varieties: NTCDm, TBN, and Jasmine 85, this stage occurred in about 53-59 DAS, 48-54 DAS, and 43-50 DAS, respectively.

During this period, spikelet primordium continued to grow and form primary branch primordium and secondary branch primordium. It could be seen that in the branch differentiation stage of aromatic rice (NTCDm and TBN), there was lobulation

at the branch primordium (Fig. 3) while the control was not lobulated.

Spikelet differentiation stage:

At the stage of spikelet differentiation, the branch primordium continued to grow. Then, spikelet primordium, lodicule primordium, upper glume primordium, and rachilla primordium also continued to grow. This stage occurred from about 49-57, 59-67, 54-62, and 50-58 DAS, respectively corresponding to the non-aromatic rice (IR28), NTCDm, TBN, and Jasmine 85. In this phase, spikelet primordium grew to pistil primordium (Fig. 4), which then continued to grow to the pistil and stamens.

The young panicle could be seen with the naked eye for the first time in the early stages of differentiation of the secondary rachis-branches. The panicle at that time was about 0.5-0.9 mm long. A panicle that had grown 1.0 mm, had already entered the spikelet differentiation stage, and this was consistent with the results of other research [5].

After spikelet primordium in the first of the top buds developed fully such as lodicule primordium, upper glume

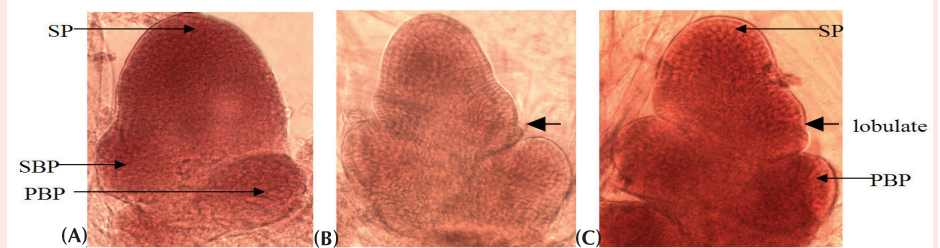


Fig.3. Branch differentiation stage (X100); samples were collected at 8:30 am. (A) IR28; (B) NTCDm; (C) TBN. SP, Spikelet primordium; PBP, Primary branch primordium; SBP: Secondary branch primordium.

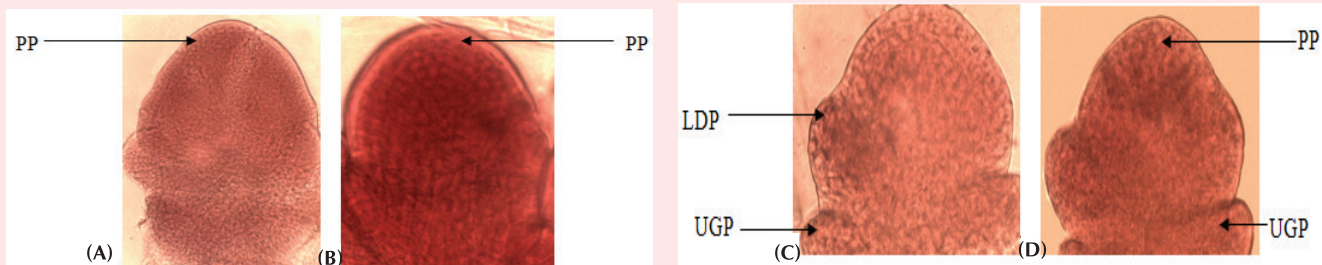


Fig. 4. Early stage (X100); samples were collected at 8:30 am. (A) IR28; (B) NTCDm; (C) IR28; (D) Jasmine 85. LDP, Lodicule primordium; PP, Pistil primordium; UGP, Upper glume primordium.

primordium, and lower glume primordium, the young spikelets neighborhood continued to grow (Fig. 5). Upper glume primordium continued to grow creating sterile lemmas. Lower glume primordium continued to grow creating rudimentary glume. At this stage, rachilla primordium was formed.

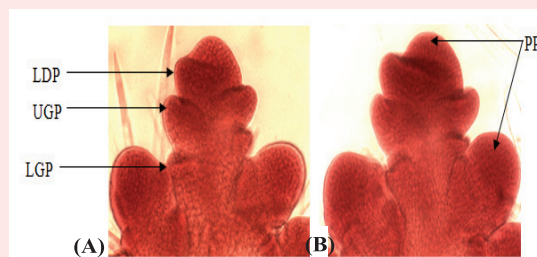


Fig. 5. Middle stage (X40); samples were collected at 8:30 am. (A) IR28; (B) NTCDm.
LDP, Lodicule primordium; LGP, Lower glume primordium; PP, Pistil primordium; UGP, Upper glume primordium.

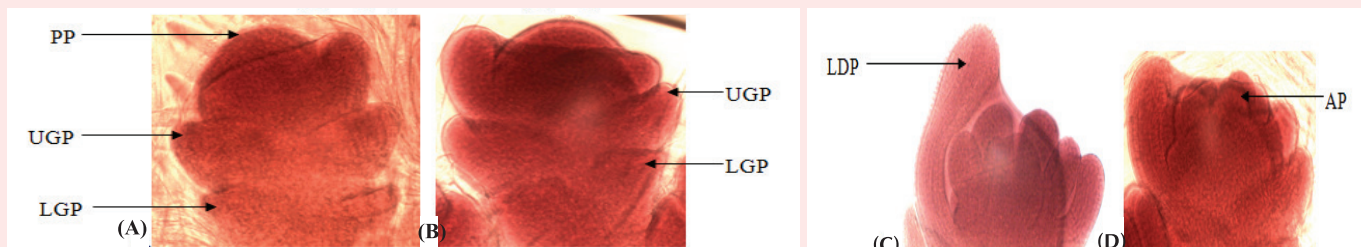


Fig. 6. Late stage (X100); samples were collected at 8:30 am. (A) IR28; (B) NTCDm; (C) IR28; (D) Jasmine 85.

AP, Anther primordium; LDP, Lodicule primordium; LGP, Lower glume primordium; PP, Pistil primordium; UGP, Upper glume primordium.

After LDP, UGP, and LGP, rachilla primordium continued developing and eventually created rudimentary glume, rachis, and rachilla. PP continued developing to create stamens primordium and pistil spikelet primordium. Stamens primordium continued developing to create anther primordium and filament. Pistil spikelet primordium continued to grow creating ovary, style, stigma, and pistil primordium lodicule. At this stage, lodicule primordium and upper glume primordium kept to grow. It could be seen that lodicule primordium forming a thin membrane surrounded inside anther primordium (Fig. 6).

Pollen mother cell differentiation stage:

In the stage of the differentiation pollen mother cells, the parts of the flower had been segmented and developed quite fully. The anthers insided containing pollen mother cells that were preparing to enter the meiosis stage. As for the non-aromatic rice variety IR28, this stage appeared from 57-60 days after sowing; however, it was 67-69 DAS, 62-65 DAS, and 58-61 DAS for NTCDm, TBN, and Jasmine 85, respectively.

In this stage, palea and lemma surrounded stamens and pistil (Fig. 7). The only stamens at this stage were still very

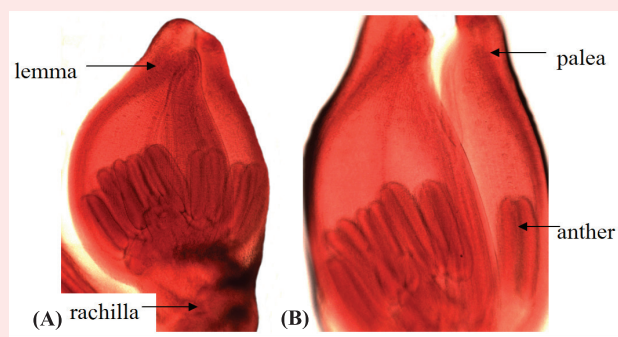


Fig. 7. A spikelet of rice (NTCDm) in Pollen mother cell differentiation stage (A) and Reduction division stage of pollen mother cell (B).

short, six anthers insided containing pollen mother cells preparing to enter the meiosis stage.

Reduction division stage of pollen mother cell:

At the stage of meiosis, pollen mother cells inside the anther started dividing and reduced to enter the process of pollen formation (Fig. 8). For non-aromatic rice (IR28), this stage appeared from 60-62 days after sowing vs aromatic rice NTCDm 69-71 DAS, TBN 65-67 DAS and Jasmine 85 63-65 DAS. The only longer stamens developed at this stage and the pollen mother cells inside anther started dividing reduced.

A bivalent number appeared in the diplotene stage showing differences (Fig. 9). As for non-aromatic rice (IR28), it had 11-12 bivalents staining, while the aromatic rice (NTCDm, TBN and Jasmine)

had 7-8 bivalents staining.

The amount of homologous chromosomes was different in the aromatic rice varieties and the control variety. This might have been due to the configuration of the Rab1 chromosome in the arrangement of the aromatic rice centromere location and unusual tips. Because of the findings of a report [6, 7], Rab1 configuration in rice were found in the wood tissue cells and undifferentiated cells in anthers. The change of Histon and DNA methylation patterns influenced chromosome arrangements. Santos and his colleagues suggested that the DNA dimethylation in rice was caused by the non-aggregation induced chromatin configuration Rab1 in the presence of abnormal tissue. These things started happening at the stage of cell division. The finding of their report [8] showed that the arrangement of chromosome

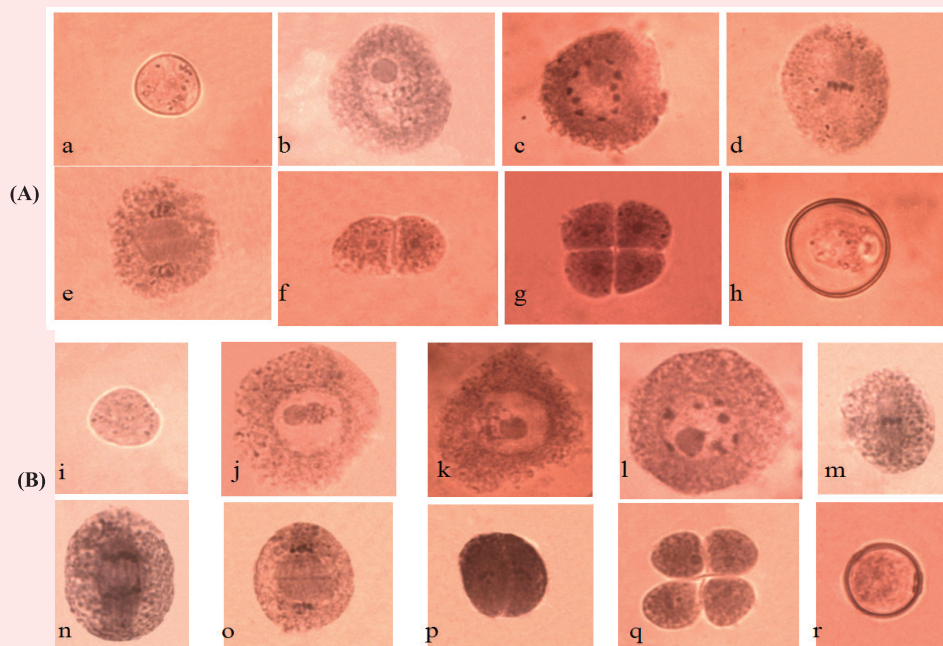


Fig. 8. Pollen formation process of IR28 (A) and TBN (B); pollen mother cell (a, i); leptotene (j); zygotene (b); pachytene (k); diplotene (c, l); metaphase I (d, m); anaphase I (n); early telophase I (e, o); telophase I (f); metaphase II (p); telophase II (g, q); pollen grains (h, r).

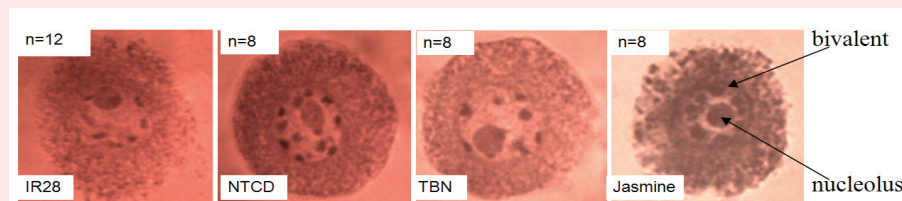


Fig. 9. Bivalent number appears in diplotene stage (X100).

territories within the nucleus exhibits dynamic changes in response to various internal and external conditions. Histone modification and DNA methylation patterns were expected to affect chromosome organization, although data on this subject is still scarce. Nevertheless, it had been shown that in rice DNA demethylation causes chromatin decondensation and induced Rab1 configuration in those tissues in which Rab1 was not normally presented. The structure no longer showed Histon heterochromatin. Heterochromatin's active and inactive chromatin caused no chromatin condensation. The results were of the chromosome being dye stained or faintly dye stained. The bivalent diplotene stage in aromatic rice varieties were not dye stained (or faded dye stained), they did not appear (or sometimes faintly appeared) at this stage.

Extine formation stage:

In the extine formation stage, the majority of maternal cells were split to form four spores. As for non-aromatic rice (IR28), this stage appeared from 62-64 days after sowing vs aromatic rice NTCDm 71-73 DAS, TBN 67-69 DAS and Jasmine 85 63-65 DAS. During this period, filament and style developed longer. Anther switched from white to pale yellow. Palea and lemma were thicker and stiffer.

Ripe pollen stage:

In the ripe pollen stage, pollen grains were preparing to go into the process of forming spores. As for non-aromatic rice (IR28), this stage appeared from 64-71 days after sowing while an aromatic rice NTCDm 73-80 DAS, TBN 69-76 DAS and Jasmine 85 65-72 DAS. In this phase, the anthers were yellow, inside anther contained pollen

ripening process of preparing to enter form gametes.

Conclusion and suggestion

In the formation and development of rice spikelet, there were two clear points of differentiation between the aromatic rice and the non-aromatic rice: the small lobes were positioned differently and the number of homologous chromosomes stained were different. In the non-aromatic rice (IR28), there were no small lobes at the branch primordium, and the number of bivalents staining appeared with 7-8 pairs, while the opposite was viewed in the aromatic rice, there were small lobes at the branch primordium, and the number of bivalents staining appeared 11-12 pairs in diplotene stage.

This report is only the beginning. More research should continue on to understand rice flavor. It might help rice breeders for use as a monitoring tool for exact selections of aromatic rice.

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REFERENCES

- [1] Dinh Van Lu (1978), *Rice plant book*, Agriculture Publisher, 128 pp. (in Vietnamese).
- [2] Nguyen Ngoc De (2008), *Rice Plant Book*, Can Tho University, 243 pp. (in Vietnamese).
- [3] Tran Cong Khanh (1980), *Microscopy techniques*, Medicine Publisher, Hanoi, 134 pp. (in Vietnamese).
- [4] S. Matsushima (1970), *Crop Science in Rice - Theory of yield determination and its application*, Fuji Publishing Co., Ltd., Tokyo, Japan.
- [5] Shouichi Yoshida (1981), *Fundamentals of rice crop science*, The International Rice Research Institute, Los Bãnos, Laguna, Philippines, P.O. Box 933, Manila, Philippines, 268 pp.
- [6] P. Prieto, A.P. Santos, G. Moore, P. Shaw (2004), "Chromosomes associate premeiotically and in xylem vessel cells via their telomeres and centromeres in diploid rice (*Oryza sativa*)", *Chromosoma*, **112**, pp.300-307.
- [7] A.P. Santos, P. Shaw (2004), "Interphase chromosomes and the Rab1 configuration: does genome size matter?", *J. Microsc.*, **214**, pp.201-206.
- [8] A.P. Santos, L. Ferreira, J. Maroco, M.M. Oliveira (2011), "Abiotic stress and induced DNA hypomethylation cause interphase chromatin structural changes in rice rDNA loci", *Cytogenet Genome Res*, **132**(4), pp.297-303.

Research and development of acacia hybrids for commercial planting in Vietnam

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Abstract:

“Acacia hybrids” refers to the inter-specific hybrids of *A. mangium* and *A. auriculiformis*, including natural, artificial and polyploid ones. The superiorities of selected acacia hybrid are fast growth, straight stem form, small branches, high productivity, and high ratio of wood utilisation. Acacia hybrids are recognized as having a higher pulping potential and greater soil improvement ability than that of the parental species, which may be shown to have 2.5-13 times larger numbers of nitrogen - fixing nodules on its roots in nursery stage. Mass propagation technology using both cutting and tissue culture has been successfully developed for acacia hybrid, enabling large-scale clonal forestry to improve plantation productivity and quality. The area of acacia hybrid plantations up to 2016 was estimated to be 500,000 ha, with an annual increase of 30,000-35,000 ha, making it the most widely planted forest tree variety in Vietnam. Acacia hybrids and propagation technologies have also been introduced in Malaysia, Indonesia, Thailand, Laos, and Cambodia. The research and development of acacia hybrid breeding can be considered as a revolution in the forestry sector and has created new and advanced approaches for both research and training in tree breeding in Vietnam.

Keywords: *Acacia auriculiformis*, *Acacia hybrid*, *Acacia mangium*, cutting propagation, nodules, tissue culture.

Classification number: 3.1

Introduction

“Acacia hybrid” (“keo lai” in Vietnamese language) is a common name used to refer to the interspecific hybrids between *A. mangium* and *A. auriculiformis*. The name refers to several types of hybrids, including natural, artificial and polyploid ones.

The study of breeding and deployment of acacia hybrid varieties for commercial planting in Vietnam began in the 1990s when the area of land covered by forests had been reduced to 25%, and the yield of plantations was very poor (approx. 5-8 m³/ha/year). At that time, there was no appropriate forest planting

varieties selected, planting was mostly focused on “reforestation”, and cutting propagation was being implemented only at an experimental scale, with no mass - production of clonal planting stock. The huge areas of denuded hills and barren land were mostly planted with a land race of *Eucalyptus camaldulensis* derived from the Binh Dinh area of Vietnam having very poor productivity, but using more water per unit volume of wood produced than other species, leading to just a few scattered planting areas; and thusly, this eucalypt variety was not accepted for production forestry in Vietnam.

At that time, *E. camaldulensis* (Petfordp rovenance) gave the highest yield of available planting varieties, but the yield was still less than 15 m³/ha/year and this variety proved to be susceptible to leaf blight diseases, such as *Cylindrocladium* and *Kirramyces*, which defoliated the canopy of many plantations, resulting in a major loss of wood production.

Natural acacia hybrids have been observed in Malaysia [1, 2], Papua New Guinea [3] and Thailand [4]. Propagation of these acacia hybrids by tissue culture propagation was studied [5, 6]. However there was a propensity to use either seeds or untested clones of acacia hybrids for planting, and as a consequence, acacia hybrids were not developed for commercial planting in those countries.

Natural acacia hybrids were detected in 1993 in *A. mangium* plantations in some regions of Vietnam [7]. Although the acacia hybrid was found later than in other countries, it was quickly selected and developed for forestry production in Vietnam through the application of progresses in genetics and cytology.

With support from the Ministry of Agriculture and Rural Development (MARD), the Ministry of Science and Technology (MOST), and relevant international organizations, as well as the active engagement of forest growers, there are now more than 500,000 ha of acacia hybrid plantations throughout the country.

The superior characteristics of acacia hybrids

Fast growth, straight stem form and small branches

Acacia hybrids have proven to be superior to both *A. mangium* and *A. auriculiformis* for their traits, that provide both high plantation productivity and commercial wood yield, as observed in trials in Vietnam [8]. In morphological characteristics of phyllodes, flowers, pods, and bark, acacia hybrids are intermediate between *A. mangium* and *A. auriculiformis* (Fig. 1).

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Fig. 1. Phyllode (above) and young pod (below) of *A. mangium* (left), acacia hybrid (middle), and *A. auriculiformis* (right).

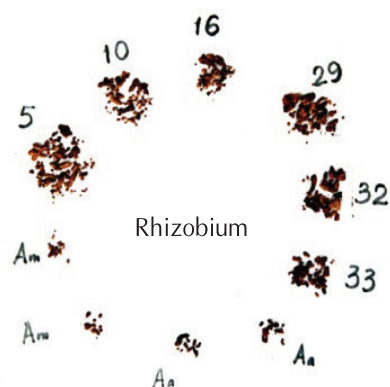


Fig. 2. Nodules on roots of acacia hybrids of its parental species at the nursery stage.

1. 5, 10, 16, 29, 32, 33 are acacia hybrid clones: BV5, BV10, BV16, BV29, BV32, BV33.

2. Am means *A. mangium* cutting; Am means *A. mangium* seedling.

3. Aa means *A. auriculiformis* cutting; Aa means *A. auriculiformis* seedling.

Higher pulping potential

Kraft pulp yield of acacia hybrids was 51.1%, whereas that of both *A. auriculiformis* and *A. mangium* was less than 48%. Paper produced from acacia

hybrids has a tensile-strength and folding-strength ranging from 7,700-8,420 m and 2,000-3,000 times, respectively. These values are higher than the corresponding values of 5,460 m and 1,200 times for *A. mangium* and 6,270-6,300 m and 1,700-2,000 times for *A. Auriculiformis* [9].

Better nitrogen fixing potential

At the nursery stage, the number of nitrogen - fixing nodules on acacia hybrid roots range from 39.9-80.3 nodules per sapling, 2-13 times greater than the values for the parental species (Fig. 2) and equal to 0.39-0.47 g per sapling in weight, which is 2.6, 70 times greater than the parental species (0.075-0.15 g per sapling). The total number of bacteria (*Rhizobium*) in one gram of soil from under an acacia hybrid is 1,760 million, 5-17 times higher than that of the parental species (101-386 million), and 96 times higher than the soil samples collected in barren land (18.4 million). These parameters indicated that acacia hybrids have a significantly higher potential for soil improvement than both *A. mangium* and *A. auriculiformis* [10].

Research on acacia hybrids and plantation expansion over time

Research on breeding and development

of acacia hybrid varieties for commercial planting in Vietnam can be described as to occur during two major periods:

The period of 1993-2000

Natural acacia hybrids in *A. mangium* trial areas was discovered in Vietnam.

Biological, morphological characteristics, and variations in growth, pulping potential, wood properties, and soil improvement abilities of natural acacia hybrid were determined.

The segregation and regression of second generation (F_2) acacia hybrids that demonstrated the need for vegetative propagation of selected clones was studied.

Research and the development of techniques for cutting and tissue culture propagation were performed.

A clonal test of acacia hybrids at large scales in different ecological regions throughout the country was established.

Research on artificial hybridization, and evaluating the differences among acacia hybrid varieties by molecular markers was performed.

The period of 2000-2015

Protocols for cutting-tissue propagation for acacia hybrids were completed, installed, and widely applied in many forest tree enterprises, as well as the development of acacia hybrid germplasms in Vietnam.

Research on artificial hybridization was continued, breeding new acacia varieties using new strategies, such as generating acacia triploids that are expected to be sterile and fast growing (Fig. 3), complete with early selection and testing trials.

The transfer of germplasm and propagation technology for some forest research and production units in the country was implemented; for instance, the Nguyen Hanh Company in Binh Dinh conducted the WB3 Project in the five provinces of Central Vietnam, and other South East Asian countries, including Indonesia, Thailand, Cambodia, and Laos.



Fig. 3. Segregation of F_2 acacia hybrid seedlings exhibits the morphology of *A. mangium*, *A. auriculiformis*, and others.

Major research activities for acacia hybrids in Vietnam

After discovering and completing basic research, acacia hybrids were propagated via cuttings. Clonal tests were established in many regions in Vietnam, meanwhile, other research was being carried out, including studies of tissue culture propagation, fertilizer application, drought tolerance assessment, and genetic fingerprinting of clones using molecular markers.

Clonal tests

Acacia hybrid clonal tests were established from 2000 to 2015 in many provinces of Vietnam, including in Yen The (Bac Giang), Ba Vi (Ha Noi), Yen Thanh (Nghe An), Binh Dien and Phu Loc (Thua Thien - Hue), Quy Nhon (Binh Dinh), Long Thanh (Dong Nai), and Bau Bang (Binh Duong). All of these tests verified the superior productivity of these acacia hybrid clones, with mean annual incremental growth of 2-3 times that of the best provinces of *A. mangium* and 3-10 times the best provenances of *A. auriculiformis* [11-16] (Table 1).

Fingerprinting of acacia hybrid clones by molecular markers

At the end of the 1990s, with support provided by Australian molecular scientists [17], a set of molecular markers was used to recognize the identity of acacia hybrid clones selected and field - tested in North Vietnam (BV5, BV10, BV16, BV23, BV27, BV32, and BV33). Two microsatellite markers, namely Am030 and Am435, proved to be suitable to identify the differences among the seven tested acacia hybrid clones. At later stages, in addition to

these two markers, another eight markers: Am136, Am164, Am387, Am396, Am460, Am484, Am502, and Am770, also proved suitable to recognize the differences and identity of all (both previous, and newly selected and field-tested) acacia hybrid clones [18].

Research on artificial hybridization between *A. mangium* and *A. auriculiformis*

Methods from recent research of artificial hybridization was implemented aiming to generate cross-combinations between either *A. mangium* and *A.*

Table 1. Growth of acacia hybrids in some clonal tests in the period of 2000-2015.

No.	Germplasm	Growth traits			Mean annual increment (m ³ /ha/year) (75% survival)
		<i>D</i> _{BH} (cm)	<i>H</i> (m)	<i>V</i> (dm ³)	
A Natural acacia hybrid (Nah) clones					
1	<i>Ba Vi (Ha Noi) (2000-2009)</i>				
	7 best Nah clones	16.5-19.2	16.5-16.8	178.3-249.7	24.7-34.5
	<i>A. mangium</i> (Pongaki)	11.9	11.8	76.8	10.6
	<i>A. auriculiformis</i> (Coen R.)	6.3	7.9	14.6	2.0
2	<i>Yên Thanh (Nghe An) (2000-2008)</i>				
	7 best Nah clones	15.2-17.6	18.8-20.7	194.4-260.4	30.3-40.5
	<i>A. mangium</i> (Pongaki)	12.0	15.0	100.7	15.7
	<i>A. auriculiformis</i> (Coen R.)	7.4	8.2	19.1	3.0
3	<i>Bau Bang (Binh Duong) (1999-2004)</i>				
	7 best Nah clones	13.7-14.3	17.8-21.1	144.0-164.4	33.5-41.1 ⁽¹⁾
	<i>A. mangium</i> (Pongaki)	122.4	16.0	120.0	14.5 ⁽¹⁾
	<i>A. auriculiformis</i> (Coen R.)	9.4	12.2	106.9	4.1 ⁽¹⁾
4	<i>Long Thanh (Dong Nai) (2005-2010)</i>				
	5 best Nah clones	14.4-14.7	-	452.4-500.9	42.2-43.3
5	<i>Quy Nhon (Binh Dinh) (2008-2015)</i>				
	6 best Nah clones	14.6-16.0	18.6-20.1	175.3-208.4	30.3-38.5
	<i>A. mangium</i> (Pongaki)	11.6	15.6	103.2	10.3
	<i>A. auriculiformis</i> (Coen R.)	9.3	13.8	56.6	4.8
B New natural acacia hybrid (NNah) clones					
6	<i>Phu Loc (Thua Thien - Hue) (3/2011-9/2014)⁽²⁾</i>				
	3 best NNah clones	13.2-13.5	11.9-12.6	83.3-89.0	29.5-31.7
	BV10	13.2	12.5	87.3	31.0
7	<i>Ba Vi (Ha Noi) (2011-2014)</i>				
	4 best NNah clones	11.3-12.2	10.1-11.0	61.3-73.6	25.4-30.5
	BV32, BV33, and BV73	11.0-11.1	9.8-10.4	47.3- 55.4	19.6-23.0
8	<i>Yên The (Bac Giang) (2012-2015)</i>				
	5 best NNah clones	10.5-11.5	13.1-13.3	57.3-68.4	23.9-28.4
	BV16, BV33, and BV73	9.7-10.1	12.8-13.7	48.6-52.9	20.2-21.9
C Artificial acacia hybrid (Aah) clones					
9	<i>Ba Vi (Hanoi) (2001-2008) (at Cam Quy)</i>				
	3 best Aah clones	13.7-14.0	13.0-13.3	97.9-108.8	15.4-16.2 ⁽¹⁾
	<i>A. mangium</i> (Pongaki)	10.3	10.8	53.7	8.4 ⁽¹⁾
	<i>A. auriculiformis</i> (Coen R.)	7.8	9.0	25.1	3.9 ⁽¹⁾
10	<i>Binh Dien (Thua Thien - Hue) (2003-2008)</i>				
	3 best Aah clones	12.0-12.5	12.7-13.3	78.1-81.0	27.8-28.8
	BV16	12.1	13.3	80.8	28.7
D Triploid acacia hybrid (Tah)					
11	<i>Song May (Dong Nai) (8/2014-11/2015)</i>				
	TahX101	7.51	7.53	16.87	-
	BV10	6.66	6.75	12.44	-
	BV16	6.21	7.27	11.18	-

Note: (1) Productivity was calculated based on survival; (2) New acacia hybrid clones recently selected.

auriculiformis, or reciprocal backcrosses to the parent species. In a period from 1997-2015, many cross - combinations were produced and tested in the field. Some outstanding individual clones were selected in comparison with the best provenances of the parental species (Table 1) [11, 19].

Initial research on breeding acacia hybrid triploids

Within the framework of research cooperation between Vietnam's Institute of Forest Tree Improvement and Biotechnology (IFTIB) and Australia's University of Tasmania (UTAS) and Commonwealth Scientific and Industrial Research Organization (CSIRO), under sponsorship of the Australian Centre for International Agriculture Research (ACIAR), research on breeding of acacia triploids commenced in 2003.

Acacia triploids were created by hybridization between 4n *A. mangium* which are quite slow-growing [20] and the fast-growing 2n *A. auriculiformis* in the hybrid orchard at Bau Bang (Binh Duong province). Preliminary results of field tests at Song May (Dong Nai province) showed that at the age of 15 months after planting, triploid hybrid clone X101 is growing faster than (diploid) acacia hybrids BV10 and BV16, whereas at Dong Ha (Quang Tri province) at the age of one year X101 was growing faster than acacia hybrid BV10, but slightly slower than BV16 [21] (Fig. 4).

Fertilizer application and drought tolerance of acacia hybrid clones

Three different fertilizer treatments that were applied before planting consisted of 2 kg of cattle manure + 100 g superphosphate; 2 kg of cattle manure + 300 g NPK (5:10:3), and 6 kg of cattle manure that indicated that in Ba Vi, acacia hybrid stem volume increased by 63-119% compared with a control sample (no fertilizer) at a three year-old plantation. Treatment of 2 kg of cattle manure + 200-300 g superphosphate increased volume by only 20% over the control [8]. Although fertilizers, such as NPK and superphosphate, that incorporate phosphorus increased growth rate of acacia hybrids in the first one to three years after planting, and the addition of a large dose of P does not greatly increase wood yield of acacia hybrids over a full crop rotation, as shown by the results of more recent experiments in Binh Phuoc [22] and Quang Tri.



Fig. 4. Acacia hybrid triploid and BV16 (15 months) at Song May commune (picture from Nghiem Quynh Chi, 2015).

Identification of drought tolerance through some cytological indices, e.g. transpiration intensity, osmotic pressure of the leaf, wilting rate..., determined that the most drought-tolerant clone at the nursery stage was BV32.

Cutting and tissue culture propagation

Regression and segregation of acacia hybrid in the second generation (F_2):

In terms of growth, tree height and diameter at breast level over bark (D_{BH}) of F_1 acacia hybrid cuttings at 22 months, reached 5.8 m and 6.1 cm, respectively, at Ba Vi, North Vietnam. By comparison, F_2 acacia hybrid seedlings and pure species seedlings ranged from 3.8-4.3 m in height and 3.7-4.5 cm in diameter (60-70% of the values of the F_1). Regarding phyllode morphology, the segregation of F_2 acacia hybrid seedlings yielded 16.4% similar to

A. mangium, 50.1% intermediate between *A. angium* and *A. auriculiformis*; 27.3% similar to *A. auriculiformis*; and 6.2% were misshapen [8]. It was concluded that F_2 seedlings collected from acacia hybrid trees should never be used for plantation forestry because of the strong regression and segregation (Fig. 4).

Acacia hybrid vegetative propagation by cuttings and tissue culture:

Tissue culture in acacia hybrids reported by Darus using basic Murashige and Skooge (MS) medium supplemented with 6-Benzylaminopurine (BAP) 0.5 mg/l for shoot multiplication and river sand for rooting, obtained a 70% rooting rate [5, 6]. In Vietnam, tissue culture propagation was first studied by Nguyen Ngoc Tan, *et al.* [23], and studies were continued by Doan Thi Mai, Ngo Minh Duyen, Le Son, and others (Fig. 5).



Fig. 5. Acacia hybrid tissue culture plantlets (left) and cuttings (right)
Note: Tissue culture plantlets have bipinnates, pinnates and phyllodes whereas the cuttings just have phyllodes (picture from Doan Thi Mai).

Another effective propagation method is by rooting stem cuttings. This was first implemented by Le Dinh Kha and others to propagate the first acacia hybrid clones in Vietnam. In late 1999, Le Dinh Kha *et al.* used tissue culture plantlets of seven acacia hybrid clones to root directly on sterile river sand in Malaysia and obtained a rooting rate of 97.8-100% after one month [11]. Plants that are re-captured into tissue culture from clonal ramets grown in the field and propagated by tissue cultures display rejuvenation, in comparison with plants produced by repeated serial rooting of cuttings. The technology combining tissue culture and cutting (*tissue culture - cutting propagation technology*) was therefore recommended as the most effective propagation method to introduce acacia hybrids into mass-production, and also to maintain the physiological vigour of acacia hybrid clones.

Outstanding achievements in acacia hybrid research and development

Application of genetic principles and cytological technologies on forest tree breeding has led to the key successes of acacia hybrid research and development in Vietnam, getting its start from the discovery until deployment and utilization of hybrid vigor together with clonal forestry for plantations. This success contributed to a new approach in forest tree improvement of other species.

Acacia hybrid research and development programs have utilized natural variations, which are characteristics of long-lived tree species, as well as actively generating new sources of variation through artificial hybridization, tetraploid induction and infertile triploid production, early selection and molecular genetic application. Some triploid clones now under field testing are of great interest to national and international forest tree breeding organizations.

In general, selected acacia hybrid varieties have demonstrated higher yield, better stem quality, higher pulp yield, and potential for soil improvement than the parental species (in spite of their being developed 12-15 years later than in other countries).

At present, the package of acacia hybrid germplasms and propagating technologies have been transferred to many forest tree production units, leading to a



Fig. 6. Cuttings area of acacia hybrids with mist sprinklers in Binh Dinh.

mass movement of acacia hybrid planting in Vietnam that contributed remarkably to increase deplantation productivity, enhanced awareness of the importance of tree breeding to plantation forestry, decrease deforestation, and increase forest cover as well as protecting environmental values in Vietnam.

Development of acacia hybrids in Vietnam and other regional countries

Procedure for acacia hybrid propagation and clonal plantation

Acacia hybrids have rapidly developed into an operational scale after being successfully mass-propagated by cutting and tissue culture technology. The practical procedure for acacia hybrid propagation and clonal plantation was written by the Research Centre of Forest Tree Improvement (RCFTI) and issued by Ministry of Agriculture and Rural Development (MARD) under Decision No. 3092 QD/BNN-KNCN dated 22/10/2006. Then, a series of training courses on cutting-tissue culture technology and germplasm transfer for a number of relevant organizations in Vietnam was organized through collaboration between RCFTI and the Department of Agriculture and Forestry Extension of MARD (Fig. 6).

Germplasm and propagating technology transfer

The period of 1996-2000:

Acacia hybrid varieties and propagation technology were transferred to the Japanese company, Oiji Pulp and Paper Corporation, located on Quy Nhon (Binh Dinh), Ho Chi Minh City Seeds Joint Stock Enterprise,

Yen Lap (Quang Ninh), Quy Nhon (Binh Dinh), and Luong Son Agro-Forestry Companies (Hoa Binh).

The period of 2000-2015:

The implementation of transfer courses to numerous forest tree research and production centers in the whole country continue on a scale from two to ten million saplings per year.

The technical courses, together with a semi-automatic sprinkler irrigation system, were transferred to many Forestry Farms and even households, particularly in Binh Dinh (Fig. 6). 152 million acacia hybrid plantlets were also produced in 2014, but that still did not meet the demand for varieties for plantation forestry within the province and other Central Highland provinces.

Protocols for rejuvenation of some major acacia hybrid planting clones such as BV10, BV16, and BV32 were completed; following these protocols, they have retained their superiority in growth rate and other stem quality traits over 20 years.

At present, the Institute of Forest Tree Improvement and Biotechnology (IFTIB) has played consultative role in acacia hybrid breeding and development for Vietnam Paper Corporation, Tan Mai Paper Corporation, An Hoa Paper Company, and Vietnam Forest Corporation.

Development of acacia hybrids for plantation forestry in provinces of Vietnam

In 1997, the area of acacia hybrid plantations was 1,300 ha, however by 2001,

Table 2. Estimates of current areas and ratio of acacia hybrids in the period of 2010-2014 in some provinces of central Vietnam [24].

Province	2010		2011		2012		2013		2014		Mean ratio (%)
	Area (ha)	Ratio (%)	Area (ha)	Ratio (%)	Area (ha)	Ratio (%)	Area (ha)	Ratio (%)	Area (ha)	Ratio (%)	
Quang Binh	1,938	40.5	2,911	55.5	3,167	64.0	2,100	48.8	4,080	58.4	53.4
Quang Tri	959	20.5	-	-	1,670	26.5	2,000	34.8	3,000	50.1	33.0
Th.Thien - Hue	3,800	87.8	4,220	84.6	3,543	84.3	3,510	88.1	2,807	69.3	82.8
Da Nang	275	29.5	196	65.2	605	62.1	350	70.0	150	21.4	49.6
Quang Nam	5,106	16.4	-	-	295	18.0	-	-	1,179	64.9	33.1
Quang Ngai	6,400	76.2	4,707	73.0	3,930	70.5	5,000	71.4	-	-	72.8
Binh Dinh	8,665	89.1	-	-	9,296	96.4	9,164	96.1	9,103	93.3	93.7
Phu Yen	7,719	93.0	1,506	47.1	2,469	61.3	-	-	4,749	77.4	69.7
Khanh Hoa	550	43.7	478	74.9	1,450	73.2	1,050	53.1	1,300	76.2	64.2
Binh Thuan	2,483	59.1	1,863	62.8	2,573	80.8	-	-	2,500	78.1	70.2
Total area	37,895		15,881		28,998		23,174		28,868		62.3

it had increased to 10,200 ha. According to Vietnam Forestry Administration's statistical data in 20 provinces, the total area of acacia hybrid plantations reached 179,890 ha in the period 2010-2014 [24].

Another report by the Australia International Economy Centre (funded by ACIAR) estimated that total area of acacia hybrid up to 2004 was 127,000 ha with an annual increase of 37,000-46,000 ha occupying 24% of total forest plantation area in Vietnam.

Following the data issued by Forestry Departments of 20 provinces, it was 25,000-45,000 ha, occupying 30-40% of total forest areas in country. In only 10 provinces located from North Central to Coastal South Central Vietnam such as Quang Ngai, Thua Thien - Hue and Binh Dinh, where the harbors were suitable for wood chip export, and having active Forestry Projects of WB3 funded by World Bank, acacia hybrid planting areas increased to 70-90% of total annual planting area (Table 2).

Transferring acacia hybrid clones and propagation technology to foreign counterparts

Many regional forestry organizations noted the results of research and development of acacia hybrids in Vietnam.

Since 1996 acacia hybrid varieties have been introduced for testing and planting through multinational companies such as the Oiji Pulp and Paper Corporation of Japan located in Quy Nhon (Binh

Dinh), and the Ta Ann Sarawak Plywood Production Corporation of Malaysia (1999), Indonesia (2002), and Cambodia (2003).

Subsequently, acacia hybrid varieties were transferred or exchanged to Thailand Tree Breeding Research Centre (Royal Forestry Department), Forestry Research Institute of Malaysia (FRIM), Guangzhou Tropical Forestry Research Institute (China) via a collaboration of RCFTI, and Salwood Ltd. Company (Australia).

Recently, technology transfer courses for Kasetsart University of Thailand and Forestry University of Laos as well as Stora Enso (Sweden - Finland) and Birla (India) corporations in Laos have been implemented.



Fig. 7. ACIAR's research program managers at a pruning trial in Long Dai Forestry Company in Quang Binh 2003. Dr. C. Hardner (left) and former manager Dr. J. Fryer (center).

Benefits from acacia hybrid research

Scientific and technological benefits

Research of acacia hybrids has created a new approach to forest tree breeding, which leads to numerous studies of plant physiology, biotechnology, silviculture, and wood processing. As a result, there have been a series of national and international projects implemented in Vietnam, and many scientific papers published, as well as MSc & PhD candidates trained (Fig. 7 and Table 3).

Table 3. Publications related to acacia hybrid.

Type of publication	Number
<i>A Author group</i>	
1 Monograph books	7
2 Papers published on national journals	28
3 Papers published on international journals	11
4 MSc theses	4
5 PhD theses	1
<i>B Other authors</i>	
1 Books	1
2 Papers published on national journals	88
3 Papers published on international journals	17
4 MSc theses	62
5 PhD theses	5

Socio - economic and other benefits

Economic benefits:

The productivity levels of highest quality acacia hybrid clones is 20-40 m³/ha/year, higher than that of *A. mangium* at 12-18 m³/ha/year (Table 1).

Local timber markets reported that mean productivity of acacia hybrids was 25 m³/ha/year while *A. mangium* was only 15 m³/ha/year.

Given the current economic conditions, acacia hybrid plantations could benefit by 280 billion VND per year compared with *A. Mangium*, because annual total areas of acacia hybrid plantation harvested in Vietnam is 35,000 ha with stable price of 800,000 VND/m³ (35,000 ha x 10 m³/ha/year x 800,000 VND/m³ = 280,000,000,000 VND).

Social and environmental benefits:

Apart from faster growth rates, higher productivity, a high measure of wood utilization, and greater paper strength,

acacia hybrids carry more nitrogen - fixing nodules than *A. mangium* and *A. auriculiformis* resulting in better soil quality and adaptation. In addition, acacia hybrids are easy to propagate via cuttings; making selected clones readily available; therefore, it has been adopted well by growers for planting over the country generating a national planting movement.

Planting acacia hybrids is not only for reforestation and short - term harvest, but also for increasing local people's income, especially people living in remote areas. It has also contributed significantly to hunger and poverty alleviation and environmental improvement.

It can be said that development and use of acacia hybrids has created a movement in forestry research and training in Vietnam.

Conclusion

"Acacia hybrid" is a common name to refer to the interspecific hybrids of *A. mangium* and *A. auriculiformis*, and can be separated into natural, artificial and polyploid hybrids.

The superiority of acacia hybrids over the parent species is present in its fast growth, straight stem form, small branches, high productivity, and high recovery of commercial wood.

Acacia hybrids have been recognized as having a higher pulping potential and greater capacity for soil improvement.

Mass propagation through cutting and tissue culture technologies has been successfully developed for acacia hybrids, generating uniform planting material of selected clones to improve plantation productivity and quality.

Up to 2016 year, the area of acacia hybrid plantations are estimated to be about 500,000 ha and this is expanding at about 30,000-35,000 ha per year, making it the most widely planted forest tree variety in Vietnam. Its propagation technology has also been introduced into other ASEAN countries.

The research and development of acacia hybrid breeding can be considered as a revolution in the forestry sector and has created new and advanced approaches for both research and training in tree breeding in Vietnam.

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REFERENCES

- [1] K.C. Tham (1976), "Introduction to Plantation Species. *A. mangium* Wild", *Proceeding of the 6th Malaysian Forestry Conference*, Kuching, Sarawak, Malaysia, Sarawak Forest Department, pp.153-158.
- [2] C.W. Rufelds (1988), "*A. Mangium* and *A. Auriculiformis* and Hybrid *A. mangium* x *A. auriculiformis* Seedling Morphology Study", *Forest Research Centre Publication*, **41**, p.109.
- [3] J.W. Turnbull, P.N. Martensz, N. Hall (1986), "Notes on Lesser - Known Australian Trees and Shrubs with Potential for Fuelwood and Agroforestry" In J.W. Turnbull ed, *Multipurpose Australian Tree and Shrubs: Lesser Known Species for Fuelwood and Agroforestry*, ACIAR, Canberra, pp.81-113.
- [4] S. Kijkar (1992), *Handbook on Vegetative Propagation of A. mangium x A. auriculiformis*, ASEAN - Canada Forest Tree Seed Centre, Saraburi, Thailand, p.19.
- [5] H.A. Darus (1991), "Micropropagation Techniques for *A. mangium* x *A. auriculiformis* Breeding Technologies for Tropical Acacias", *ACIAR Proceedings*, **37**, pp. 119-121.
- [6] H.A. Darus (1993), "Large Scale Production of *A. mangium* x *A. auriculiformis* Hybrids Plantlets by Micropropagation Techniques", *Proceedings of the Regional Symposium on Recent Advances in Mass Clonal Multiplication of Forest Trees for Plantation Programmes*, FAO, FORTIP, UNDP Los Banos, Philippines, pp.204-269.
- [7] Le Dinh Kha, Nguyen Dinh Hai, Pham Van Tuan (1993), "Natural Hybrid Between *A. mangium* and *A. auriculiformis*", *Forestry Review*, **7**, pp.18-19.
- [8] Le Dinh Kha (1999), *Studies on The Use of Natural Hybrids Between A. mangium and A. auriculiformis in Vietnam* (Vietnamese), Agriculture Publishing House, Hanoi, 207p (English, 2001, 171p).
- [9] Le Dinh Kha, Le Quang Phuc (1995), "Paper Pulp Potential of Acacia Hybrid", *Forestry Review*, **3**, pp.6-7.
- [10] Le Dinh Kha, Ngo Dinh Que (2000), "Soil Improvement Ability of Acacia Hybrid and Some Other Acacia Species Planted on Bare Hills", *Forestry Review*, **6**, pp.11-14.
- [11] Le Dinh Kha (2003), *Selection, Breeding and Propagation of Some Main Plantation Tree Species in Vietnam* (Vietnamese), Agriculture Publishing House, Hanoi, 291p.
- [12] Le Dinh Kha, C. Harwood, C.S. Baltunis, Nguyen Duc Kien, Nguyen Dinh Hai, Ha Huy Thinh (2012), "Growth and Wood Basic Density of Acacia Hybrid Clones at Three Locations in Vietnam", *New Forests*, **43**, pp.13-19.
- [13] Le Dinh Kha, Nguyen Thi Thanh Huong, Nguyen Van Du, Tran Ho Quang, Mai Trung Kien (2013), "Results of Clonal Test for New Acacia Hybrids at Dong Trieu, Phu Loc and Vinh Cuu", *Science and Technology Journal of Agriculture and Rural Development*, Special issue on crops and domestic animals, **1(12)**, pp.255-268.
- [14] Ha Huy Thinh, Le Dinh Kha, Phi Hong Hai, Nguyen Duc Kien, Doan Thi Mai, Tran Ho Quang (2011), *Selection, Breeding and Propagation of Some Main Plantation Tree Species in Vietnam*, Agriculture Publishing House, Hanoi, **3**, 181p.
- [15] Ha Huy Thinh, Phi Hong Hai, Nguyen Duc Kien (2011), *Selection, Breeding and Propagation of Some Main Plantation Tree Species in Vietnam*, Agriculture Publishing House, **4**, 155p.
- [16] Ha Huy Thinh, Collaborators (2015), "Selection, Breeding, and Propagation of Some Main Plantation Tree Species in Vietnam", *Scientific Report of the Project of the MARD*.
- [17] Butcher (2001), *Letter to Research Centre for Forest Tree Improvement on the Use of Microsatellites in Forest Tree Improvement* (see Le Dinh Kha, 2003, Vietnamese, p.88).
- [18] Tran Ho Quang, Le Dinh Kha (2012), *Report on Identification of New Acacia Hybrids Differences by Molecular Marker* (Scientific Report for Project on Propagation and Test of Newly Selected Natural Acacia and Eucalypt Hybrids in Vietnam, 2009-2013).
- [19] Nguyen Viet Cuong (2015), *Hybridization of Eucalypts, Melaleucas, Acacias, Pines, and Testing for Selection of Hybrids*, Agriculture Publishing House, 202p.
- [20] Le Dinh Kha, R. Griffin, Ha Huy Thinh, J. Harbard, Le Son, Duong Thanh Hoa, Nghiem Quynh Chi (2009), "Research on Identification of Some *A. mangium* Tetraploid's Characteristics in Comparison with Diploid Clones in Vietnam", *Science and Technology Journal of Agriculture and Rural Development*, **9**, pp.114-120.
- [21] Nghiem Quynh Chi (2015), *Information on Research of Acacia Triploid Hybrids of A. mangium and A. auriculiformis in Vietnam*.
- [22] P.V. Bon, C.E. Harwood (2016), "Effects of Stock Plant Age and Fertiliser Application at Planting on Growth and Form of Clonal Acacia Hybrid", *Journal of Tropical Forest Science*, **28(2)**, pp.182-189.
- [23] Nguyen Ngoc Tan, Tran Ho Quang, Ngo Minh Duyen (1997), "Acacia Hybrid Propagation by Meristem Tissue Culture", *Scientific Results of Research on Forest Tree Breeding*, Agricultural Publishing House, **2**, pp.60-66.
- [24] Doan Ngoc Dao (2015), *Planted Area of Acacia Hybrids in Some Provinces in the Years from 2010 to 2014* (Completed data of Vietnam administration).

Advances in research on Rotavin-M1

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Abstract:

“Rotavin-M1” is an oral live-attenuated vaccine that prevents diarrhea in children under five years old, produced from rotavirus strains G1P [1] on Vero cells. This vaccine has been studied for 16 years beginning with monitoring the local circulating strain and eventually establishing a seed lots system. The safety and immunogenicity of the vaccine were found equivalent to internationally-imported vaccines.

Keywords: G1P, Rotavin-M1, vaccine.

Classification number: 3.2

Introduction

The discovery of the rotavirus as one of the major causes of diarrhea in children has led to the expansion of research in order to develop vaccines to prevent or reduce the incidents and mortality from this disease. Epidemiological studies of diarrhea caused by rotavirus were particularly useful as prerequisites for research into a vaccine. Specific preventative measures in Vietnam support and protect general public health, especially that of infants and young children. According to statistic data, the annual incidence of diarrhea caused by rotavirus accounts for over 50% of children under age of five years old hospitalized in pediatric hospitals in Vietnam, and about 5,300 - 6,800 deaths

were reported annually in children under five years old, accounting for 8 to 11% of the mortality rate among children of the same age. Among about 1.64 million of those born annually, it is estimated that 820,000 clinical visits, 122,000 to 140,000 cases of hospitalizations, and 2,900-5,400 deaths were due to diarrhea caused by rotavirus. Rotavirus causes great damage to the national economy. Annual cost used for the treatment of rotavirus diarrhea in Vietnam amounted to US\$ 5.3 million, of which US\$ 3.1 million was direct medical expenses, US\$ 685,000 was the costs spent in other sectors than health, and US\$ 1.5 million was used for indirect costs. “Rotavin-M1” is an oral live-attenuated vaccine preventing diarrhea in children

under five years old, produced from rotavirus strains G1P [1] KH0118 on Vero cells as identified at the Center for Research and Production of Vaccines and Biologicals - Ministry of Health.

Materials and Methods

Materials

- Vero cells from ATCC Vero cell bank of the WHO;
- Primary monkey kidney cells of *Macaca mullata*;
- MA104 cells provided by the US CDC;
- Rotaclon Kit;
- Reagents for determining the concentration of antigen by creating clusters of the rota necrosis and immunofluorescence method;
- RT-PCR Kit;
- Production strain type G1P8 (KH0118);
- DMEM cell culture (Dulbecco's Modified Eagle Medium) - Gibco, Cat. No 31600 pH 6.8 to 7.0, 5% fetal calf serum;
- DMEM cell washing (Dulbecco's Modified Eagle Medium) - Gibco, Cat. No 31600 pH 6.8 to 7.0, no fetal calf serum, no trypsin, no herpes;
- DMEM (Dulbecco's Modified Eagle Medium) - Gibco, Cat.No 31600 pH from 7.0 to 7.15, Herpes 0,0125 mM, trypsin 20 µg/ml;
- Medium 199, Gibco, Cat.No 31100;
- Fetal calf serum (Fetal Bovine Serum-Certified, HI Gamma Irradiated) - MP Biomedical LLC, Germany, Formula number: 2916454;
- 0.25% trypsin solution 1x, Gibco, Cat.No.15050-065;

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- Solution Hanks' Balanced Salt Solution (HBSS) 1x, Gibco, Cat. No.14175-103;
- Neomycin antibiotic solution, Sigma, N1142, Lot 104K2321;
- Plastic Bottle 225 cm³;
- Incubators, plastic pipette using 01 types, pipe aid and other tools;
- Medium dispenser;
- Other equipment and materials sufficient for the research process.

Methods

Step 1: Monitoring of diarrhea caused by the rotavirus was conducted at the Pediatric hospitals in Vietnam and pathogenic circulating strains were identified by the RT-PCR method.

Step 2: Establishment of an attenuated virus seed strains system is performed by cloning the virus, multiple culture passages of virus lines, Vero cell adaptive virus line, and virus purification.

Step 3: Establishment of a rotavaccine production process in a laboratory and laboratory and animal experiment evaluation.

Step 4: Evaluation of the safety and immunogenicity of the vaccine by three phase clinical trials using volunteers as under the GCP process issued by the Ministry of Health.

Step 5: Vaccine production after licensing in accordance to approved procedures.

Results and discussion

Surveillance of rotavirus caused diarrhoea in Vietnam [1-14]

Vietnam is one of the countries in Southeast Asian that participates in monitoring diarrheal diseases caused by the rotavirus. This network is organized by the World Health Organization (WHO). Since 1998, the surveillance system has been set

up in three regions of the country, at the Paediatric Hospital and Saint Paul Hospital in Hanoi, the Children's Hospital in Hai Phong, Khanh Hoa General Hospital, and the Children's Hospital I and II in Ho Chi Minh City. Monitoring results have shown that among children with diarrhea caused by rotavirus, children of 6-24 months of age accounted for 90% of cases. The rotavirus strain has been found circulating in South and Central Vietnam throughout the year at higher rates than the North. In the North, due to the four distinct seasons at the subtropical climate zone, the incidence of diarrhea due to rotavirus have been found to fluctuate according to seasonal changes, with a maximum peak lasting from November to May (winter - spring season) and decreasing considerably in other seasons. The detection rate of rotavirus diarrhea in patients was 55.64% at the Paediatric Hospital in Hanoi, 49.84% at Saint Paul Hospital, 59.28% at the Children Hospital in Hai Phong, 58.32% at Khanh Hoa General Hospital, and 58.82% at the Children's Hospital I, and 58.65% at the Children's Hospital II in Ho Chi Minh City. The average incidence of children with rotavirus acute diarrhea was 57.39% nationwide, and rotavirus strains circulating in the country in 1998-2011 period were mainly P [1] and G1.

Establish the seed lost system for rota virus vaccine production [15, 16]

Based on the results obtained from epidemiological surveillance during the 1998-2011 period, rotavirus strains G1P [1] have been chosen through selective cloning and by multiple tissue culture passages; first in MA104 cells, then in primary monkey kidney cells (pMKC) and in Vero cells. The purified virus on Vero cells was used to establish the master seed virus (MSV) and working seed virus (WSV). The obtained seed strain systems was confirmed via gene sequence and tested for adventitious agents at the Center for Prevention and Disease Control (CDC-USA),

the Vietnam Academy of Science and Technology, and the National Institute for Vaccine and Bio-medical products. The strain system has been tested successfully in monkeys of 6-12 months old in safety and in immunogenicity and certified by the National Institute for Vaccine and Bio-medical products for use in rotavirus vaccine production in Vietnam since 2007.

The virulent strains of rotavirus used to establish the system of MSV was the strain code KH0118. This rotavirus strain was isolated from stool samples of patients with acute gastroenteritis caused by the rotavirus. KH0118 strain creation process is summarized as follows:

KH0118 rotavirus strains isolated from clinical specimens KH0118 using three continual isolations on MA104 cells in 1-2 µg trypsin/ml supplemented DMEM media not contained fetal bovine serum, according to rotavirus isolation procedures developed by CDC (Atlanta, USA). This strain is preserved at the Center for Research and Production of Vaccines and Biologicals (POLYVAC), located at 135 Lo Duc, Hanoi, Vietnam, to be used as raw materials to produce master seed rotavirus strains.

Cloning method (according to CDC's protocol): Each clone was inoculated into 0.1 ml medium culture suspension, then the infected MA104 cells were put into 2 ml DMEM and incubated for 72 hours at a temperature of 37°C, in a shake-condition of 4 cycles/min, in a 5% CO₂ incubator. The rotavirus genetically homogeneous clones with the highest titers were then selected.

Attenuated rotavirus master seed strain by multiple passages: The MA104 cells in 10 g trypsin/ml supplemented DMEM were infected with 0.25 ml of obtained genetically homogeneous rotavirus and were cultured in a condition of 5% CO₂, and shook with rotation speed of 4 cycles/min for 72

hours at 37°C. After the incubation, rotavirus lines with the highest titers obtained from six repeated subcultures in the same culture conditions were selected for use in the next step.

In order to adapt rotavirus strain on primary monkey kidney cells, 12 passages were performed on primary monkey kidney cells in 10 mg trypsin/ml supplemented DMEM. Samples were incubated for 72 hours at 37°C, in 5% CO₂ and shake condition of 4 rounds/min. The rotavirus culture clones with the highest titers were selected.

To adapt the rotavirus strain on Vero cells, 0.25 ml of the attenuated virus suspension was adapted in primary monkey kidney cells and passaged 17 times on the Vero cells in 20 micrograms of trypsin/ml supplemented DMEM by using the same culture condition for each culture passage (72 hours of incubation at 37°C in a 5% CO₂ incubator, and shaken at 4 cycles/min).

Isolation of adapted to Vero cells rotavirus master seed strain: The isolated Vero cells that adapted to the rotavirus master seed strains were obtained using a double cloning procedure.

First cloning: The Vero cell adapted virus suspensions were diluted from 10⁻¹ to 10⁻⁷. The concentrations from 10⁻² till 10⁻⁷ were used to infect the Vero cells, and the later were incubated in a shaking condition of 3-5 rounds/minute at 37°C. After the virus was harvested, virus concentration was determined by EIA and the virus samples with highest optical index (OD) of concentration of 10⁻⁶ were chosen for second cloning.

Second cloning: Using the same procedure as for the first cloning. The harvested virus suspension with the highest OD were selected and used as purified attenuated rotavirus strains type G1P [1].

Establish attenuated rotavirus seed strains: For obtain attenuated rotavirus

seed strains, the purified attenuated rotavirus strain G1P [1] has been subcultured five times consecutively on Vero cells, then stored at -70°C at the POLYVAC. This seed virus strain is used to produce working seed rotavirus strain for production of vaccine.

Development of vaccine production process and establishment of standard requirements [5]

“Rotavin-M1” is an oral live-attenuated vaccine used for the prevention of diarrhea in children under five years old, caused by rotavirus strains G1P [1] on Vero cells, identified at the POLYVAC.

“Rotavin-M1” production process:

(a) Culture the monolayer of Vero cells in plastic bottles in a 5% fetal calf serum supplemented DMEM and incubate at 37°C for three days to obtain enough cell layers for vaccine production; after washing two times with DMEM without trypsin and Herpes, pH of 6.8 to 7.0, incubate the harvested cells in new DMEM at 37°C for three hours;

(b) Activate the WSV strains G1P [1] KH0118 using trypsin with concentrations of 15 µg/ml at 37°C for 30 minutes (in 37°C thermal bath). Before this step, CaCl₂ (300 g/l) a concentration of two µl/ml is added to the cell solution at room temperature for at least 30 minutes;

(c) Virus absorption: Empty the cell culture bottles prepared in step ‘a’, add 3 ml of virus suspension activated in step ‘b’ into the culture bottle to obtain concentrations of infected cells reached to 0.006 FFU/ml. Let absorb for one hour at 37°C, then slightly shake the culture vessels for 15 minutes each;

(d) Add the fresh medium to the infected cell cultures. The culture vessels, after absorption step, are met with 70 ml of 20 µg trypsin/ml supplemented DMEM, pH 7.0 to 7.15; then incubate

the vessels at 37°C in a static state;

(e) Harvest the vaccine Virus suspension: Virus suspension is harvested at day three, after adding the fresh medium from step ‘d’. Before the harvest, shake the culture bottle. Put the culture bottles at -20°C and then thaw them. Transfer the virus solution from culture bottles into plastic bottle at 2.5 liters. The pool cell solution is preserved at -60°C, and then thaw out once again;

(f) After being thawed, virus suspension is pooled in a big tank. A crude sampling of 50-100 ml is taken for inspection. Finally vaccine virus suspension is filtered using housing filters with diameters of 0.65 µm. Semi-finished vaccine solutions are preserved at <-60°C;

(g) Prepare vaccine dilution to have G1P [1] virus concentration in each dose (2 ml) greater or equal to 10^{6.3} PFU/ml with 35% sucrose;

(h) Fill the Rotavin-M1 in glass vials of single dose, 2 ml per dose, storage at ≤-20°C.

Rotavin-M1 component:

Each 2 ml dose of vaccine contains:

Live human Rotavirus, attenuated strain of G1P [1]: ≥ 10^{6.3} PFU

Sucrose: 35%

Kanamycin: ≤10 µg/ml

DMEM (Gibco).

Rotavin-M1 clinical trial [17-20]

Rotavin-M1 is produced by the POLYVAC within the frame of state projects coded as KC10.03/06-10. Three loads of vaccines are shown to have good results for safety and immunogenic when tested in a laboratory and used on experimental animals (preclinical), especially on young rhesus monkeys, Macaca mulatta. At the same time, the vaccine was checked by the National Institute of Vaccines and Biologicals

in 3/2009 and approved by the Ethics Council of the Ministry of Health for clinical trials with three phases according to the Health Ministry's GCP. The vaccine was used by 30 adults, and 1,000 infants each of 6-12 weeks old in Thanh Son, Phu Tho province and Thai Binh City. Results confirmed the safety of the vaccine in adults, and children aged 6-12 weeks, which is the equivalent of this seen in Belgium's Rotarix vaccine. Rotavin-M1 is also showed to have a high immune response, equivalent of that of Belgium Rotarix vaccine.

Safety:

- Out of 30 adult volunteers at Thanh Son, Phu Tho

During the trial, no unwanted reactions were seen, no cases were lost, and no side effects appeared noticeable after 28 days after each vaccine dose was administered. After the first vaccine dose, two volunteers with viruses from the stool samples from day ten were isolated, but not of type G1. After the second vaccine dose administration, no stool samples were taken from ten days of continuous isolation with the virus. The blood and biochemical test data, including red blood cells, leukocytes, platelets, SGOT, SGOP, and urea from after the first dose one and second dose administration revealed no difference compared to that of before taking the vaccine [17].

- Out of 200 healthy infants aged 6-12 weeks old in Thanh Son, Phu Tho [18]

The biochemical and blood cell indicators (red blood cells, leukocytes, platelets, SGOT, SGOP, and urea) after each vaccine dose administration were at normal level. Within 30 minutes after vaccine intake, no cases of symptoms appeared in place. In the first seven days after taking dose 1, 2, and 3, fever and vomiting occurred negligibly in some cases. From day 8-30 after second and

third dose administration, the rate of cases with fevers were found as the same in different groups. 2.5% of the children got diarrhea, but none of these cases were isolated with the vaccine virus. The same results were observed with the group of children taking Rotavin 10⁶ FFU. Some cases of diarrhea have isolated strains of the vaccine virus in the feces of those taking Rotavin (10^{6.3}FFU). About excreted the vaccine virus in their stool, within seven days after the first dose, the percentage of children isolated with vaccine virus in stool varied from 47.5 to 55%. This rate was highest on day six and day seven. After the second dose, the proportion of children excreting virus was reduced compared with those who did after dose one (<20%). After the third dose, this rate had increased compared with the data observed after the second dose (approximately 45%), but lower than the rate after first dose and there was no difference between the proportion of children excreted virus among the group administered vaccine dose of 10⁶ or 10^{6.3} FFU/ml. In 60-90 days after the first dose, none of case hospitalized due to unwanted reactions.

- Out of 400 children in Thanh Son, Phu Tho and 400 children in Thai Binh province [18]

None of the children appeared to have undesirable reactions after 30 minutes of vaccination. No vomiting, abdominal pains, or allergies were seen in the children during the first seven days after the first dose of the vaccination in both study sites, excepted 1.3% of cases with fever (2% in placebo group), 2.67% with diarrhea (3.02% in placebo group), 0.17% with anorexia or refused the feeding (0.5% in placebo group); 1.5% of children crying (3% in placebo group), and 1% with cough (2.51% in placebo group). seven days after the second vaccination dose, none of the children were vomiting, had loss of appetite or not eating, but the children

experienced fever 2.12% (2.72% in the placebo group), 1.24% of children with had pepper flow (placebo 0.54%), 0.18% of the children had abdominal pains (placebo 0%), 1.42% of the children experienced crying (placebo 1.09%), 0.88% of the children had a cough (placebo 0.54%), and 0.18% of the children experienced allergic reactions (none in placebo group).

From 8 to 30 days after taking first vaccine dose, none of children at both study sites had allergic reactions, but 10.67% of them had fevers (7.04% in placebo group), 0.17% had vomiting, 2% had diarrhea (2.01% in placebo group), 0.17% had abdominal pain (0.5% in placebo group), 0.83% had anorexia or refused feeding; 10.83% cried (7.04% in placebo group) and 2.5% experienced a cough (2% in placebo group). Within 8-30 days after the second dose, no abdominal pain cases were observed, but 11.33% of children had fevers (8.15% in placebo group), 0.35% had vomiting, 0.71% had diarrhea (2.17% in placebo group), 1.59% had anorexia and refusal of feeding, 9.56% cried (7.61% in placebo group), 3.09% had a cough (1.09% in placebo group) and 0.18% had allergies. In summary, 15.22% of any unwanted reactions were observed in children during the 30 days of vaccine administration, while this rate in group taken the placebo was 14.67%, no statistically significant difference between these two ratios was found.

From day 0 to 30 days, at two trial sites, after taking one dose of vaccine, no allergic cases were found, 11.50% of children had fevers (8.04% in the placebo group), 0.17% had vomiting, 4.17% had diarrhea (4.52% in placebo group), 0.17% had abdominal pain (0.5% in placebo group), 0.83% had anorexia or refusal of feeding (0.5% in placebo); 11.33% had crying (8.04% in placebo) and 3% had a cough (3.02% in placebo group). In 30 days after taking

the second dose of vaccine, 12.74% had fevers (9.78% in placebo group), 0.35% had vomiting (0.54% in placebo group), 1.95% had diarrhea (2.72% in placebo group), 0.18% had abdominal pain (none in placebo group), 1.59% had anorexia or refused to feed (0.54% in placebo group); 10.44% were crying (8.15% in placebo group), 3.72% had a cough (1.63% in placebo group) and 0.35% had a cough.

So in 30 days after taking the first and second doses of the vaccine, at both study sites, the proportion of children with symptoms such as vomiting, fever, diarrhea, abdominal pain, coughing, or crying, were low and no statistical significance difference between the groups of children receiving vaccines and placebo.

Among the 95 cases with diarrhea, it appeared during the follow-up time (30 days after each dose), four children were isolated with rotavirus in their feces, including three typed as the vaccine virus G1P [1] strain. All these diarrhea cases were observed within the virus excretion period after vaccination, other symptoms of gastroenteritis related were not found.

Immunogenicity:

IgA antibody:

Results of the phase II study on 200 infants in comparison to those who received Belgium's Rotarix vaccine showed that the IgA antibody titer after vaccination is as following:

Rotavin-M1 10^{6.3} FFU, two doses at two months interval: 72.7%

Rotavin-M1 10^{6.3} FFU, three doses at one month interval: 65.6%

Rotavin -M1 10⁶ FFU, two doses at one month interval: 60.5%

Rotavin-M1 10⁶ FFU, three doses at one month interval 55.9%

Belgium Rotarix two doses at one

month interval: 59%

Results of phase III of the study on 800 children in Phu Tho and Thai Binh provinces compared with results from the placebo group showed that the mean percentage of children that were positive with the rotavirus-specific serum IgA in the vaccine group of 80.7% (ranging from 77.3% in Phu Tho to 84.3% in Thai Binh children). Meanwhile, in the placebo group, this rate was 13.3% (from 11.1 to 15.2% respectively in Phu Tho and in Thai Binh), corresponding to the natural virus infection of children. After vaccination with two doses, antibody titres (geometric mean) reached 85.9 (95% CI: 74.5 to 99.1), 54.5-60.1% of these had a titer ≥ 80 .

IgA antibodies immune response level produced by the vaccine batch of high-titer (from 160 to 640) accounted for 42.35% while that produced by the batch of good titer levels accounted for only 8.55% and 14.31% produced by the vaccine batch of moderate titer reached. The batch with very high titer levels stimulated IgA immuno response in 17.69%.

IgA antibody dynamic after one year vaccinated with 10^{6.3} FFU of Rotavin or Rotarix showed almost stable with 54.84% in group received Belgium's Rotarix and 66.67% in those vaccinated with Rotavin-M1.

IgG antibody:

Although 100% of the children have the RV-specific IgG antibody before vaccination (transferred from mother), the proportion of children having the IgG antibody response after vaccination reached 72.8 to 85.3%. The geometric mean of the IgG titer has increased 1.4 times compared to that seen before vaccination while it decreased from 7.6 to 8.7 times in children of placebo group in both study sites.

Dose and schedule of vaccine administration:

Children of 6-12 weeks of age get the first dose with following vaccination schedule:

Rotavin-M1 10^{6.3} FFU, two doses at two months interval: 80.7%

Rotavin-M1 10^{6.3} FFU, three doses at one month interval: 65.6%

Rotavin -M1 10⁶ FFU, two doses at one month interval: 60.5%

Rotavin-M1 10⁶ FFU, three doses at one month interval: 55.9%

Belgium Rotarix, two doses at one month interval: 59%.

Licensed Rotavin-M1 vaccine, production and use of vaccine after licensed

The vaccine was licensed to the manufacture and used widely with high effective for disease prevention and economic efficiency. Currently, rotavirus vaccine is not included yet as part of the National Expanded Immunization program, but is being used as a health care socialized service. Before Rotavin-M1 is licensed, Rotarix and RotaTeq were the rotavaccines used in the Vietnamese market. Two of these vaccines are imported vaccines that have very high costs, so can be used mainly the big cities for people with good economic conditions. Rotavin-M1 vaccine with similar quality and with the price of 1/3 imported vaccine's price, will be highly response to the needs of Vietnamese community.

Since 2012 after Rotavin-M1 was licensed, more than 500,000 doses of the vaccine and 18 lots of the bulk vaccine amounted 200 liters equivalent to 400,000 doses has been produced. The production line and vaccine testing schedule have been established with over 60 scientists and technical staff. Several new technologies have been applied and routinely deployed in the POLYVAC as plaque cloning technique, technical limits diluted concentrations,

PCR, Sequencing etc.

Rotavin-M1 vaccine was officially approved as the national product by Decision 2441/QĐ-TTg of the Prime Minister. With this program Rotavin-M1 vaccine would be produced for mass serving in national vaccination programs and exporting to world markets.

Since being approved in May 2012, the Rotavin-M1 vaccine has been used in almost all provinces and cities nationwide. More than 500,000 doses of vaccine have been used, effectively preventing infection for about 250,000 children. POLYVAC has gained 40 billion in sales, benefiting about 90 billion for society in comparison to using of imported vaccines.

Conclusions

The vaccine “Rotavin-M1” is an oral live-attenuated vaccine to prevent diarrhea disease for children under five years old, and has been produced from rotavirus strain G1P [1] on Vero cells at the POLYVAC through the Vietnamese Ministry of Health. The Rotavin-M1 vaccine has been established and developed through five stages: i) Monitoring the circulating of rotavirus strain; ii) Establishing the seed virus strain system; iii) Establishing the production process, testing and vaccine standard criteria according to WHO; iv) Implementing the clinical trials; and v) Licensing and posting of the vaccine licensure surveillance. All of these stages were performed according to the process requirement of WHO. Rotavin-M1 is safe and effective for children under five years old to prevent from the disease.

REFERENCES

[1] Nguyen Dang Hien, Le Thi Luan (2011), “Monitoring circulating strains of rotavirus in Vietnam in 2010”, *Journal of Preventive Medicine*, **Vol.XXI, No.5 (123)**, pp.71-77.

[2] Le Thi Luan and Nguyen Nu Anh Thu (2003), “Genotype and phenotype of rotavirus caused acute gastroenteritis in children under 5 years old in

Khanh Hoa Academy of Pediatrics, 2002”, *Provision Medical Journal*, **Vol.XIII, No.4(61)**, pp.49-51.

[3] Le Thi Luan and Nguyen Nu Anh Thu (2004), “The biological characteristics of rotavirus caused diarrhea in children under 5 years old at the Children’s Hospital Haiphong (7/2001-6/2002)”, *Provision Medical Journal*, **Vol.XIV, No.1(64)**, p.27.

[4] Le Thi Luan and Nguyen Thuy Huong (2003), “Identify and type of rotavirus in diarrhea pediatric patients at Children’s Hospital Swedish first 9 months of 2003”, *Practical Journal of Medicine*, **4(451)**, pp.64-66.

[5] Le Thi Luan, Nguyen Dang Hien (2011), *Rotavin-M1 vaccine to protect diarrhea. Safety and immunity response*, Medical Publishing House.

[6] Nguyen Dang Hien, Le Thi Luan, et al. (2012), “Circulating strains of rotavirus in 2010 in Vietnam”, *Journal of Preventive Medicine*, **Vol.XXII, No.4(131)**, pp.17-21.

[7] Nguyen Dang Hien, Nguyen Thi Mai Huong, Bui Duc Nguyen, Dang Duc Anh, Le Thi Luan (2010), “Monitoring pathogenic strains of rotavirus acute gastroenteritis in children under 5 years of 2008”, *Journal of Preventive Medicine*, **Vol. XX, No.5(113)**, pp.23-27.

[8] Nguyen Dang Hien, Nguyen Thi Mai Huong, Pham Thi Phuong Thao, Le Thi Luan (2011), “Monitoring results due to rotavirus in 2009 in Vietnam”, *Journal of Preventive Medicine*, **Vol.XXI, No.1(119)**, pp.10-15.

[9] Nguyen Dang Hien, Pham Thi Phuong Thao, Le Thi Luan (2009), “Rota monitoring circulating strains cause diarrhea in Vietnam from 1998 to 2009”, *Journal of Preventive Medicine*, **Vol. XXI, No.1(119)**, pp.5-9.

[10] Joseph Bresee, Nguyen Van Man, Le Thi Luan, et al. (2004), “First Report from the Asian Rotavirus Surveillance network”, *Emerging Infectious Diseases*, **10(6)**, pp.988-995.

[11] Nguyen Van Man, Le Thi Luan, Dang Duc Trach, Nguyen Thi Hien Thanh, Phan Van Thu, Nguyen Thanh Long, Dang Duc Anh, Jon R. Gentsch, Roger Glass (2005), “Epidemiological Profile and Burden of Rotavirus Diarrhea in Vietnam: 5 Years of Sentinel Hospital Surveillance, 1998-2003”, *JID*, **192**, Supplement 1, S127-132.

[12] Nguyen Van Man, Le Thi Luan, Tran Hong Thuy, et al. (2004), *Immunocytochemical study of the rotavirus interaction with host cells in the culture*, Publishing House of Vietnam National University, Hanoi, Asean-MC4, pp.6-10.

[13] Nguyen Van Man, Nguyen Van Trang, Huynh Phuong Lien, Dang Duc Trach, Le Thi Luan, et al. (2001), “The Epidemiology and Disease Burden of rotavirus in Vietnam: Sentinel Surveillance at 6

hospitals”, *The Journal of Infectious Disease*, **183**, pp.1707-1712.

[14] Nguyen Van Man, Nguyen Van Trang, Le Thi Luan, Huynh Phuong Lien, Dang Duc Trach, et al. (2004), *The Epidemiology and burden of Rotavirus diarrhea in Vietnam: Five years of Sentinel Hospital Surveillance 1998-2003*, Vietnam National University Publishers, Hanoi, The proceeding of The 2nd Vietnam-Lao-Cambodia, pp.20-30.

[15] Le Thi Luan, Nguyen Thuy Huong, Nguyen Dang Hien, Nguyen Thanh Thuy, Nguyen Thi Minh Lien, Ennio Lucio Benedetti, Irene Dunia (2011), *Immunocytochemical Characterization of rotavirus entry into monkey kidney cells in culture. Viruses Responsible for Emerging Diseases in South - East Asia*, Jacques Monod Institute/CNRS Universite Paris Diderot - Chapter 7, pp.225-238.

[16] Luan T. Le, Trang V. Nguyen, Phuong M. Nguyen, Nguyen T. Huong, Ngo T. Huong, et al. (2009), “Development and characterization of candidate rotavirus vaccine strains derived from children with diarrhea in Vietnam”, *The official Journal of the International society for Vaccine*, **27**, Supplement 5, pp.130-138.

[17] Dang Duc Anh, Nguyen Van Trang, Vu Dinh Thiem, Nguyen Hien Anh, Nguyen Dang Hien, Le Thi Luan, Nguyen Van Mao (2010), “The safety of vaccines Rotavin-M1 produced in POLYVAC on adult volunteers”, *Provision Medical Journal*, **Vol.XX, No.7(115)**, pp.19-28.

[18] Dang Duc Anh, Nguyen Van Trang, Vu Dinh Thiem, Nguyen Hien Anh, Nguyen Dang Hien, Le Thi Luan, Nguyen Van Mao, Bui Duc Nguyen, Vu Thi Bich Hau, Le Thi Hong Nhung, Le Thi Kim Anh (2010), “The safety of Rotavin-M1 vaccine on children under 6-12 weeks old”, *Provision Medical Journal*, **Vol.XX, No.10(118)**, pp.5-14.

[19] Vu Dinh Thiem, Nguyen Van Trang, Nguyen Thi Hien Anh, Le Huy Hoang, Nguyen Dang Hien, Le Thi Luan, Thien Anh Tong, Nguyen Van Mao, Nguyen Van Thom, Tran Van Dui, Bui Duc Nguyen, Vu Thi Bich Hau, Le Thi Hong Nhung, Le Thi Kim Anh, Ngo Thi Thanh Hoa, Nguyen Anh Tuan, Dang Duc Anh (2011), “The safety of the Rotavin-M1 in children under 6 to 12 weeks old at the Phu Tho and Thai Binh”, *Journal of Preventive Medicine*, **Vol.XXI, No.2(120)**, pp.99-111.

[20] Dang Duc Anh, Nguyen Van Trang, Vu Dinh Thiem, Nguyen Thi Hien Anh, Nguyen Duc Mao, Baoming Jiang, Nguyen Dang Hien, Le Thi Luan (2012), “A dose-escalation safety and immunogenicity of a new live attenuated human rotavirus vaccine (Rotavin-M1) in Vietnamese children”, *Vaccine*, A114-A121.

Utility of ^{18}F -FDG PET/CT in metabolic response assessment after CyberKnife radiosurgery for early stage non-small cell lung cancer

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Abstract:

Objective: To assess metabolic tumor response using ^{18}F -FDG PET/CT scan in early stage non-small cell lung cancer (NSCLC) treated by CyberKnife radiosurgery. **Materials and Methods:** 30 patients were diagnosed proven by biopsy and inoperable stage I NSCLC, and were enrolled into this study. ^{18}F -FDG PET/CT was performed prior to the program, and at three months following the radiosurgery treatment. The tumor maximum standardized uptake value (SUVmax) was recorded for each time point and the PERCIST criteria was applied to assess tumor response. **Results:** 30 patients with NSCLC, stage I after CyberKnife radiosurgery was followed-up after 12 months. The 1-year Kaplan-Meier local control estimate was 96.7%, the cut-off of SUVmax was 10, and revealed the local tumor control to have a statistically significant difference. Mean tumor SUVmax before treatment was 10.5 ± 3.25 (range, 5.0 to 20). During early follow-up the mean SUVmax in the tumor remained high due to peritumoral radiation-induced pneumonitis visible on CT imaging. After radiosurgery for six months, ^{18}F -FDG PET/CT images showed that 21 of 30 patients (70%) had a partial metabolic response, 8 of 30 patients (26.7%) had stabilized diseases, and one patient (0.3%) had disease progression. Meanwhile, CT could not reveal the progressed patient. **Conclusions:** Local control following CyberKnife radiosurgery for stage I NSCLC is acceptable. Transient increases in tumor SUVmax are likely related to radiation-induced pneumonitis. The value of ^{18}F -FDG PET/CT imaging for early metabolic tumor response after stereotactic body radiation therapy (SBRT) could be higher than anatomic response on CT.

Keywords: CyberKnife radiosurgery, non-small cell lung cancer, SBRT, ^{18}F -FDG PET/CT.

Classification number: 3.2

Introduction

Stereotactic Body Radiation Therapy (SBRT) is a proven treatment option for inoperable stage I NSCLC [1]. Several techniques have been employed to treat these potentially mobile tumors. Treatments require accurate, safe, and swift delivery of extremely high doses of radiation. As anticipated, SBRT has improved local control and overall survival rates relative to historical controls. Up to now, the enhanced accuracy and flexibility of the CyberKnife method facilitated the safe delivery of dose distributions designing to eradicate both gross tumor and known microscopic disease radiating. Focal radiation-induced pneumonitis and fibrosis may be seen as a side effect of treatment, hampering the assessment of the tumor response using CT and ^{18}F -FDG PET imaging [2]. However, approximately 10% of these patients developed local recurrences after high-doses of SBRT. Tumor hypoxia also plays an important role in radio-resistance. In recent studies, reductions of the diameters of CT suggestive hypoxic conditions within a tumor have been shown to correlate with local recurrence [3]. However, metabolic response was found in a few studies, having a significant impact on the biological behaviors of malignant tissue including NSCLC [4]. Metabolic response may have higher sensitivity in diagnostic and assessment treatment response. The relationship between pre-treatment and post-treatment glucose metabolism measurements has not yet been fully elucidated in NSCLC. In Vietnam, to our best knowledge, there has not been any articles related to this topic published. Following the reasons mentioned above, the aim of this study was to investigate the utility of ^{18}F -FDG PET/CT in the assessment of treatment responses and the prognostic impacts of SUVmax on local control (LC) in patients with SBRT-treated NSCLC.

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Materials and methods

This study was approved by the hospital institutional review board. 30 patients were consecutively treated on a single institution prospective protocol with inoperable biopsy proven clinical stage I NSCLC, and were evaluated. Inoperability was defined as a post-operative predicted forced expiratory volume in one second (FEV1) of less than 40%, heart disease, diabetes, and patients refusal of operation. The performance status is rather good with ECOG 0-2. The patients in stage II, III, IV, FEV1 < 1,000 ml/minute, ECOG 3-4 were excluded. Patients were treated according to protocol using at the CyberKnife Radiosurgery Center, located at 108 Military Central Hospital. Briefly, fine-cut (1-mm) treatment planning CTs were obtained over 7-10 days after a CT-guided percutaneous biopsy and fiducial placement. Gross tumor volumes (GTV) were contoured utilizing lung windows. The GTV margin was expanded by 5 mm to establish the planning treatment volume (PTV). A treatment plan was generated using the CyberKnife non-isocentric, inverse-planning algorithm with tissue-density heterogeneity corrections for lungs. The radiation dose ranged from 42-60 Gy in three fractions, and was prescribed to an isodose line that covered at least 95% of the PTV and resulted in the 30-Gy isodose contour extending a minimum of 1 cm from the GTV.

^{18}F -FDG PET/CT imaging was performed two weeks prior to CyberKnife radiosurgery and at three months following the radiation treatment. CT was used for attenuation correction of the PET emission image data. Quantitative values of tumor metabolic activity were expressed as tumor SUVmax, defined as the maximum standardized uptake value within the tumor. Values were obtained using three-dimensional regions of interest placed on lung lesions, which were anatomically defined by combined review of the PET and CT images. Local tumor recurrence was defined as unequivocal progression on serial ^{18}F -FDG PET/CT imaging. Biopsy was required to confirm recurrence if needed. Clinical follow-up was consecutively at 6 and 12 months afterward. For patient preparation, the serum glucose levels were checked to exclude hyperglycemia. Afterwards, the patients were allowed to rest in the waiting room before an intravenous injection of 2.5 MBq/kg body weight ($\pm 10\%$) of ^{18}F -FDG PET and low-dose CT scans from cranial top to the mid-thigh were performed 60 min after the ^{18}F -FDG injection was given, as is standard procedure. In general, ^{18}F -FDG PET/CT was read independently by one of two nuclear medicine physicians with thorough knowledge about the patient's clinical history; then, the other physician reviewed all lesion-related findings and impressions. Disagreements were resolved by consensus. A positive lesion on ^{18}F -FDG PET/CT imaging was defined as a

focal ^{18}F -FDG uptake with relatively higher activity than that of the surrounding normal tissue or when the SUVmax of the lesion was revealed to be more than 2.5. Treatment response criteria based on RECIST 1.1 and PERCIST as prescribed on articles published previously [5].

Data was analyzed and graphs were prepared with the SPSS 18.0 statistical package. The follow-up duration was defined as the time from the date of completion of treatment to the last date of recurrence or at the end of study (12 months). Actuarial local control was calculated from the conclusion of treatment using the Kaplan-Meier method. The T-test and Mann-Whitney Tests were used for mean and median comparison. The confidence intervals (95%) were determined.

Results

Table 1. Clinical characteristics of NSCLC patients.

Clinical characteristics	Number (n = 30)	Percentage (%)
Mean age $\pm$ SD	66.3 $\pm$ 10.74	
Age < 60	7	23.3
Age $\geq$ 60	23	76.7
Gender		
Male	24	80.0
Female	6	20.0
Histopathology		
Adenocarcinoma	16	53.3
Squamous cell	7	23.3
Large cell	4	13.3
Others	3	10.0
T-Stage		
T1a	2	6.7
T1b	6	20
T2a	22	73.3

The total patients in this study were 30 objects, followed-up over 12 months (Table 1). The median age and SD were 66.3 $\pm$ 10.74 (range, 55-80). The group of age were divided in to two subgroups under 60 (23.3%) and over 60 (76.7%). The percentage of male patients was four-fold higher than that of

female patients. Among histopathologic types of non-small cell lung cancer in this study, adenocarcinoma occurred in more than half of cases. According to T-stage, T2a was seen more frequently with 73.3%. This figure is much higher than those of T1a and T1b.

Table 2. Characteristics of NSCLC tumors on ^{18}F -FDG PET/CT imaging.

Characteristics of tumors		Number (%)	SUVmean $\pm$ SD	p
Location of tumor	Right lung	21 (70)	10.2 $\pm$ 3.5	> 0.05
	Left lung	9 (30)	9.5 $\pm$ 3.46	
	Peripheral	20 (67)	9.6 $\pm$ 2.67	> 0.05
	Central	10 (33)	11.2 $\pm$ 5.7	
Longest diameter of tumor	Mean $\pm$ SD	3.71 $\pm$ 0.95	-	> 0.05
	<20 mm	25 (75)	7.5 $\pm$ 3.52	
	>20 mm	5 (25)	11.6 $\pm$ 4.31	
Histopathology	Adenocarcinoma	16 (53.4)	15.7 $\pm$ 4.32	p = 0.022
	Squamous cell	7 (23.3)	10.4 $\pm$ 3.67	
	Others	7 (23.3)	7.68 $\pm$ 4.33	

The primary tumor was observed to be 70% on the right and 67% at the peripheral lung, the percentage was even higher than that on the left and the central lung (Table 2). The mean of the longest diameter of the tumor was 3.7 $\pm$ 0.95, and the diameter under 20 mm was seen more frequently than those larger than 20 mm. Among all of histopathology types, adenocarcinoma (AD) was the most popular with 53.4%, squamous cell (SCC) and others was 23.3% for each of the types. There were no significant difference in the SUVmean $\pm$ SD between positions of the tumor and diameters of the tumor ($p > 0.05$). However, the significant difference between the histopathologic types was noted ($p = 0.02$).

After three months of SBRT, almost SUVmax had been going down. However, there were several cases in which SUVmax had transient elevations (Fig. 1). Mean $\pm$ SD of SUVmax before treatment was decreased from 10.5 $\pm$ 3.25 to 5.3 $\pm$ 4.1 after treatment of three months ($p < 0.05$).

Assessing by RECIST criteria on CT (anatomic criteria), statistics shows 18 of 30 patients had partial response, 12 of 30 patients had disease stability, and disease progression was not seen in any patient. Regarding the PERCIST criteria (metabolic criteria), the number of partial responses was 21 of 30 higher than those of RECIST, and the number of stable diseases had decreased (Fig. 2). Moreover, ^{18}F -FDG PET/CT scan revealed

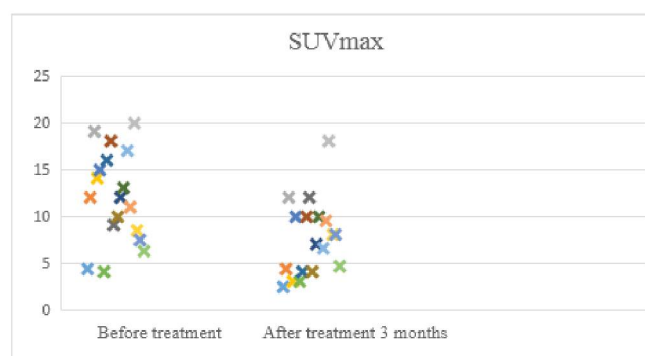


Fig. 1. The change of SUVmax in primary NSCLC tumors before and after radiosurgery.

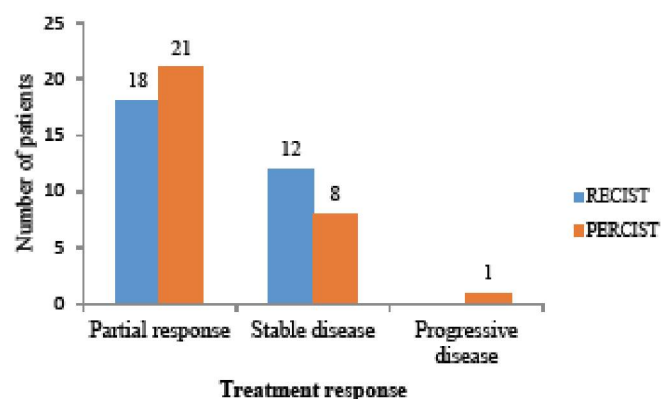


Fig. 2. Comparison of metabolic and anatomic treatment response assessment.

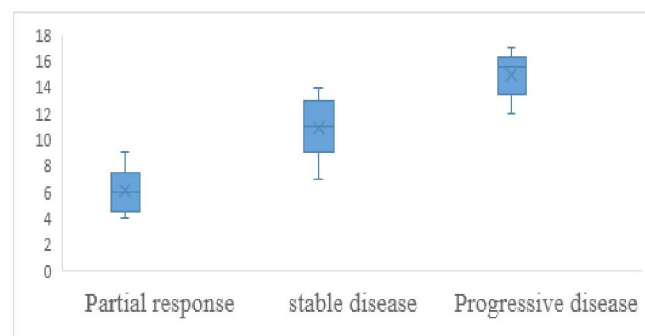


Fig. 3. The relation between the SUVmax and levels of treatment response.

one patient with distant metastases and recurrence after treatment for three months.

The SUVmax mean measured on the primary tumor of partial response, stabling diseased and progressing diseased patients, was 6.1 $\pm$ 2.1, 10.3 $\pm$ 3.21 and 15.2 $\pm$ 2.42 respectively. The SUVmax of the primary tumor in progressing diseased patients tended to be greater than that of the primary tumor in partial response patients ($p < 0.05$) (Fig. 3).

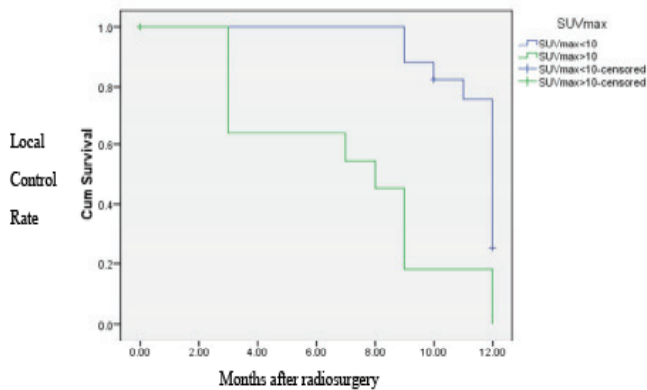


Fig. 4. Kaplan - Meier curves of local tumor control with a cut-off SUVmax at 10.

Following-up by CT after three months, six months, and 12 months after the SBRT, there were significant difference in local control estimations between patients with SUVmax under ten and above ten measured on primary tumor before treatment (Fig. 4).

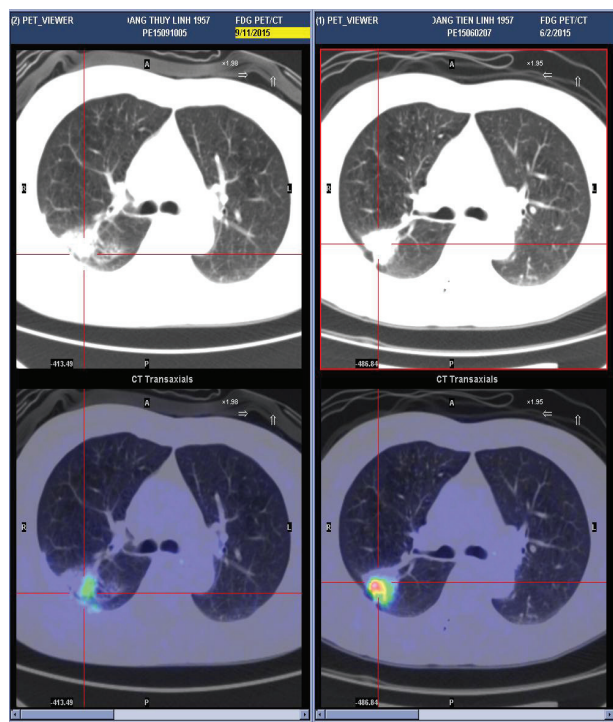


Fig. 5. NSCLC patient (78-years old, man with adenocarcinoma of lower right lobe of lung, T1aN0M0) was treated with CyberKnife radiosurgery with three fractions.

Before treatment (left), ^{18}F -FDG PET/CT showed a tumor with 25 x 28 mm in diameter, SUVmax: 15.8. After three months radiosurgery (right), SUVmax decreased to 3.0 although the diameters seem to be significantly unchanged.

Discussion

Several studies have published reports that documented deficiencies with CT tumor response assessment using the SBRT by the CyberKnife radiosurgery protocol for inoperable stage I NSCLC patients [2, 6]. CyberKnife radiosurgery delivered to lung tumors with adequate marginal damages to the peritumoral lung tissue, and often causes acute radiation pneumonitis. The lung injury has been shown to be repaired typically by inflammation in asymptomatic focal lung parenchyma fibrosis in the region corresponding to the high-dose radiation volume. Evidence of focal radiation induced pneumonitis and fibrosis was consistently observed within the target volumes of our patients during follow-up as well. ^{18}F -FDG PET/CT is the standard imaging staging for NSCLC at our hospital. It is both more sensitive and specific than conventional imaging for the detection of primary lung tumors, involved regional lymph nodes and distant metastases. Primary lung tumors with a SUVmax greater than 2.5 are considered malignant until proven otherwise. However, preliminary evidence suggested that like CT imaging, ^{18}F -FDG PET imaging is limited in assessing local tumor control following SBRT due to early elevations in tumor SUVmax, which are thought to be related to acute radiation induced pneumonitis. Therefore, prior to starting protocol therapy, the decision was made to routinely observe inoperable NSCLC patients with early transient elevations in tumor SUVmax following radiosurgery. Understanding this mechanism is very important to assess treatment response, in this study there were several cases when SUVmax increased after three months of SBRT. However, the CT imaging features of pneumonitis has been realized and the patients should be follow-up further. Pulmonary injury following radiation may commonly be seen in a metabolically active ^{18}F -FDG-avid lesion, rising transiently after treatment of SBRT up to two months. In our study, the cut-off SUVmax may be due to pneumonitis is 4.5. Most evidence supported a SUVmax of approximately 5.0 as a clinically useful threshold for the distinction between recurrence and fibrosis [7].

Recommendations for imaging follow-up after SBRT are generally based on retrospective evidence and expert opinion. The aim of follow-up actions serve three major goals including the detection of local recurrence and metastatic lesions occurred approximately of 2-10% per person-year [8, 9]. Tumor response assessment following definitive treatment is typically categorized according to Response Evaluation Criteria in

Solid Tumors (RECIST) 1.1 as complete (disappearance of the target), partial ($\geq 30\%$ decrease), stable disease, or progression ($\geq 20\%$ increase) according to the diameter of the target tumor [10]. However, RECIST 1.1 has limitation, since the target lesion may actually represent lung fibrosis, and response may be misdiagnosis. ^{18}F -FDG PET scans are recommended in lung cancer diagnosis and re-staging, metabolic imaging currently has a limited clinical trial data in the evaluation of tumor response and detection of local recurrence. Nevertheless, metabolic criteria assessed by ^{18}F -FDG PET/CT may reveal the earlier treatment response than anatomic response. In our study, there was no complete metabolic response due to SUVmax transient elevation. Based on PET/CT imaging the number of patients of partial response was higher than that on CT imaging. The reasons could be understood that the biomarker imaging on PET is more sensitive than anatomic imaging. Although the diameters of primary lung tumors were unchanged significantly, the SUVmax was sharply decreased. Since, then the whole-body PET/CT is dominant of detection of distant metastases, this modality also revealed a progressive patient with suspicious recurrent on CT imaging. Generally, there is not any publications reported the status of tumor response but almost papers describe the rate of local control after SBRT. As can be seen on Kaplan Meier curve, the cutoff SUVmax in primary tumor is 10 in this study. The difference of local control between groups of SUVmax under 10 is significant higher than that of SUVmax upper 10. In contrast to other studies, this investigation is related to serial imaging and follow-up. Routine biopsy was not justified following radiosurgery and the risk associated with biopsy in this inoperable patient population. Therefore, confirmation of radiographic impressions was limited to a single biopsy in one patient following an increase in tumor SUVmax; biopsies were not taken to confirm the absence of the disease in cases in which tumor SUVmax remained low. Therefore, it is likely that the true local control rate in this study is less than our reported 95% rate. Furthermore, this difference in local control rates could be considerable in patients with low pre-treatment tumor SUVmax values. Shibamoto et al. presented that, a higher SUVmax according to pretreatment ^{18}F -FDG PET/CT in NSCLC was found to be a significant predictor of local recurrence after SBRT [7]. In our study, SUVmax mean in progressive disease was higher than that of stable disease and partial response patients.

Conclusions

Local control and treatment response following CyberKnife radiosurgery for stage I NSCLC is acceptable. However, transient SUVmax elevation in acute radiation induced pneumonitis may hinder early metabolic tumor response assessment. The value of ^{18}F -FDG PET/CT imaging for survival long term following lung SBRT should be deserved by further study.

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REFERENCES

- [1] J.A. Katzel, M.P. Fanucchi, Z. Li (2009), "Recent advances of novel targeted therapy in non-small cell lung cancer", *J Hematol Oncol.*, **2**, p.2.
- [2] T. Takeda, et al. (2004), "Radiation injury after hypofractionated stereotactic radiotherapy for peripheral small lung tumors: serial changes on CT", *AJR Am J Roentgenol.*, **182**(5), pp.1123-1128.
- [3] M. Aoki, et al. (2016), "Prognostic impact of average iodine density assessed by dual-energy spectral imaging for predicting lung tumor recurrence after stereotactic body radiotherapy", *J Radiat Res.*, **57**(4), pp.4-12.
- [4] P. Baumann, et al. (2009), "Outcome in a prospective phase II trial of medically inoperable stage I non-small-cell lung cancer patients treated with stereotactic body radiotherapy", *J Clin Oncol.*, **27**(20), pp.3290-3296.
- [5] Wahl, L. Richard, et al. (2009), "From RECIST to PERCIST: evolving considerations for PET response criteria in solid tumors", *Journal of nuclear medicine*, **50**, Suppl 1, pp.122S-150S.
- [6] Nakajima, Naomi, et al. (2013), "Differentiation of tumor recurrence from radiation-induced pulmonary fibrosis after stereotactic ablative radiotherapy for lung cancer: characterization of ^{18}F -FDG PET/CT findings", *Annals of Nuclear Medicine*, **27**(3), pp.261-270.
- [7] Y. Shibamoto, et al. (2012), "Stereotactic body radiotherapy using a radiobiology-based regimen for stage I non-small cell lung cancer: a multicenter study", *Cancer.*, **118**(8), pp.2078-2084.
- [8] M. Dachele, et al. (2011), "Radiological changes after stereotactic radiotherapy for stage I lung cancer", *J Thorac Oncol.*, **6**(7), pp.1221-1228.
- [9] F. Lou, et al. (2013), "Patterns of recurrence and second primary lung cancer in early-stage lung cancer survivors followed with routine computed tomography surveillance", *J Thorac Cardiovasc Surg.*, **145**(1), pp.75-81.
- [10] E.A. Eisenhauer, et al. (2009), "New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1)", *Eur J Cancer*, **45**(2), pp.228-247.

Outstanding achievements of medicine and pharmacy in Vietnam during the period of 2011-2015

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Abstract:

Based on the success of research that applies advanced international medical and pharmaceutical technology to projects of Vietnam's Ministry of Science and Technology, the author presents some outstanding achievements in science and technology in medicine and pharmacy during 2011-2015. These results contribute significantly to the healthcare of the community; raises Vietnam's medical science to keep up with developed countries, provides a great socio-economic significance, and also indicates the important position of science and technology as well as the benefits of scientific investment into medical and pharmaceutical fields.

Keywords: advanced medical and pharmaceutical technology, science and technology, Vietnam.

Classification numbers: 3.2, 3.3

In the past five years, thanks to science and technology programs from the Ministry of Science and Technology, the level of Vietnam's science and technology advancement in the medical and pharmaceutical sectors has significantly progressed. It might be said so far, that most of the new technologies, innovative applications for diagnosis, treatments, and preventions of diseases that other countries are using, have already been deployed in Vietnam, including many techniques that have achieved a comparable level with those in developed countries. This paper presents some of the outstanding achievements of medical and pharmaceutical science and technology reached in the last five years.

Biological technology

Across the world, modern biotechnology was accepted into medical and pharmaceutical fields very early on and has achieved incredible success. In the middle of the 1970s, during the last century, due to the

success of monoclonal antibodies, scientists revolutionized biotechnology by forming medicines, and now, the revolution has fully exploded. Many achievements in medicine have been reached. Many nascent techniques have been used to help diagnose life threatening diseases early and accurately, and several new treatments have been created to cure those diseases. Biotechnology has established some new specialties including molecular medicine, molecular pathology, and methods that have unraveled the many mysteries of the microscopic world of disease. Vietnam's biotechnology's lag by about 30 years behind the rest of the world, but until recently, that lag time has shortened. We can say the essential biotechnologies used for diagnosis, treatment and prevention of diseases used in the rest of the world has been implemented in the country.

Successful application of genetic engineering techniques for the diagnosis, treatment and prevention of diseases, for example:

+ Applied multi-primer PCR to identify EML4-ALK & EGFR genes targeting therapy for non-small cell lung cancer (Crizotinib) [1]. Applied FISH techniques to determine HER2 in breast cancer to help specify the exact target in selecting drugs [2]. This was a new horizon in cancer treatment, and is highly effective.

+ Applied ASB realtime PCR technique for the detection of T1799A BRAF gene mutations to diagnose papillary thyroid cancer [3].

+ Created multi-primer PCR protocol (Multiplex PCR) for the detection of common sepsis pathogens [4].

+ Used a gene sequencing technique to identify a number of genes involved in the antibiotic resistance of 13 common strains of pathogenic bacteria found in Vietnam [5].

+ Used chromatography and FISH to establish a protocol to engineer three neonatal disease screenings: Hypothyroidism congenital adrenal hyperplasia and lack of GDP-6 [6].

+ Protocolled diagnosis and screening of common Vietnamese genetic diseases before embryo transfer (Pre-implantation Genetic Diagnosis) in vitro fertilization [7].

Application of stem cells in treatment

We have mastered the technique of isolating stem cells from different sources to treat some blood disorders, cardiovascular diseases, osteoarthritis, respiratory issues, and cancers; and those preliminary and initial results are similar to countries in other parts of the

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world [8].

Techniques of Ionizing radiation

Ionizing radiation is used mainly for three specialties: nuclear medicine, X-ray and oncology. In recent years, a number of modern techniques of ionizing radiation have been launched. These techniques have helped early diagnosis, accurate and early detection of metastases, cancer recurrence, and accurate diagnosis of stage of diseases. Therefore, the treatments are correct, appropriate, effective and safe. These techniques have changed over 30% of initial treatment plans into proper therapies, causing a breakthrough in cancer treatment. Here are some outstanding results:

- The application of Intense Modulated Radiation Therapy (IMRT) using PET/CT image scanning to simulate radiation therapy planning to the treatment of throat cancer, lower throat larynx cancer, and esophagus and lung cancer [9]. IMRT is a technique that uses adjusting doses of radiation beams based on tumor morphology, and changes the intensity of the radiation beams according to the density of the cancer cells, thereby optimizing the high doses at the tumor while minimizing the doses on surrounding healthy organs. Therefore, treatment efficiency is higher and safer. This is the top technique for radiation currently used around the world; only a few developed countries implement this technique, such as the United States, Germany, Italy, Australia.

- The application of radiosurgery techniques using the rotating gamma knife technique for the treatment of brain tumors and some other brain diseases [10]. The rotating gamma knife procedure has the accuracy of classical gamma knife system, but uses Co-60 radiation sources and cubism radiation techniques based on the accelerator, forming a cubism radio-surgery approach based on the principle of using the powerful radiation sources of Co-60, and is focused and correctly localized to the tumor or pathological brain region. The radiation beam is rotated and focused at different trajectories, so tumors and

lesions receive the highest doses of radiation, but surrounding healthy tissue received very low radiation doses. So the radiosurgery system with gamma knife is an ideal piece of equipment used in the current rotating set of radiosurgery techniques.

The application of stereotactic body radiotherapy using cyber knife has enhanced the effectiveness of treatments and is comparable to surgery.

- The implantation of radioactive I-125 seeds (Permanent radioactive seed implant) in the treatment of prostate cancer has begun: This is a new technique, that is modern, and overcomes the disadvantages of previous radiation therapies. This new technique has been implemented in a few countries around the world, and was first implemented in Vietnam at Bach Mai Hospital in April, 2015.

- The application of ^{18}F -FDG PET/CT used for diagnosing and monitoring treatment outcomes of cardiovascular disease and cancer, so that the right treatment is indicated brings high treatment outcomes [11].

Pharmaceutical sector

Applications of high-tech in manufacturing and apothecary

- The successful apothecary of injecting liposomes with two cancer drugs, including doxorubicine and amphotericin B [12]. Liposome, progressed technology in pharmaceutical applications, is a new technology used worldwide which was originally applied in Vietnam. This technology increases a drug's efficacy and reduces toxicity, through the mechanism of targeted therapy.

- The successful apothecary of long-acting pills used to treat cardiovascular diseases and diabetes, which is designed for extended-release for the purpose of reducing the number of medications that patients must take, and improve the treatment efficacy and reduce side effects of drugs [13].

- The successful apothecary of injecting lyophilized carboplatin for the

treatments of cancer on an industrial scale [14]. This form of medicine easily helps the preservation and use of drugs.

Production of vaccines

We have mastered the technology for producing the vaccine Rotavin-M1, used to prevent diarrhea in children caused by Vero cells [15]. The drug has since been confirmed for safety and efficacy by the CDC. This result has named Vietnam as the fourth country in the world to produce the Rota vaccine, after the United States, Belgium and China. Thanks to domestic drug production with low costs, the vaccines have been put into expanding immunization programs.

Production of medical biological agents of high value used for diagnosis

- The primers PCR kit has three target genes that act for rapid diagnosis of TB and drug-resistant TB [16]. Thanks to the three target genes, this kit has a higher sensitivity and specificity than imported kits.

- The rapid, accurate diagnosis kit for simultaneous multiple organ fungi has helped clinicians accurately diagnose patients with fungal organs that previously often would be overlooked [17].

Application of biomass technology for producing Ngoc Linh ginseng root cells [18]

Ngoc Linh panax is a rare medicinal herb that has been exhaustively exploited. Advantages in cell biomass has shown a very short incubation period of only about 10-20 days, reduced affect by weather, epidemics, select potential cell with high biologically active substances and stable material quality so consistent with drug production according to GMP standards. Although natural Ngoc Linh panax does not fully meet the demand, thanks to this technology the market still has many products from biomass Panax that are preferred by clinicians.

Organ transplantation [19-21]

Transplantation in Vietnam was applied 50 years later than across the rest of the world, and 20 years later than other countries in the region. The first

successful kidney transplant in Vietnam was performed in 1992; then, after 18 years of effort, in 2010, transplantation in Vietnam achieved advanced techniques of organ transplants equal to the rest of the world. That means that we have gained control of the common techniques of organ transplant, including kidney, liver and heart transplant from living donors and brain dead donors. However, by 2010, we still had some outdated technologies that the rest of the world hadn't used for nearly 20-50 years. Technologies to perform lung and pancreas transplants, and techniques for donations after cardiac death (DCD) and multi-organ transplants. To solve this problem, KC10 2011-2015 program designed scientific projects to be used for transplantation. Since then, transplantation in Vietnam has really kept up with the rest of the world and created a breakthrough for the development of organ transplant in the future.

- Resolved issues with organ transplant from DCD (non-heart-beating donors). This has contributed to solving the problem of organ shortage, which is a big challenges for organ transplant. Therefore, the source of organ donation, now, is not only from living donors (brain dead), but also from non-heart-beating donors. Organ donation from a non-heart-beating donor is easier than the brain dead donors while their hearts are still beating.

- Performed successful implementation of simultaneous pancreas, kidney transplants used for the treatment of last stage renal failure for patients who have diabetes. This result terminated Vietnam's 48-year lag behind the rest of the world's pancreas transplant technology (the first pancreas transplant in the world was performed in 1966).

- Performed successful multi-organ transplants (simultaneously transplanted two organs in a patient) including a simultaneous kidney, pancreas transplant at now available at 103 hospitals, simultaneous heart-lung transplant at Hue Central Hospital, and demonstrated competence in techniques and transplant management.

- For the first time, successfully

implemented an artificial heart transplant (heartware) used to extend a patient's life while waiting for a heart transplant.

Thanks to these advances, transplants in the last five years have become a frequent technique, increasing the number of transplants. There are about 1,500 transplants that have been made in Vietnam, more than five times the amounts of transplants during the previous 17 years. In December 2015 alone, there were 96 cases of kidney transplants. In Viet-Duc hospital, four cases of transplants were performed within one day (one heart, one liver and two kidney transplants). The number of hospitals which can perform the organ transplants has increased from 12 to 17 nationwide.

Transplantation was not only achieved in technical progress, but also in management skill; this is especially clear with transplant coordination. In two years, there have been three times that organ donors from Ho Chi Minh City provided organs for transplants for patients located thousands of kilometers away in Hue and Hanoi.

Interventional radiology

Interventional radiology was developed from angiography diagnosis. It was firstly applied on January 16th, 1964, when Charles Dotter (US), for the first time, used percutaneous intravascular catheters for angioplasty to treat a patient with severe femoral arterial stenosis, which resulted in toe necrosis. The patient was saved from leg amputation. Today, interventional radiology has replaced many surgical treatments used for cardiovascular, gastrointestinal, kidney, urinary, respiratory, obstetrics and gynecology, and others diseases. This is a minimally invasive technique, anesthesia is not necessary; therefore, patients might recuperate quickly. Thanks to this advantage that many severe patients who were unable to perform operation, interventional radiology has rescued them.

Interventional radiology was started late in Vietnam, at the end of the 1990s

of the previous century (which is later than the rest of the world by about 30 years), but after ten years, many vascular intervention techniques, which were implemented across the world, were performed in the country. Especially in the last five years, interventional radiology has been widely applied to all specialties: cardiology, digestive, respiratory, urinary, neurosurgery and obstetric intervention. Many complicated techniques, which were not widely implemented across the rest of the world have also been implemented such as vascular intervention treatment of congenital heart disease, thoracic and abdominal aortic aneurysm, cerebrovascular diseases, trans-jugular intrahepatic porto-systemic shunts (TIPS), trans-catheter arterial chemoembolization (TACE) and trans venous embolization (TVE) [22-24]. Most specifically, interventional radiology for cardiovascular disease has had great progress, on par with other countries in the region and the world. Through this experience, Bach Mai Cardiovascular Institute has trained more than 30 doctors from the United States, France, Japan, China, Korea, India, Singapore, Malaysia, and Myanmar on a variety of techniques that have been developed, including enlargement of mitral valve stenosis, congenital heart interventions.

Laparoscopic surgery

The first laparoscopic surgery in the world began with a case of cholecystectomy by Erich Muhe (Germany) in 1985. Seven years later than the rest of the world, Vietnam has adopted techniques for laparoscopic surgery. Today, Vietnam's approach to laparoscopic surgery is an equal level with the rest of the world. After 18 years, especially in the last year, laparoscopic surgery has made great development in Vietnam. Complicated abdominal laparoscopic surgery, such as gastrotomy, hepatectomy, and the Whipple procedure, has become routine in many hospitals. Laparoscopic surgery outside abdominal procedures has also been performed, such as thoracic

surgery, neurosurgery, thyroid, bone & joint surgery. Vietnam has performed regular techniques, such as single hole laparoscopic surgery (single port), natural hole surgery (Natural orifice transluminal endoscopic surgery: NOTES) [25]. Vietnam is one of the first countries in the world to perform cancer colectomy through an anus, and the first country in the world to perform colectomy through a vagina. These techniques have been reported at an international laparoscopic surgery conference held in Moscow in 2014, and was a point of interest with colleagues. Especially in the last five years, we have implemented a number of robotic surgery methods, a modern surgical approach, and ensured high accuracy. This surgery is not common in the rest of the world. Many laparoscopic surgeries have been advanced by Vietnam, including thyroid surgery, some choledochal cysts surgery in pediatric, congenital megacolon, diaphragmatic hernia surgery and new endoscopic surgeries such as single port laparoscopic surgery, laparoscopic surgery through a natural hole. Therefore, in recent years many foreign colleagues have come to Vietnam for learning, exchange of experiences and invited Vietnamese experts to foreign countries for teaching and performing surgery.

Conclusion

Thanks to science and technology, in the last five years, many techniques and advanced technologies in the medical and pharmaceutical sector have been implemented in Vietnam. It can be said until now, that most valuable high-tech in the diagnosis, treatment and prevention of diseases around the world have been performed in Vietnam. This is an important contribution to improving the quality of protection and health care for communities, and bringing a great economic efficiency, a great social significance, raised the level of domestic medicine to keep up the level of international medicine. These results show the significance and importance of science and technology and also

demonstrate the effectiveness of science and technology investment in medicine.

REFERENCES

- [1] 108 Military Central Hospital (2011-2015), *The National project KC10.21/11-15 named The research on application of PET/CT and Cyberknife in the diagnosis and treatment of differentiated thyroid cancer, prostate cancer and lung cancer.*
- [2] K Hospital (2011-2015), *The National project KC10.17/11-15 named The research on application of advanced breast cancer: diagnosis and treatment.*
- [3] 108 Military Central Hospital (2011-2015), *The National project KC10.TN14/11-15 named The Research on application of the value of the detection of T1799A BRAF gene mutations to diagnose papillary thyroid cancer.*
- [4] 108 Military Central Hospital (2011-2015), *The National project KC10.TN12/11-15 named The Research on application of multiplex PCR technique in detection of common sepsis pathogens.*
- [5] National Hospital of Tropical Diseases (2011-2015), *The National project KC10.18/11-15 named The Research on application of molecular biology techniques to identify the antibiotic resistance of common strains of pathogenic bacteria found in Vietnam.*
- [6] Institute of Biotechnology, Vietnam Academy of Science and Technology (2011-2015), *The National project KC10.TN17/11-15 named Study on molecular genetics of hypothyroidism congenital adrenal hyperplasia disease in children.*
- [7] Military Medical University (2011-2015), *The National project KC10.35/11-15 named Study on the procedure of diagnosis and screening of common Vietnamese genetic diseases before embryo transfer (Pre-implantation Genetic Diagnosis) in vitro fertilization.*
- [8] National Institute of Burns (2011-2015), *The National project KC10.TN06/11-15 named Study on the isolation procedure of mesenchymal stem cells from fatty tissue and Manufacture and testing the biological products for the treatment of injuries, burns;* University of Medicine and Pharmacy at Ho Chi Minh city (2011-2015), *The National project KC10.TN07/11-15 named The Experiment of culture and isolation of dental pulp stem cells on tooth tissue regeneration in immature teeth.*
- [9] Central Lung Hospital, (2011-2015), *The National project KC10.29/11-15 named The Research on application of advanced technique in screening, early diagnosis and targeted therapy to treat lung and bronchus cancer in Vietnam.*
- [10] Bach Mai Hospital (2011-2015), *The National project KC10.39/11-15 named The Research on application of Gamma knife treatment for brain tumors, vestibular schwannoma, and brain metastasis.*
- [11] 108 Military Central Hospital (2011-2015), *The National project KC10.23/11-15 named The Application of ¹⁸F-FDG PET/CT used for diagnosing and monitoring treatment outcomes of cardiovascular disease, lymphoma, and colorectal cancer.*
- [12] Hanoi University of Pharmacy (2011-2015), *The National project KC10.14/11-15 named Apothecary of injecting liposomes with two cancer drugs, including doxorubicine and amphotericin B.*
- [13] Hanoi University of Pharmacy (2011-2015), *The National project KC10.15/11-15 named Apothecary of long-acting pills used to treat cardiovascular diseases and diabetes using HPMC (hydroxypropyl methylcellulose).*
- [14] Binh Dinh Pharmaceutical and Medical Equipment Joint Stock Company (2011-2015), *The National project KC10.DA04/11-15 named Perfecting the production process of injecting lyophilized carboplatin for cancer treatment.*
- [15] The Company for vaccine and biological production No.1 (2011-2015), *The National project KC10.DA07/11-15 named Perfecting the production process of the vaccine Rotavin-M1 to prevent diarrhea caused by Vero cells in children.*
- [16] Viet A Technologies Joint Stock (2011-2015), *The National project KC10.DA11/11-15 named Perfecting the production process of the PCR primers kit for rapid diagnosis of TB and drug-resistant TB.*
- [17] Military Medical University (2011-2015), *The National project KC10.32/11-15 named The Research on application of molecular biology techniques for accurate diagnosis on patients with fungal organs.*
- [18] Military Medical University (2011-2015), *The National project KC10.DA02/11-15 named The Application of biomass technology for producing Ngoc Linh ginseng root cells and Vinatonic.*
- [19] Cho Ray Hospital (2011-2015), *The National project KC10.28/11-15 named Kidney transplant from non-heart-beating donors.*
- [20] Military Medical University (2011-2015), *The National project KC10.27/11-15 named Experimental study of simultaneous pancreas-kidney transplant from brain dead donors.*
- [21] Hue Central Hospital (2011-2015), *The National project KC10.26/11-15 named Study on heart-lung transplant on a patient implanted with a left ventricular assist device.*
- [22] Viet Duc Hospital (2011-2015), *The National project KC10.02/11-15 named The Research on application of vascular intervention treatment for liver and kidney injuries.*
- [23] Cho Ray Hospital (2011-2015), *The National project KC10.34/11-15 named The Research on application of vascular intervention treatment for cardiovascular diseases.*
- [24] Cho Ray Hospital (2011-2015), *The National project KC10.38/11-15 named The Research on application of vascular intervention treatment for cerebral ischemia.*
- [25] Hue Central Hospital (2011-2015), *The National project KC10.31/11-15 named The Research on application of single port laparoscopic surgery and natural orifice transluminal laparoscopic surgery (NOTES) for treatment of colorectal cancer.*



Promising results of application-oriented basic research on nanomedicine in Vietnam

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Abstract:

During the present decade application-oriented basic research on nanomedicine has rapidly developed in Vietnam. This work is a review of this development. It was directed towards following scientific topics: Biomedical utilization of PLA-TPGS and PLA-PEG, dendrimer-based anticancer drugs, special drug delivery nanosystems, various utilizations of nanocurcumin in nanomedicine, biomedical application of hydrogel nanocomposites, biosensors and biosensing methods, toxicity and antibacterial activity of different types of nanoparticles. Obtained scientific results demonstrated that although Vietnamese application-oriented basic research on nanomedicine began to develop only in this decade, it has achieved very promising successes.

Keywords: anticancer, biosensor, dendrimer, drug delivery, hydrogel.

Classification numbers: 5.1, 5.2, 5.4

Introduction

At the beginning of present century the US President Bill Clinton has announced the National Nanotechnology Initiative NNI. Having been encouraged by this bright initiative, in the year 2002 Ministry of Science and Technology of Vietnam has decided to open a new prior interdisciplinary scientific direction, the Nanotechnology, in the National Basic Science Research Programme. The application of the achievements of nanotechnology to medicine has resulted in the emergence of nanomedicine in Vietnam since the beginning of the present decade. The purpose of this work is to review the development application-oriented basic research on nanomedicine in Vietnam during this first decade.

The subsequent Section II is devoted to the review of the research on the use of poly(lactide)-d- α -tocopheryl poly(ethylene glycol) succinate (PLA-TPGS) and poly(lactide)-poly(ethylene glycol)(PLA-PEG) copolymers. Some special drug delivery nanosystems are presented in Section IV. The role of curcumin (Cur) is presented in Section V. Section VI is devoted to the review on biomedical applications of hydrogel composites. The content of Section VII is the presentation on biosensors

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and biosensing methods. The subject of Section VIII is the toxicity and antibacterial activity of some types of nanoparticles. The Conclusion and Discussion are presented in Section IX.

Biomedical utilization of PLA-TPGS and PLA-PEG

The utilization of PLA-TPGS in nanomedicine began in Vietnam since 2012. Ha Phuong Thu, Le Mai Huong, et al. [1] studied apoptosis induced by PLA-TPGS in Hep-G2 cell.

Paclitaxel is an important anticancer drug in clinical use for treatment of a variety of cancers. The clinical application of paclitaxel in cancer treatment is considerably limited due to its serious poor delivery characteristics. In this study paclitaxel-loaded copolymer poly(lactide)-d- α -tocopheryl polyethylene glycol 1000 succinate (PLA-TPGS) nanoparticles were prepared by a modified solvent extraction/evaporation technique. The characteristics of the nanoparticles, such as surface morphology, size distribution, zeta potential, solubility and apoptosis were investigated *in vitro*. The obtained spherical nanoparticles were negatively charged with a zeta potential of about -18 mV with the size around 44 nm and a narrow size distribution. The ability of paclitaxel-loaded PLA-TPGS nanoparticles to induce apoptosis in human hepatocellular carcinoma cell line (Hep-G2) indicates the possibility of developing paclitaxel nanoparticles as a potential universal cancer chemotherapeutic agent.

Subsequently, *in vitro* apoptosis enhancement of Hep-G2 cells by PLA-TPGS and PLA-PEG block copolymer encapsulated Curcumin nanoparticles were investigated by Le Mai Huong, Ha Phuong Thu, et al. [2]. In this work nanodrug systems containing curcumin (Cur) encapsulated with block copolymers poly(lactide)-d- α -tocopheryl poly(ethylene glycol) 1000 succinate

(PLA-TPGS) and poly(lactide)-poly(ethylene glycol) (PLA-PEG) were prepared and characterized by infrared and fluorescence spectroscopy, field-emission scanning electron microscopy (FE-SEM), and dynamic light scattering (DLS). Upon encapsulation, the highest solubility of Cur-PLA-TPGS and Cur-PLA-PGE dried powder was calculated as high as 2.40 and 2.20 mg ml⁻¹, respectively, an increase of about 350-fold compared to that of Cur (6.79 μ g ml⁻¹). The antitumor assays (cytotoxic and antitumor-promoting assays) on Hep-G2 cells of copolymer-encapsulated Cur nanoparticles showed the apoptotic activity due to the remarkable changes in size, morphology, and angiogenesis ability of tumor cells in all cases of the tested samples as compared with the control.

In Ref. [3] Le Quang Huan, et al. investigated anti-tumor activity of docetaxel PLGA-PEG nanoparticle with a novel anti-HER2 single chain fragment (scF). The authors developed pegylated (poly(D,L-lactide-co-glycolide) (PLGA-PEG) nanoparticles for loading docetaxel and improving active target in cancer cells because they have advantages over other nanocarriers such as excellent biocompatibility, biodegradability and mechanical strength and these nanoparticles were conjugated with molecules of a novel anti-HER2 single chain fragment (scF) by a simple carbodiimide modified method. ScF have potential advantages over whole antibodies such as more rapid tumor penetration and clearance. In addition, to investigate cellular uptake of targeted nanocarriers, many studies have been performed by linking with fluorescent factors, but in this study 6-histidine-tag fused with novel anti-HER2 scF antibodies was used to purify protein and to study binding activity and cellular uptake of targeting nanoparticles. Furthermore, cytotoxicity of these nanoparticles was also investigated in

BT474 (HER2 overexpress) and MDA-MB-231 (HER2 underexpress) cells.

In vitro and *in vivo* targeting effect of folate decorated paclitaxel loaded PLA-TPGS nanoparticles was investigated by Ha Phuong Thu, et al. [4]. The authors noted that paclitaxel is one of the most effective chemotherapeutic agents for treating various types of cancer. However, the clinical application of paclitaxel in cancer treatment is considerably limited due to its poor water solubility and low therapeutic index. Thus, it requires an urgent solution to improve therapeutic efficacy of paclitaxel. In this study folate decorated paclitaxel loaded PLA-TPGS nanoparticles were prepared by a modified emulsification/solvent evaporation method. The obtained nanoparticles were characterized by FESEM, Fourier transform infrared (FTIR) and DLS method. The spherical nanoparticles were around 50 nm in size with a narrow size distribution. Targeting effect of nanoparticles was investigated *in vitro* on cancer cell line and *in vivo* on tumor bearing nude mouse. The results indicated the effective targeting of folate decorated paclitaxel loaded copolymer nanoparticles on cancer cells both *in vitro* and *in vivo*.

In Ref. [5] Ha Phuong Thu, et al. studied enhanced cellular uptake and cytotoxicity of folate decorated doxorubicin (DOX) loaded PLA-TPGS nanoparticles. DOX is one of the most effective anticancer drugs for treating many types of cancer. However, the clinical applications of DOX were hindered because of serious side-effects resulting from the unselective delivery to cancer cell including congestive heart failure, chronic cardiomyopathy and drug resistance. Recently, it has been demonstrated that loading anti-cancer drugs onto drug delivery nanosystems helps to maximize therapeutic efficiency and minimize unwanted side-effects via passive and active targeting mechanisms. In this study the authors

prepared folate decorated DOX loaded PLA-TPGS nanoparticles with the aim of improving the potential as well as reducing the side-effects of DOX. Characteristics of nanoparticles were investigated by FESEM, DLS and FTIR. Anticancer activity of the nanoparticles was evaluated through cytotoxicity and cellular uptake assays on HeLa and HT29 cancer cell lines. The results showed that prepared drug delivery system had size around 100 nm and exhibited higher cytotoxicity and cellular uptake on both tested HeLa and HT29 cells.

Previous studies have been performed by linking with fluorescent factors, but in this study 6-histidine-tag fused with novel anti-HER2 scF antibodies was used to purify protein and to study binding activity and cellular uptake of targeting nanoparticles. Furthermore, cytotoxicity of these nanoparticles was also investigated in BT474 (HER2 overexpress) and MDA-MB-231 (HER2 underexpress) cells.

In Ref. [6] Ha Phuong Thu, et al. studied characteristics and cytotoxicity of folate-modified curcumin loaded PLA-PEG micellar nano systems with various PLA/PEG ratios. Targeting delivery system using natural drugs for tumor cells is an appealing platform help to reduce the side effects and to enhance the therapeutic effects of the drug. In this study, the authors synthesized curcumin (Cur) loaded Poly lactic - Poly ethylenglycol micelle (Cur/PLA-PEG) with the ratio of PLA/PEG of 3:1, 2:1, 1:1, 1:2 and 1:3 (w/w) and another micelle modified by folate (Cur/PLA-PEG-Fol) for targeting cancer therapy. The PLA-PEG copolymer was synthesized by ring opening polymerization method. After loading onto the micelle, solubility of Cur increased from 0.38 to 0.73 mg ml⁻¹. The average size of prepared Cur/PLA-PEG micelles was from 60 to 69 nm (corresponding to the ratio difference of PLA/PEG) and the drug encapsulating efficiency was from 48.8 to 91.3%.

Compared with the Cur/PLA-PEG micelles, the size of Cur/PLA-PEG-Fol micelles were from 80 to 86 nm and showed better *in vitro* cellular uptake and cytotoxicity towards HepG2 cells. The cytotoxicity of the NPs, however, depends much on the PEG component. The results demonstrated that folate-modified micelles could serve as a potential nano carrier to improve solubility, anti-cancer activity of Cur and targeting ability of the system.

Targeted drug delivery nanosystems based on TPGS for cancer treatment were investigated by Ha Phuong Thu, et al. [7]. Along with the development of nanotechnology, drug delivery nanosystems (DDNSs) have attracted a great deal of concern among scientists over the world, especially in cancer treatment. DDNSs not only improve water solubility of anticancer drugs but also increase therapeutic efficacy and minimize the side effects of treatment methods through targeting mechanisms including passive and active targeting. Passive targeting is based on the nano-size of drug delivery systems while active targeting is based on the specific bindings between targeting ligands attached on the drug delivery systems and the unique receptors on the cancer cell surface. In this article the authors present some results in the synthesis and testing of DDNSs prepared from copolymer poly(lactide)-tocopheryl polyethylene glycol succinate (PLA-TPGS), which carry anticancer drugs including curcumin, paclitaxel and doxorubicin. In order to increase the targeting effect to cancer cells, active targeting ligand folate was attached to the DDNSs. The results showed copolymer PLA-TPGS to be an excellent carrier for loading hydrophobic drugs (curcumin and paclitaxel). The fabricated DDNSs had a very small size (50-100 nm) and enhanced the cellular uptake and cytotoxicity of drugs. Most notably, folate-decorated paclitaxel-loaded

copolymer PLA-TPGS nanoparticles (Fol/PTX/PLA-TPGS NPs) were tested on tumor-bearing nude mice. During the treatment time, Fol/PTX/PLA-TPGS NPs always exhibited the best tumor growth inhibition compared to free paclitaxel and paclitaxel-loaded copolymer PLA-TPGS nanoparticles. All results evidenced the promising potential of copolymer PLA-TPGS in fabricating targeted DDNSs for cancer treatment.

Curcumin as fluorescent probe for directly monitoring *in vitro* uptake of curcumin combined paclitaxel loaded PLA-TPGS nanoparticle was studied by Ha Phuong Thu, Hoang Thi My Nhung, et al. [8]. It was well-known that theranostics, which is the combination of both therapeutic and diagnostic capacities in one dose, is a promising tool for both clinical application and research. Although there are many chromophores available for optical imaging, their applications are limited due to the photobleaching property or intrinsic toxicity. Curcumin, a natural compound extracted from the rhizome of *curcuma longa*, is well known thanks to its bio-pharmaceutical activities and strong fluorescence as biocompatible probe for bio-imaging. In this study the authors aimed to fabricate a system with dual functions: diagnostic and therapeutic, based on poly(lactide)-tocopheryl polyethylene glycol succinate (PLA-TPGS) micelles co-loaded curcumin (Cur) and paclitaxel (PTX). Two kinds of curcumin nanoparticle (NP) were fabricated and characterized by FESEM and DLS methods. The cellular uptake and fluorescent activities of curcumin in these systems were also tested by bioassay studies, and were compared with paclitaxel-oregon. The results showed that (Cur + PTX)-PLA-TPGS NPs is a potential system for cancer theranostics.

In Ref. [9] Le Quang Huan, et al. evaluated anti-HER2 scFv-conjugated

PLGA-PEG nanoparticles on tumor-spheroids of BT474 and HCT116 cancer cells. The authors noted that three-dimensional culture cells (spheroids) are one of the multicellular culture models that can be applied to anticancer chemotherapeutic development. Multicellular spheroids more closely mimic *in vivo* tumor-like patterns of physiologic environment and morphology. In previous research, the authors designed docetaxel-loaded pegylated poly(D, L-lactide-co-glycolide) nanoparticles conjugated with anti-HER2 single chain antibodies (scFv-DOX-PLGA-PEG) and evaluated them in 2D cell culture. In this study, they continuously evaluate the cellular uptake and cytotoxic effect of scFv-DOX-PLGA-PEG on a 3D tumor spheroid model of BT474 (HER2-overexpressing) and HCT116 (HER2-underexpressing) cancer cells. The results showed that the nanoparticle formulation conjugated with scFv had a significant internalization effect on the spheroids of HER2-overexpressing cancer cells as compared to the spheroids of HER2-underexpressing cancer cells. Therefore, cytotoxic effects of targeted nanoparticles decreased the size and increased necrotic score of HER2-overexpressing tumor spheroids. Thus, these scFv-DOX-PLGA-PEG nanoparticles have potential for active targeting for HER2-overexpressing cancer therapy. In addition, BT474 and HCT116 spheroids can be used as a tumor model for evaluation of targeting therapies.

In vitro evaluation of Aurora kinase inhibitor VX680 in formulation of PLA-TPGS nanoparticles was performed by Hoang Thi My Nhung, et al. [10]. In this work polymeric nanoparticles prepared from poly(lactide)-tocopheryl polyethylene glycol succinate (PLA-TPGS) were used as potential drug carriers with many advantages to overcome the disadvantages of insoluble anticancer

drugs and enhance blood circulation time and tissues. VX680 is an Aurora kinase inhibitor and is also the foremost Aurora kinase inhibitor to be studied in clinical trials. In this study, the authors aimed to investigate whether VX680-loaded PLA-TPGS nanoparticles (VX680-NPs) are able to effectively increase the toxicity of chemotherapy. Accordingly, the authors first synthesized VX680-loaded nanoparticles and NP characterizations of morphology, mean size, zeta potential, and encapsulation efficiency were spherical shape, 63 nm, -30 mV and 76%, respectively. Then, they investigated the effects on HeLa cells. The cell cytotoxicity was evaluated by the xCELLigence real-time cell analyzer allowing measurement of changes in electrical impedance on the surface of the E-plate. Analysis of nucleus morphology and level of histone H3 phosphorylation was observed by confocal fluorescence scanning microscopy. Cell cycle distribution and apoptosis were analyzed by flow cytometry. The results showed that VX680-NPs reduced cell viability with half maximal inhibitory concentration (IC_{50}) value lower 3.4 times compared to free VX680. Cell proliferation was inhibited by VX680-NPs accompanied by other effects such as high abnormal changes of nucleus, a decrease of phospho-histone H3 at Ser10 level, an increase of polyploid cells and resulted in higher apoptotic cells. These results demonstrated that VX680-NPs had more cytotoxicity than as treated with VX680 alone. Thus, VX680-NPs may be considered as promising drug delivery system for cancer treatment.

Dendrimer-based anticancer drugs

The demonstration of a high efficiency for loading and releasing dendrimer-based anticancer drugs against cancer cells *in vitro* and *in vivo* was performed by Tran Ngoc Quyen, Nguyen Cuu Khoa, et al. [11]. In this work pegylated polyamidoamine

(PAMAM) dendrimer at generation 3.0 (G 3.0) and carboxylated PAMAM dendrimer G 2.5 were prepared for loading anticancer drugs. For loading cisplatin, carboxylated dendrimer could carry 26.64 wt/wt% of cisplatin. The nanocomplexes have size ranging from 10 to 30 nm in diameter. The drug nanocarrier showed activity against NCI-H460 lung cancer cell line with IC_{50} of $23.11 \pm 2.08 \mu\text{g ml}^{-1}$. Pegylated PAMAM dendrimers (G 3.0) were synthesized below 40 nm in diameter for carrying 5-fluorouracil (5-FU). For 5-FU encapsulation, pegylated dendrimer showed a high drug-loading efficiency of the drug and a slow release profile of 5-FU. The drug nanocarrier system exhibited an antiproliferative activity against MCF-7 cells (breast cancer cell) with a IC_{50} of $9.92 \pm 0.19 \mu\text{g ml}^{-1}$. *In vivo* tumor xenograft study showed that the 5-FU encapsulated pegylation of dendrimer exhibited a significant decrement in volume of tumor which was generated by MCF-7 cancer cells. The positive results from this study our studies could pave the ways for further research of drugs dendrimer nanocarriers toward cancer chemotherapy.

Cationic dendrimer-based hydrogels for controlled heparin release were prepared by Nguyen Cuu Khoa, Tran Ngoc Quyen, et al. [12]. In this work the authors introduced a PAMAM dendrimers and tetronic (Te) based hydrogels in which precursor copolymers were prepared with simple methods. In the synthetic process, tyramine-conjugated tetronic (TTe) was prepared via activation of its four terminal hydroxyl groups by nitrophenyl chloroformate (NPC) and then substitution of tyramine (TA) into the activated product to obtain TTe. Cationic PAMAM dendrimers G3.0 functionalized with p-hydroxyphenyl acetic acid (HPA) by use of carbodiimide coupling agent (EDC) to obtain Den-HPA. Proton nuclear magnetic

resonance ($^1\text{H-NMR}$) spectroscopy confirmed the amount of HPA and thermal analysis conjugations. The aqueous TTe and Den-HPA copolymer solution rapidly formed the cationic hydrogels in the presence of horseradish peroxidase enzyme (HRP) and hydrogen peroxide (H_2O_2) at physiological conditions. The gelation time of the hydrogels could be modulated ranging from 7 to 73 secs, when the concentrations of HRP and H_2O_2 varied. The hydrogels exhibited minimal swelling degree and low degradation under physical condition. *In vitro* cytotoxicity study indicated that the hydrogels were highly cytocompatible as prepared at 0.15 mg ml^{-1} HRP and 0.063 wt% of H_2O_2 concentration. Heparin release profiles show that the cationic hydrogels can sustainably release the anionic anticoagulant drug. The obtained results demonstrated a great potential of the cationic hydrogels for coating medical devices or delivering anionic drugs.

In Ref. [13] Nguyen Cuu Khoa, Tran Ngoc Quyen, et al. applied $^1\text{H-NMR}$ spectroscopy as an effective method for predicting molecular weight of polyaminoamine dendrimers and their derivatives. They have established two formulas to predict molecular weight of polyaminoamine dendrimers and their alkylated derivatives, based on the theoretical number of protons at specific positions in the dendrimers and the true value of the integral values of these protons appearing in proton nuclear magnetic resonance spectra. Calculated results indicated that molecular weight of the dendrimers is approximately equal to results from mass spectrometry. Degrees of alkylation were easily calculated for each dendrimer-alkylated derivative. According to the obtained results, the authors confirm that the use of the proton spectra can be an effective method to predict molecular weight of dendrimers.

An improved method for preparing

cisplatin-dendrimer nanocomplex and its behavior against NCI-H460 lung cancer cell were investigated by Tran Ngoc Quyen, Nguyen Cuu Khoa, et al. [14]. The effect of anticancer drugs could be significantly enhanced if it is encapsulated in drug delivery vehicles such as liposomes, polymers, dendrimers and other materials. For some conventional cisplatin encapsulating methods, however, suffers from low loading efficiency. Therefore, in order to overcome this limitation, in this study sonication was used in preparation of the nanocomplex of a species of aquated cisplatin and carboxylated PAMAM dendrimer G3.5 to evaluate loading capacity as well as platinum release behavior using FTIR, UV-Vis, NMR, inductively coupled plasma atomic absorption spectroscopy (ICP-AES), and transmission electron microscopy (TEM). The results showed that 25.20 and 27.83 wt/wt% of cisplatin were loaded under stirring and sonication respectively, a remarkably improvement in loading efficiency compared to that of conventional method that used of cisplatin. *In vitro* study showed that this drug-nanocarrier complex also help reduce cisplatin's cytotoxicity but can still keep sufficient antiproliferative activity against lung cancer cell, NCI-H460, with IC_{50} at $0.985 \pm 0.01 \mu\text{M}$.

Highly lipophilic pluronics-conjugated polyamidoamine dendrimer nanocarriers as potential delivery system for hydrophobic drug were investigated by Nguyen Cuu Khoa, Tran Ngoc Quyen, et al. [15]. In this work four kinds of pluronics (P123, F68, F127 and F108) with varying hydrophilic-lipophilic balance (HLB) values were modified and conjugated on 4th generation of dendrimer PAMAM. The obtained results from FTIR, $^1\text{H-NMR}$, gel permeation chromatography (GPC) showed that the pluronics effectively conjugated on the dendrimer. The molecular weight of four PAMAM G4.0-Pluronic

and its morphologies are in range of 200.15-377.14 KDa and around 60-180 nm in diameter by TEM, respectively. Loading efficiency and release of hydrophobic fluorouracil (5-FU) anticancer drug were evaluated by high performance liquid chromatography (HPLC). Interesting that the dendrimer nanocarrier was conjugated with a highest lipophilic pluronic P123 (G4.0-P123) exhibiting a highest drug loading efficiency (up to 76.25%) in comparison with another pluronics. Live/dead fibroblast cell staining assay mentioned that all conjugated nanocarriers are highly biocompatible. The drug-loaded nanocarriers also indicated a highly anti-proliferative activity against MCF-7 breast cancer cell. The obtained results demonstrated a great potential of the highly lipophilic pluronics-conjugated nanocarriers in hydrophobic drugs delivery for biomedical applications.

Special drug delivery nanosystems

In Ref. [16] Nguyen To Hoai, Dang Mau Chien, et al. attempted to fabricate a nanoparticle formulation of ketoprofen (Keto)-encapsulated cucurbit [6] (CB [6]) uril nanoparticles, to evaluate its *in vitro* dissolution and to investigate its *in vivo* pharmaceutical property. The CB [6]-Keto nanoparticles were prepared by emulsion solvent evaporation method. Morphology and size of the successfully prepared nanoparticles were then confirmed using a transmission electron microscope and dynamic light scattering. It was shown that they are spherical with hydrodynamic diameter of 200-300 nm. The *in vitro* dissolution studies of CB [6]. Keto nanoparticles were conducted at pH 1.2 and 7.4. The results indicated that there is a significant increase in Keto concentration at pH 7.4 compared to pH 1.2. For the *in vivo* assessment, CB [6]. Keto nanoparticles and referential profenid were administered by oral gavages to rabbits. The results implied that CB[6]-Keto nanoparticles remarkably increased area under the

curve compared to profenid.

As new copolymer material for oral delivery of insulin Ho Thanh Ha, Dang Mau Chien, et al. [17] used poly(ethylene glycol)-grafted chitosan. In this work a new scheme of grafting poly (ethylene glycol) onto chitosan was proposed in this study to give new material for delivery of insulin over oral pathway. First, methoxy poly(ethylene glycol) amine (mPEGa MW 2000) were grafted onto chitosan (CS) through multiples steps to synthesize the grafting copolymer PEG-g-CS. After each synthesis step, chitosan and its derivatives were characterized by FTIR, ¹H-NMR. Then, insulin loaded PEG-g-CS nanoparticles were prepared by cross-linking of CS with sodium tripolyphosphate (TPP). Same insulin loaded nanoparticles using unmodified chitosan were also prepared in order to compare with the modified ones. Results showed better protecting capacity of the synthesized copolymer over original CS. CS nanoparticles (10 nm of size) were gel like and high sensible to temperature as well as acidic environment while PEG-g-CS nanoparticles (200 nm of size) were rigid and more thermo and pH stable.

Targeted drug delivery nanosystems based on poly(lactide)-tocopheryl polyethylene glycol succinate for cancer treatment were studied by Ha Phuong Thu, et al. [18]. The authors noted that along with the development of nanotechnology, drug delivery nanosystems (DDNSs) have attracted a great deal of concern among scientists over the world, especially in cancer treatment. DDNSs not only improve water solubility of anticancer drugs but also increase therapeutic efficacy and minimize the side effects of treatment methods through targeting mechanisms including passive and active targeting. Passive targeting is based on the nano-size of drug delivery systems while active targeting is based on the specific bindings between targeting

ligands attached on the drug delivery systems and the unique receptors on the cancer cell surface. In this article the authors present some of our results in the synthesis and testing of DDNSs prepared from copolymer poly(lactide)-tocopheryl polyethylene glycol succinate (PLA-TPGS), which carry anticancer drugs including curcumin, paclitaxel and doxorubicin. In order to increase the targeting effect to cancer cells, active targeting ligand folate was attached to the DDNSs. The results showed copolymer PLA-TPGS to be an excellent carrier for loading hydrophobic drugs (curcumin and paclitaxel). The fabricated DDNSs had a very small size (50-100 nm) and enhanced the cellular uptake and cytotoxicity of drugs. Most notably, folate-decorated paclitaxel-loaded copolymer PLA-TPGS nanoparticles (Fol/PTX/PLA-TPGS NPs) were tested on tumor-bearing nude mice. During the treatment time, Fol/PTX/PLA-TPGS NPs always exhibited the best tumor growth inhibition compared to free paclitaxel and paclitaxel-loaded copolymer PLA-TPGS nanoparticles. All results evidenced the promising potential of copolymer PLA-TPGS in fabricating targeted DDNSs for cancer treatment.

Chitosan-grafted pluronic® F127 copolymer nanoparticles containing DNA aptamer for PTX delivery to treat breast cancer cells were investigated by Nguyen Kim Thach, Le Quang Huan, et al. [19]. It was well-known that HER-2/ ErbB2/Neu(HER-2), a member of the epidermal growth factor receptor family, is specifically overexpressed on the surface of breast cancer cells and serves a therapeutic target for breast cancer. In this study, the authors aimed to isolate DNA aptamer (Ap) that specifically bind to a HER-2 overexpressing SK-BR-3 human breast cancer cell line, using SELEX strategy. They developed a novel multifunctional composite micelle with surface modification of Ap for targeted delivery of paclitaxel. This

binary mixed system consisting of Ap modified pluronic®F127 and chitosan could enhance PTX loading capacity and increase micelle stability. Polymeric micelles had a spherical shape and were self-assemblies of block copolymers of approximately 86.22±1.45 nm diameter. PTX could be loaded with high encapsulation efficiency (83.28±0.13%) and loading capacity (9.12±0.34%). The release profile were 29-35% in the first 12 h and 85-93% after 12d at pH 7.5 of receiving media. The IC₅₀ doses by (3-(4,5-dimethylthiazol-2-yl) 2,5 dimethyltetrazolium bromide) (MTT) assay showed the greater activity of nanoparticles loaded paclitaxel over free paclitaxel and killed cells up to 95% after 6 h. These results demonstrated unique assembly with the capacity to function as an efficient detection and delivery vehicle in the biological living system.

In Ref. [20] Nguyen Tuan Anh, Dang Mau Chien, et al. demonstrated micro and nano liposome vesicles containing curcumin for using as a drug delivery system. In this work micro and nano liposome vesicles were prepared using a lipid film hydration method and a sonication method. Phospholipid, cholesterol and curcumin were used to form micro and nano liposomes containing curcumin. The size, structure and properties of the liposomes were characterized by using optical microscopy, TEM, UV-Vis and Raman spectroscopy. It was found that the size of the liposomes was dependent on their composition and the preparation method. The hydration method created micro multilamellars, whereas nano unilamellars were formed using the sonication method. By adding cholesterol, the vesicles of the liposome could be stabilized and stored at 4°C for up to 9 months. The liposome vesicles containing curcumin with good biocompatibility and biodegradability could be used for drug delivery applications.

Hierarchical self-assembly of heparin-PEG end-capped porous silica as a redox sensitive nanocarrier for doxorubicin delivery was demonstrated by Nguyen Cuu Khoa, Nguyen Dai Hai, et al. [21]. The authors noted that porous nanosilica (PNS) has been attracting a great attention in fabrication carriers for drug delivery system (DDS). However, unmodified PNS-based carriers exhibited the initial burst release of loaded bioactive molecules, which may limit their potential clinical application. In this study the surface of PNS was conjugated with adamantylamine (A) via disulfide bonds (PNS-SS-A) which was functionalized with cyclodextrin-heparin-polyethylene glycol (CD-HPEG) for redox triggered doxorubicin (DOX) delivery. The modified PNS was successfully formed with spherical shape and diameter around 50 nm determined by TEM. DOX was efficiently trapped in the PNS-SS-A@CD-HPEG and slowly released in phosphate buffered saline (PBS) without any initial burst effect. Importantly, the release of DOX was triggered due to the cleavage of the disulfide bonds in the presence of dithiothreitol (DTT). In addition, the MTT assay data showed that PNS-SS-A@CD-HPEG was a biocompatible nanocarrier and reduced the toxicity of DOX. These results demonstrated that PNS-SS-A@CD-HPEG has great potential as a novel nanocarrier for anticancer drug in cancer therapy.

Various utilizations of nanocurcumin in nanomedicine

In Section II we have presented the combinations of curcumin with paclitaxel loaded PLA-TPGS nanoparticles, PLA-PEG micellar nanosystems and PLA-TPGS and PLA-PEG block copolymer. In Section IV the micro and nano liposome vesicles drug delivery system containing curcumin was also presented. Beside above-mentioned combinations containing curcumin there are other biomedical

utilizations of nanocurcumin. In Ref. [22] Le Mai Huong, Ha Phuong Thu et al. investigated antitumor activity of curcumin encapsulated by 1,3- β -glucan isolated from Vietnam medicinal mushroom *Hericium erinaceum*. It was known that the clinical application of curcumin in cancer treatment is considerably limited due to its serious poor delivery characteristics. In order to increase the hydrophilicity and drug delivery capability, the authors encapsulated curcumin into 1,3- β -glucan isolated from Vietnam medicinal mushroom *Hericium erinaceum*. The 1,3- β -glucan-encapsulated curcumin nanoparticles (Cur-Glu) were found to be spherical with an average size of 50 nm, being suitable for drug delivery applications. They were much more soluble in water not only than free curcumin but also than other biodegradable polymer-encapsulated curcumin nanoparticles. An antitumor-promoting assay was carried out, showing the positive effects of Cur-Glu on tumor promotion of Hep-G2 cell line *in vitro*.

Folate attached, curcumin loaded Fe_3O_4 nanoparticles as a novel multifunctional drug delivery system for cancer treatment were prepared and investigated by Ha Phuong Thu, Nguyen Xuan Phuc, et al. [23]. In this work the authors studied the role of folic acid as a targeting factor on magnetic nanoparticle Fe_3O_4 based curcumin loading nanosystem. Characteristics of the nanosystems were investigated by FTIR and FESEM, X-ray diffraction (XRD), thermal gravimetric analysis (TGA) and vibrating sample magnetometer (VSM), while targeting role of folic acid was accessed *in vivo* on tumor bearing mice. The results showed that folate attached Fe_3O_4 based curcumin loading nanosystem has very small size and exhibits better targeting effect compared to the counterpart without folate. In addition, magnetic induction heating of this nanosystem evidenced its potential for cancer hyperthermia.

In Ref. [24] Ha Phuong Thu, Nguyen Xuan Phuc, et al. investigated Fe_3O_4 /o-Carboxymethyl Chitosan/Curcumin-based nanodrug system for chemotherapy and fluorescence imaging in HT29 cancer cell line. In this work a multifunctional nanodrug system containing Fe_3O_4 , o-carboxymethyl chitosan (OCMCs), and curcumin (Cur) has been prepared and characterized by infrared and fluorescence spectroscopy, XRD and FE-SEM. The fluorescent staining experiments showed that this system not only had no effect on the cell internalization ability of curcumin but also successfully led curcumin into the HT29 cells as expected. From real-time cell analysis (RTCA), the effect of Fe_3O_4 /OCMCs/Cur on this cancer cell line was found to be much stronger than that of pure curcumin. This system contained magnetic particles and, therefore, could be also considered for hyperthermia therapy in cancer treatment.

A novel nanofiber curcumin-loaded polylactic acid constructed by electrospinning was investigated by Mai Thi Thu Trang, Tran Dai Lam, et al. [25]. Curcumin (Cur), extracted from the *Curcuma longa* L. plant, is well known for its anti-tumor, anti-oxidant, anti-inflammatory and anti-bacterial properties. Nanofiber mats of polylactic acid (PLA) loading Cur (5 wt%) were fabricated by electrospinning (e-spinning). Morphology and structure of the fibers were characterized by FE-SEM and FTIR spectroscopy, respectively. The diameters of the obtained fibers varied from 200 to 300 nm. The release capacity of curcumin from curcumin-loaded PLA fibers was investigated in phosphate buffer saline (PBS) containing ethanol. After 24 h, 50% of the curcumin was released from curcumin-loaded PLA fibers. These results of electrospun (e-spun) fibers exhibit the potential for biomedical application.

In Ref. [26] Ha Phuong Thu, Nguyen Xuan Phuc, et al. prepared polymer-

encapsulated curcumin nanoparticles and investigated their anti-cancer activity. It is well-known that curcumin (Cur) is a yellow compound isolated from rhizome of the herb *Curcuma longa*. Curcumin possesses antioxidant, anti-inflammatory, anti-carcinogenic and antimicrobial properties, and suppresses proliferation of many tumor cells. However, the clinical application of curcumin in cancer treatment is considerably limited due to its serious poor delivery characteristics. In order to increase the hydrophilicity and drug delivery capability, the authors encapsulated curcumin into copolymer PLA-TPGS, 1,3- β -glucan (Glu), O-carboxymethyl chitosan (OCMCS) and folate-conjugated OCMCS (OCMCS-Fol). These polymer-encapsulated curcumin nanoparticles (Cur-PLA-TPGS, Cur-Glu, Cur-OCMCS and Cur-OCMCS-Fol) were characterized by infrared (IR), fluorescence (FL), photoluminescence (PL) spectra, FE-SEM, and found to be spherical particles with an average size of 50-100 nm, being suitable for drug delivery applications. They were much more soluble in water than not only free curcumin but also other biodegradable polymer-encapsulated curcumin nanoparticles. The anti-tumor promoting assay was carried out, showing the positive effects of Cur-Glu and Cur-PLA-TPGS on tumor promotion of Hep-G2 cell line *in vitro*. Confocal microscopy revealed that the nano-sized curcumin encapsulated by polymers OCMCS and OCMCS-Fol significantly enhanced the cellular uptake (cancer cell HT29 and HeLa).

Curcumin-loaded pluronic F127/Chitosan nanoparticles for cancer therapy were prepared by Le Quang Huan, et al. [27]. In this work curcumin-loaded NPs have been prepared by an ionic gelation method using CS and pluronic®F-127 (PF) as carriers to deliver curcumin to the target cancer cells. Prepared NPs were characterized using Zetasizer,

fluorescence microscopy, SEM and TEM. The results showed that the encapsulation efficiency of curcumin was approximately 50%. The average size of curcumin-loaded PF/CS NPs was 150.9 nm, while the zeta potential was 5.09 mV. Cellular uptake of curcumin-loaded NPs into HEK293 cells was confirmed by fluorescence microscopy.

In a subsequent work [28] Le Quang Huan, et al. investigated docetaxel and curcumin-containing poly(ethylene glycol)-block-poly(ϵ -caprolactone) polymer micells. In this work nanoparticles (NPs) prepared from poly(ethylene glycol)-block-poly(ϵ -caprolactone) (PEG-PCL) were fabricated by the modified nanoprecipitation method with and without sonication to entrap DOX and curcumin (Cur). NPs were characterized in terms of morphology, size distribution, zeta potential, encapsulation efficiency and cytotoxicity. The particles have a ~45-80 nm mean diameter with a spherical shape. The cellular uptake of the NPs was observed after 2 and 4 h of incubation by fluorescence of curcumin loaded with docetaxel. The cell viability was evaluated by an MTT assay on the Hela cell line. DOX and DOX-Cur NPs had higher cytotoxicity and a much lower IC_{50} value compared with free DOX or Cur after 24 and 48 h of incubation. Doc and Cur incorporated into the PEG-PCL NPs had the highest cytotoxicity in comparison with all other NPs and may be considered as an attractive and promising drug delivery system for cancer treatment.

Biomedical application of hydrogel nanocomposites

Tetronic-grafted chitosan hydrogel as an injectable and biocompatible scaffold for biomedical applications was investigated by Tran Ngoc Quyen, Nguyen Cuu Khoa, et al. [29]. In recent years, injectable chitosan-based hydrogels have been widely studied towards biomedical applications because

of their potential performance in drug/cell delivery and tissue regeneration. In this study, the authors introduce a simple and organic solvent-free method to prepare tyramine tetronic-grafted chitosan (TTeCS) via activation of four terminal hydroxyl groups of tetronic, partial tyramine conjugate into the activated product and grafting remaining activated moiety of tetronic-tyramine onto chitosan. The grafted copolymer was well-characterized by UV-Vis, 1H -NMR and TGA. The aqueous TTeC copolymer solution rapidly formed hydrogel in the presence of horseradish peroxidase (HRP) and hydrogen peroxide (H_2O_2) at physiological conditions. The gelation time of the hydrogel was performed within a time period of 4 to 60 sec when the concentrations of HRP, H_2O_2 , and polymers varied. The hydrogel exhibited highly porous structure which could be controlled by using H_2O_2 . *In vitro* cytotoxicity study with Human Foreskin Fibroblast cell using live/dead assay indicated that the hydrogel was high cytocompatibility and could play a role as a scaffold for cell adhesion. The injectable hydrogels didn't cause any inflammation after one day and 2 weeks of the *in vivo* injection. The obtained results demonstrated a great potential of the TTeCS hydrogel in biomedical applications.

Enzyme-mediated *in situ* preparation of biocompatible hydrogel composites from chitosan derivative and biphasic calcium phosphate nanoparticles for bone regeneration was performed by Nguyen Cuu Khoa, Tran Ngoc Quyen, et al. [30]. It was known that injectable chitosan-based hydrogels have been widely studied toward biomedical applications because of their potential performance in drug/cell delivery and tissue regeneration. In this study the authors introduce tetronic-grafted chitosan containing tyramine moieties which have been utilized for *in situ* enzyme-mediated hydrogel preparation. The hydrogel can be used

to load nanoparticles (NPs) of biphasic calcium phosphate (BCP), mixture of hydroxyapatite (HAp) and tricalcium phosphate (TCP), forming injectable biocomposites. The grafted copolymers were well-characterized by $^1\text{H-NMR}$. BCP nanoparticles were prepared by precipitation method under ultrasonic irradiation and then characterized by using XRD and SEM. The suspension of the copolymer and BCP nanoparticles rapidly formed hydrogel biocomposite within a few seconds of the presence of HRP and H_2O_2 . The compressive stress failure of the wet hydrogel was at 591 ± 20 KPa with the composite 10 wt% BCP loading. *In vitro* study using mesenchymal stem cells showed that the composites were biocompatible and cells are well-attached on the surfaces.

Fabrication of hyaluronan-poly(vinylphosphonic acid)-chitosan hydrogel for wound healing application was performed by Nguyen Dai Hai, Bui Chi Bao, et al. [31]. In this work new hydrogel made of hyaluronan, poly(vinylphosphonic acid), and chitosan (HA/PVPA/CS hydrogel) was fabricated and characterized to be used for skin wound healing application. Firstly, the component ratio of hydrogel was studied to optimize the reaction effectiveness. Next, its microstructure was observed by light microscope. The chemical interaction in hydrogel was evaluated by NMR spectroscopy and FTIR spectroscopy. Then, a study on its degradation rate was performed. After that, antibacterial activity of the hydrogel was examined by agar diffusion method. Finally, *in vivo* study was performed to evaluate hydrogel's biocompatibility. The results showed that the optimized hydrogel had a three-dimensional highly porous structure with the pore size ranging from about $25\ \mu\text{m}$ to less than $125\ \mu\text{m}$. Besides, with a degradation time of two weeks, it could give enough time for the formation of extracellular matrix framework during remodeling stages. Furthermore, the

antibacterial test showed that hydrogel has antimicrobial activity against *E. coli*. Finally, *in vivo* study indicated that the hydrogel was not rejected by the immune system and could enhance wound healing process. Overall, HA/PVPA/CS hydrogel was successfully fabricated and results implied its potential for wound healing applications.

In Ref. [32] injectable hydrogel composite based gelatin-PEG and biphasic calcium phosphate nanoparticles for bone regeneration was prepared by Nguyen Cuu Khoa, Tran Dai Lam, et al. Gelatin hydrogels have recently attracted much attention for tissue regeneration because of their biocompatibility. In this study the authors introduce polyethylene glycol (PEG)-grafted gelatin containing tyramine moieties which have been utilized for *in situ* enzyme-mediated hydrogel preparation. The hydrogel can be used to load nanoparticles of biphasic calcium phosphate, a mixture of hydroxyapatite and b-tricalcium phosphate, and forming injectable bio-composites. $^1\text{H-NMR}$ spectra indicated that tyramine-functionalized polyethylene glycol-nitrophenyl carbonate ester was conjugated to the gelatin. The hydrogel composite was rapidly formed *in situ* (within a few seconds) in the presence of horseradish peroxidase and hydrogen peroxide. *In vitro* experiments with biomineralization on the hydrogel composite surfaces was well-observed after 2 weeks soaking in simulated body fluid solution. The obtained results indicated that the hydrogel composite could be a potential injectable material for bone regeneration.

Biosensors and biosensing methods

Biosensor for cholesterol detection using interdigitated electrodes based on polyaniline-carbon nanotube film was demonstrated by Tran Dai Lam, et al. [33]. In this work polyaniline-carboxylic multiwalled carbon nanotubes composite film (PANi-MWCNT)

has been polymerized on the surface of interdigitated platinum electrode (fabricated by MEMS technology) which was compatibly connected to Autolab interface via universal serial bus (USB). An amperometric biosensor based on covalent immobilization of cholesterol oxidase (ChOx) on PANi-MWCNT film with potassium ferricyanide (FeCN) as the redox mediator was developed. The mediator helps to shuttle the electrons between the immobilized ChOx and the PANi-MWCNT electrode, therefore operating at a low potential of $-0.3\ \text{V}$ compared to the saturated calomel electrode (SCE). This potential precludes the interfering compounds from oxidation. The bio-electrode exhibits good linearity from 0.02 to 1.2 mM cholesterol concentration with a correlation coefficient of 0.9985.

Electrochemical immunosensors based on different serum antibody immobilization methods for detection of Japanese encephalitis virus was developed by Tran Quang Huy, Nguyen Thi Hong Hanh, et al. [34]. In this work the authors described the development of electrochemical immunosensors based on human serum antibodies with different immobilization methods for detection of Japanese encephalitis virus (JEV). Human serum containing anti-JEV antibodies was used to immobilize onto the surface of silanized interdigitated electrodes by four methods: direct adsorption (APTES-serum), covalent binding with a cross linker of glutaraldehyde (APTES-GA-serum), covalent binding with a cross linker of glutaraldehyde combined with anti-human IgG (APTES-GA-anti-HIgG-serum) and covalent binding with a cross linker of glutaraldehyde combined with a bioaffinity of protein A (APTES-GA-PrA-serum). Atomic force microscopy was used to verify surface characteristics of the interdigitated electrodes before and after treatment with serum antibodies. The output signal of the immunosensors was measured by

the change of conductivity resulting from the specific binding of JEV antigens and serum antibodies immobilized on the electrodes, with the help of horseradish peroxidase (HRP)-labeled secondary antibody against JEV. The results showed that the APTES-GA-PrA-serum method provided the highest signal of the electrochemical immunosensor for detection of JEV antigens, with the linear range from 25 ng ml⁻¹ to 1 µg ml⁻¹, and the limit of detection was about 10 ng ml⁻¹. This study showed a potential development of novel electrochemical immunosensors applied for virus detection in clinical samples in case of possible outbreaks.

Graphene patterned polyaniline-based biosensor for glucose detection was fabricated by Nguyen Van Chuc, Tran Dai Lam, et al. [35]. In this work a glucose electrochemical biosensor was layer-by-layer fabricated from graphene and polyaniline films. Graphene sheets (0.5×0.5 cm²) with the thickness of 5 nm (15 layers) were synthesized by thermal chemical vapor deposition (CVD) under ambient pressure on copper tapes. Then they were transferred into integrated Fe₃O₄-doped polyaniline (PANi) based microelectrodes. The properties of the nanocomposite films were thoroughly characterized by SEM, Raman spectroscopy, atomic force microscopy (AFM) and electrochemical methods, such as square wave voltammetry (SWV) and chronoamperometry. The above graphene patterned sensor (denoted as Graphene/Fe₃O₄/PANi/GOx) shows much improved glucose sensitivity (as high as 47 µA mM⁻¹ cm⁻²) compared to a non-graphene one (10 - 30 µA mM⁻¹ cm⁻², as previously reported in the literature). It can be expected that this proof-of-concept biosensor could be extended for other highly sensitive biodection.

Preparation of a fluorescent label tool based on lanthanide nanophosphor for viral biomedical application

was performed by Le Quoc Minh, et al. [36]. In this article the authors reported the preparation of luminescent lanthanide nanomaterial (LLN) linked bioconjugates and their application as a label tool for recognizing virus in the processing line of vaccine industrial fabrication. Several LLNs with the nanostructure forms of particles or rods/wires with europium(III) and terbium(III) ions in lattices of vanadate, phosphate and metal organic complex were prepared to develop novel fluorescent conjugates able to be applied as labels in fluorescence immunoassay analysis of virus/vaccine.

In Ref. [37] Tran Hong Nhung, et al. synthesized dye-doped water soluble silica-based nanoparticles to label bacteria *E. coli* O157:H7 and investigated their photophysical properties. In this work organically modified silicate (ORMOSIL) nanoparticles (NPs) doped with rhodamine 6G and rhodamine B (RB) dyes were synthesized by Stöber method from methyltriethoxysilane CH₃Si(OCH₃)₃ precursor (MTEOS). The NPs are surface functionalized by cationic amino groups. The optical characterization of dye-doped ORMOSIL NPs was studied in comparison with that of free dye in solution. The synthesized NPs were used for labeling bacteria *E. coli* O157:H7. The number of bacteria have been counted using the fluorescent spectra and microscope images of labeled bacteria. The results show the ability of NPs to work as biomarkers.

The fabrication of the layer-by-layer biosensor using graphene films and the application for cholesterol determination were performed by Nguyen Van Chuc, et al. [38]. In this work the preparation and characterization of graphene films for cholesterol determination are described. The graphene films were synthesized by thermal chemical vapor deposition (CVD) method. Methane gas (CH₄) and copper tape were used as carbon source and catalyst in the

graphene growth process, respectively. The integrated array was fabricated by using micro-electro-mechanical systems (MEMS) technology in which Fe₃O₄-doped polyaniline (PANi) film was electropolymerized on Pt/Gr electrodes. The properties of the Pt/Gr/PANi/Fe₃O₄ films were investigated by FE-SEM, Raman spectroscopy and electrochemical techniques. Cholesterol oxidase (ChOx) has been immobilized onto the working electrode with glutaraldehyde agent. The cholesterol electrochemical biosensor shows high sensitivity (74 µA mM⁻¹ cm⁻²) and fast response time (<5 s). A linear calibration plot was obtained in the wide cholesterol concentration range from 2 to 20 mM and correlation coefficient square (R²) of 0.9986. This new layer-by-layer biosensor based on graphene films promises many practical applications.

Electrosynthesis of polyaniline-multiwalled carbon nanotube nanocomposite films in the presence of sodium dodecyl sulfate for glucose biosensing was performed by Tran Dai Lam, et al. [39]. In this work polyaniline-multiwalled carbon nanotube (PANi-MWCNT) nanocomposites were electropolymerized in the presence of sodium dodecyl sulfate (SDS) onto interdigitated platinum-film planar microelectrodes (IDµE). The MWCNTs were first dispersed in SDS solution then mixed with aniline and H₂SO₄. This mixture was used to electro-synthesize PANi-MWCNT films with potentiostatic method at E = +0.90 V (versus SCE). The PANi-MWCNT films were characterized by cyclic voltammetry (CV) and SEM. The results show that the PANi-MWCNT films have a high electroactivity, and a porous and branched structure that can increase the specific surface area for biosensing application. In this work the PANi-MWCNT films were applied for covalent immobilization of glucose oxidase (GOx) via glutaraldehyde agent. The GOx/PANi-MWCNT/IDµE

was studied using cyclic voltammetric and chronoamperometric techniques. The effect of several interferences, such as ascorbic acid (AA), uric acid (UA), and acetaminophen (AAP) on the glucosensing at +0.6 V (versus SCE) is not significant. The time required to reach 95% of the maximum steady-state current was less than 5 s. A linear range of the calibration curve for the glucose concentration lies between 1 and 12 mM which is a suitable level in the human body.

In Ref. [40] Ngo Vo Ke Thanh, et al. demonstrated a quartz crystal microbalance (QCM) as biosensor for detecting *Escherichia coli* O157:H7. The anti-*E. coli* O157:H7 antibodies were immobilized on a self-assembly monolayer (SAM) modified 5 MHz AT-cut quartz crystal resonator. The SAMs were activated with 16-mercaptopropanoic acid, in the presence of 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDC) and ester N-hydroxysuccinimide (NHS). The result of changing frequency due to the adsorption of *E. coli* O157:H7 was measured by the QCM biosensor system designed and fabricated by ICDREC-VNUHCM. This system gave good results in the range of 10^2 - 10^7 CFU ml^{-1} *E. coli* O157:H7. The time of bacteria *E. coli* O157:H7 detection in the sample was about 50 minutes. Besides, QCM biosensor from SAM method was comparable to protein A method-based piezoelectric immunosensor in terms of the amount of immobilized antibodies and detection sensitivity.

A significant progress in the research on silica-based optical nanoparticles for biomedical application was achieved by Tran Hong Nhung, et al. [41]. This article is a review of their research results. Gold, dye-doped silica based and core-shell multifunctional multilayer (SiO_2/Au , $\text{Fe}_3\text{O}_4/\text{SiO}_2$, $\text{Fe}_3\text{O}_4/\text{SiO}_2/\text{Au}$) water-monodispersed nanoparticles were synthesized by chemical route and

surface modified with proteins and biocompatible chemical reagents. The particles were conjugated with antibody or aptamer for specific detecting and imaging bacteria and cancer cells. The photothermal effects of gold nanoshells (SiO_2/Au and $\text{Fe}_3\text{O}_4/\text{SiO}_2/\text{Au}$) on cells and tissues were investigated. The nano silver substrates were developed for surface enhanced Raman scattering (SERS) spectroscopy to detect melamine.

The preparation of gold nanoparticles by microwave heating and the study the conjugate of gold nanoparticles with *E. coli* O157:H7 antibody were demonstrated by Ngo Vo Ke Thanh, et al. [42]. In this article the authors described a method for the low cost synthesis of gold nanoparticles using sodium citrate (Na_3Ct) reduction in chloroauric acid ($\text{HauCl}_4 \cdot 3\text{H}_2\text{O}$) by microwave heating (diameter about 13-15 nm). Gold nanoparticles were functionalized with surface activation by 3-mercaptopropionic acid for attaching antibody. These nanoparticles were then reacted with anti-*E. coli* O157:H7, using N-hydroxy succinimide (NHS) and carbondimide hydrochloride (EDC) coupling chemistry. The product was characterized with UV-visible spectroscopy, FTIR spectroscopy and zeta potential. In addition, the binding of antibody-gold nanoparticles conjugates to *E. coli* O157:H7 was demonstrated using TEM.

Silicon nanowire sensor for detecting alpha-fetoprotein biomarker of liver cancer was fabricated by Pham Van Binh, Dang Mau Chien, et al. [43]. In this article the authors presented a facile technique that only uses conventional micro-techniques and two size-reduction steps to fabricate wafer-scale silicon nanowire (SiNW) with widths of 200 nm. Initially, conventional lithography was used to pattern SiNW with 2 μm width. Then the nanowire width was decreased to

200 nm by two size-reduction steps with isotropic wet etching. The fabricated SiNW was further investigated when used with nanowire field-effect sensors. The electrical characteristics of the fabricated SiNW devices were characterized and pH sensitivity was investigated. Then a simple and effective surface modification process was carried out to modify SiNW for subsequent binding of a desired receptor. The complete SiNW-based biosensor was then used to detect alpha-fetoprotein (AFP), one of the medically approved biomarkers for liver cancer diagnosis. Electrical measurements showed that the developed SiNW biosensor could detect AFP with concentrations of about 100 ng ml^{-1} . This concentration is lower than the necessary AFP concentration for liver cancer diagnosis.

Electrochemical aptasensor for detecting tetracycline in milk was demonstrated by Le Quang Huan, et al. [44]. In this article the authors developed a label-free aptasensor for electrochemical detection of tetracycline. According to the electrochemical impedance spectroscopy (EIS) analysis, there was a linear relationship between the concentration of tetracycline and the electron transfer resistance from 10 to 3000 ng ml^{-1} of the tetracycline concentration. The detection limit was 10 ng ml^{-1} in 15 min detection duration. The prepared aptasensor showed a good reproducibility with an acceptable stability in tetracycline detection. The recoveries of tetracycline in spiked milk samples were in the range of 88.1-94.2%. The aptasensor has sensitivity 98% and specificity of 100%.

Toxicity and antibacterial activity of different types of nanoparticles

Capping and *in vivo* toxicity studies of gold nanoparticles were performed by Tran Hong Nhung, et al. [45]. In this work water-dispersed colloidal gold nanoparticles (AuNPs) with



high concentration were synthesized from metal precursor HauCl_4 . The bovine serum albumin (BSA) and heterobiofunctionalized thiol polyethylene glycol acid (HS-PEG-COOH) were used as biofunctionalized layers for the synthesized AuNPs. The BSA and HS-PEG-COOH bound to the AuNPs were characterized qualitatively and quantitatively by transmission electron microscope and UV-VS spectrophotometer. The fabricated BSA and HS-PEG-COOH-capped AuNPs were introduced in mouse to study its toxicity and its availability in the liver.

Colloidal silver nanoparticles for preventing gastrointestinal bacterial infections were investigated by Le Anh Tuan, Tran Quang Huy, et al. [46]. In this work the authors have demonstrated a powerful disinfectant ability of colloidal silver nanoparticles (NPs) for the prevention of gastrointestinal bacterial infections. The silver NPs colloid was synthesized by a UV-enhanced chemical precipitation. Two gastrointestinal bacterial strains of *Escherichia coli* (ATCC 43888-O157:k:H7) and *Vibrio cholerae* (O1) were used to verify the antibacterial activity of the as-prepared silver NPs colloid by means of surface disinfection assay in agar plates and turbidity assay in liquid media. Transmission electron microscopy

was also employed to analyze the ultrastructural changes of bacterial cells caused by silver NPs. Noticeably, our silver NPs colloid displayed a highly effective bactericidal effect against two tested gastrointestinal bacterial strains at a silver concentration as low as $\sim 3 \text{ mg l}^{-1}$. More importantly, the silver NPs colloid showed an enhancement of antibacterial activity and long-lasting disinfectant effect as compared to conventional chloramin B (5%) disinfection agent. These advantages of the as-prepared colloidal silver NPs make them very promising for environmental treatments contaminated with gastrointestinal bacteria and other infectious pathogens. Moreover, the powerful disinfectant activity of silver-containing materials can also help in controlling and preventing further outbreak of diseases.

Antibacterial studies of silver core-chitosan shell nanoparticles using catechol-functionalized chitosan were performed by Tran Ngoc Quyen, et al. [47]. In this article the authors reported the preparation and stabilization of colloidal silver nanoparticle solution, with the assistance of chitosan dihydroxyphenyl acetamide (CDHPA), or oligochitosan dihydroxyphenyl acetamide (OCDHPA). The structure of the chitosan derivatives were characterized by $^1\text{H-NMR}$ spectroscopy.

The morphology of the synthesized silver core-chitosan shell nanoparticles were observed by TEM and XRD techniques, and showed a well-defined core-shell structure of polymer-coated silver nanoparticles (AgNPs). The core-shell NPs exhibited a strong antibacterial activity against *E. coli* and *S. aureus*, at a very low concentration of AgNPs (2.5 ppm).

Silver chloride nanoparticles as an antibacterial agent were investigated by Nguyen Thi Thanh Binh, et al. [48]. In this work silver chloride nanoparticles were prepared by the precipitation reaction between silver nitrate and sodium chloride in an aqueous solution containing poly(vinyl alcohol) as a stabilizing agent. Different characteristics of the nanoparticles in suspension and in lyophilized powder such as size, morphology, chemical nature, interaction with stabilizing agent and photo-stability were investigated. Biological tests showed that the obtained silver chloride nanoparticles displayed antibacterial activities against *Escherichia coli* and *Staphylococcus aureus*.

In Ref. [49] Duong Thi Thuy, Ha Phuong Thu, et al. examined the growth inhibition effect of engineered silver nanoparticles against bloom forming

cyanobacterial *M. aeruginosa* strain. AgNPs were synthesized by a chemical reduction method at room temperature and UV-Vis spectroscopy, SEM, TEM showed that they presented a maximum absorption at 410 nm and size range between 10 and 18 nm. *M. aeruginosa* cells exposed during 10 d to AgNPs to a range of concentrations from 0 to 1 mg l⁻¹. The changes in cell density and morphology were used to measure the responses of the *M. aeruginosa* to AgNPs. The control and treatment units had a significant difference in terms of cell density and growth inhibition ($p < 0.05$). Increasing the concentration of AgNPs, a reduction of the cell growths in all treatment was observed. The inhibition efficiency was reached 98.7% at higher concentration of AgNPs nanoparticles. The term half maximal effective concentration (EC₅₀) based on the cell growth measured by absorbance at 680 nm (A680) was 0.0075 mg l⁻¹. The inhibition efficiency was 98.7% at high concentration of AgNPs (1 mg l⁻¹). Image of SEM and TEM reflected a shrunk and damaged cell wall indicating toxicity of silver nanoparticles toward *M. aeruginosa*.

Microwave-assisted synthesis of chitosan/polyvinyl alcohol silver nanoparticles gel for wound dressing applications was performed by Tran Ngoc Quyen, Nguyen Dai Hai, et al. [50]. The purpose of this study was to fabricate chitosan/poly(vinylalcohol)/Ag nanoparticles(CPA) gels with microwave-assistance for skin applications. Microwave irradiation was employed to reduce silver ions to silver nanoparticles and to crosslink chitosan (CS) with polyvinyl alcohol (PVA). The presence of silver nanoparticles in CPA gels matrix was examined using UV-Vis spectroscopy, TEM and XRD. The interaction of CS and PVA was analysed by FTIR. The release of silver ions was determined by atomic absorption spectrometry. The

antimicrobial properties of CPA gels against *P. aeruginosa* and *S. aureus* were investigated using agar diffusion method. Finally, the biocompatibility and woundhealing ability of the gels were studied using fibroblast cells (*in vitro*) and mice models (*in vivo*). In conclusion, the results showed that CPA gels were successfully fabricated using microwave irradiation method. These gels can be applied to heal an open wound thanks to their antibacterial activity and biocompatibility.

Role of collagen concentration in stability of star-shaped silver@gold nanoparticles was investigated by Nguyen Dai Hai, et al. [51]. In this work star-shaped silver@gold (Ag@Au) nanoparticles were synthesized in collagen (Coll) suspensions by a seeding growth approach. The silver nanoparticles were used as seeds for Au development. Coll was used as a protecting agent and the effect of its concentration on stability was also examined. Obtained nanoparticles were then characterized by UV-Vis, TEM, XRD and FTIR. The result was confirmed by the maximum surface plasmon resonance peak at 566-580 nm for each sample indicating the formation of branched Ag@Au@Coll NPs. The average diameters of the branched Ag@Au@Coll NPs were revealed to be 30-50 nm depending on the corresponding component ratio and the pH value. It is interesting to note that the concentration of Coll plays a critical role in the stability of the star-shaped gold nanoparticles. The results offer an understanding of the handling of the electronic and the silver@gold based nanoparticles stability properties.

Conclusion and Discussion

Basic research on nanomedicine in Vietnam began about 5 years ago with the first publications in the year 2012 [1,16]. Since that time it rapidly developed and obtained promising results in following

areas of nanomedicine:

- Biomedical utilization of PLA-TPGS and PLA-PEG;
- Dendrimer-based anticancer drug;
- Various utilizations of nanocurcumin in nanomedicine;
- Biomedical application of hydrogel nanocomposite;
- Biosensors and biosensing methods;
- Toxicity and antibacterial activity of different types of nanoparticles.

Results of the research on nanocurcumin were efficiently applied to the industrial production of several food supplements such as CURMAGOLD, CURMIN Nano 22⁺, HEPOSAL B, FGC and CUMARKUL.

Further development of the basic research on nanomedicine could be directed toward two topics:

- Enrichment of the scientific contents of the basic research works;
- Implementations of the results of basic research both to the diagnosis as well as to the treatment of the diseases.

The development of nanomedicine in Vietnam requires a very large fund, a difficulty of Vietnamese science. However, this difficulty certainly will be avoided by both the great attention of the Vietnamese Government to the public health and the friendly financial support of the international community.

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REFERENCES

- [1] Hoai Nam Nguyen, Hong Ha Tran Thi, Duong Le Quang, Toan Nguyen Thi, Nhu Hang Tran Thi, Mai Huong Le, Phuong Thu Ha (2012), "Apoptosis induced by paclitaxel-loaded copolymer

PLA-TPGS in Hep-G2 cells", *Adv. Nat. Sci.: Nanosci. Nanotechnol.*, **3**, 045005.

[2] Ha Phuong Thu, Duong Tuan Quang, Mai Thi Thu Trang, Tran Thi Hong Ha, Nguyen Hoai Nam, Nguyen Xuan Phuc, Tran Thi Minh Nguyet, Phan Quoc Thong, Phan Thi Hong Tuyet, Vuong Thi Kim Oanh, Le Mai Huong (2013), "In Vitro Apoptosis Enhancement of Hep-G2 Cells by PLA-TPGS and PLA-PEG Block Copolymer Encapsulated Curcumin Nanoparticles", *Chem. Lett.*, **42**, pp.255-257.

[3] Duong Thi Thuy Le, Lua Thi Minh Dang, Nhung Thi My Hoang, Huyen Thi La, Huyen Thi Minh Nguyen, Huan Quang Le (2015), "Anti-Tumor Activity of Docetaxel PLGA-PEG Nanoparticles with a Novel Anti-HER2 scFv", *J. Nanomed. Nanotechnol.*, **6**, p.267.

[4] Ha Phuong Thu, Nguyen Hoai Nam, Bui Thuc Quang, Ho Anh Son, Nguyen Linh Toan, Duong Tuan Quang (2015), "In vitro and in vivo targeting effect of folate decorated paclitaxel loaded PLA-TPGS nanoparticles", *J. Saudi Pharma*, **23**, pp.683-688.

[5] Hoai Nam Nguyen, Thi My Nhung Hoang, Thi Thu Trang Mai, Thi Quynh Trang Nguyen, Hai Doan Do, Thi Hien Pham, Thi Lap Nguyen, Phuong Thu Ha (2015), "Enhanced cellular uptake and cytotoxicity of folate decorated doxorubicin loaded PLA-TPGS nanoparticles", *Adv. Nat. Sci.: Nanosci. Nanotechnol.*, **6**, 025005.

[6] Quoc Thong Phan, Mai Huong Le, Thi Thu Huong Le, Thi Hong Ha Tran, Xuan Phuc Nguyen, Phuong Thu Ha (2016), "Characteristics and cytotoxicity of folate-modified curcumin-loaded PLA-PEG micellar nano systems with various PLA:PEG ratios", *Inter. J. Pharma*, **507**, pp.32-40.

[7] Phuong Thu Ha, Hoai Nam Nguyen, Hai Doan Do, Quoc Thong Phan, Minh Nguyet Tran Thi, Xuan Phuc Nguyen, My Nhung Hoang Thi, Mai Huong Le, Linh Toan Nguyen, Thuc Quang Bui, Van Hieu Phan (2016), "Targeted drug delivery nanosystems based on copolymer poly(lactide)-tocopheryl polyethylene glycol succinate for cancer treatment", *Adv. Nat. Sci.: Nanotechnol.*, **7**, 015001.

[8] Hoai Nam Nguyen, Phuong Thu Ha, Anh Sao Nguyen, Dac Tu Nguyen, Hai Doan Do, Quy Nguyen Thi, My Nhung Hoang Thi (2016), "Curcumin as fluorescent probe for directly monitoring in vitro uptake of curcumin combined paclitaxel loaded PLA-TPGS nanoparticles", *Adv. Nat. Sci.: Nanosci. Nanotechnol.*, **7**, 025001.

[9] Thi Thuy Duong Le, Thu Hong Pham, Trong Nghia Nguyen, Thi Hong Giang Ngo, Thi My Nhung Hoang, Quang Huan Le (2016), "Evaluation of anti-HER2 scFv-conjugated PLGA-PEG nanoparticles on 3D tumor spheroids of BT474 and HCT116 cancer cells", *Adv. Nat. Sci.: Nanosci. Nanotechnol.*, **7**, 025004.

[10] Thi Thuy Duong Le, Phuong Thu Ha, Thi Hai Yen Tran, Dac Tu Nguyen, Hoai Nam Nguyen, Van Khanh Bui, My Nhung Hoang (2016), "In vitro evaluation of Aurora kinase inhibitor-VX680-in formulation of PLA-TPGS nanoparticles", *Adv. Nat. Sci.: Nanosci. Nanotechnol.*, **7**, 025010.

[11] Ngoc Quyen Tran, Cuu Khoa Nguyen, Thi Phuong Nguyen (2013), "Dendrimer-based nanocarriers demonstrating a high efficiency for loading and releasing anticancer drugs against cancer cells in vitro and in vivo", *Adv. Nat. Sci.: Nanosci. Nanotechnol.*, **4**, 045013.

[12] Nhat-Anh N. Tong, Thi Hai Nguyen, Dai Hai Nguyen, Cuu Khoa Nguyen, Ngoc Quyen Tran (2015), "Preparation of the Cationic Dendrimer-Based Hydrogels for Controlled Heparin Release", *J. Macromol. Sci.*, **A 52**, pp.830-837.

[13] Thi Bich Tram Nguyen, Thi Tram Chau Nguyen, Hoang Chinh Tran, Cuu Khoa Nguyen, Ngoc Quyen Tran (2015), "H-NMR Spectroscopy as an Effective Method for Predicting Molecular Weight of Polyaminoamine Dendrimers and Their Derivatives", *Int. J. Polym. Anal. Charact.*, **20**, pp.57-68.

[14] Nguyen Hoang, Nguyen Ngoc Hoa, Tran, Ngoc Quyen, Nguyen Cuu Khoa (2015), "Improved Method for Preparing Cisplatin-Dendrimer Nanocomplex and Its Behavior Against NCI-H460 Lung Cancer Cell", *J. Nanosci. Nanotechnol.*, **15**, pp.4106-4110 (5).

[15] Thi Tram Chau Nguyen, Cuu Khoa Nguyen, Thi Hiep Nguyen, Ngoc Quyen Tran (2017), "Highly lipophilic pluronic-conjugated polyamidoamine dendrimer nanocarriers as potential delivery system for hydrophobic drugs", *Mater. Sci. Eng.*, **C 70**, pp.992-999.

[16] Nguyen To Hoai, Phuong Tuyen Thi Dao, Quoc Nam Phu, Duy Dam Le, Tuan Anh Nguyen, Tai Chi Nguyen, Mau Chien Dang (2012), "Ketoprofen encapsulated cucurbit[6]uril nanoparticles: a new exploration of macrocycles for drug delivery", *Adv. Nat. Sci.: Nanosci. Nanotechnol.*, **3**, 045004.

[17] Thanh Ha Ho, Thi Nu Thanh Le, Tuan Anh Nguyen, Mau Chien Dang (2015), "Poly(ethylene glycol) grafted chitosan as new copolymer material for oral delivery of insulin", *Adv. Nat. Sci.: Nanosci. Nanotechnol.*, **6**, 035004.

[18] Phuong Thu Ha, Hoai Nam Nguyen, Hai Doan Do, Quoc Thong Phan, Minh Nguyet Tran Thi, Xuan Phuc Nguyen, My Nhung Hoang Thi, Mai Huong Le, Linh Toan Nguyen, Thuc Quang Bui, Van Hieu Phan (2016), "Targeted drug delivery nanosystems based on copolymer poly(lactide)-tocopheryl polyethylene glycol succinate for cancer treatment", *Adv. Nat. Sci.: Nanosci. Nanotechnol.*, **7**, 015001.

[19] Kim Thach Nguyen, Duc Vinh Le, Dinh

Ho Do, Quang Huan Le (2016), "Development of chitosan graft pluronic®F127 copolymer nanoparticles containing DNA aptamer for paclitaxel delivery to treat breast cancer cells", *Adv. Nat. Sci.: Nanosci. Nanotechnol.*, **7**, 025018.

[20] Tuan Anh Nguyen, Quan Duoc Tang, Duc Chanh Tin Doan, Mau Chien Dang (2016), "Micro and nano liposome vesicles containing curcumin for a drug delivery system", *Adv. Nat. Sci.: Nanosci. Nanotechnol.*, **7**, 035003.

[21] Nguyen Thi TT, Tran TV, Tran NQ, Nguyen CK, Nguyen DH (2017), "Hierarchical self-assembly of heparin-PEG end-capped porous silica as a redox sensitive nanocarrier for doxorubicin delivery", *Mater. Sci. Eng.*, **C 70**, pp.974-954.

[22] Le Mai Huong, Ha Phuong Thu, Nguyen Thi Bich Thuy, Tran Thi Hong Ha, Ha Thi Minh Thi, Mai Thu Trang, Tran Thi Nhu Hang, Do Huu Nghi, Nguyen Xuan Phuc, Duong Tuan Quang (2011), "Preparation and Antitumor-promoting Activity of Curcumin Encapsulated by 1,3-β-Glucan Isolated from Vietnam Medicinal Mushroom *Heridium erinaceum*", *Chem. Lett.*, **40**, pp.846-848.

[23] Le Thi Thu Huong, Nguyen Hoai Nam, Do Hai Doan, Hoang Thi My Nhung, Bui Thuc Quang, Pham Hong Nam, Phan Quoc Thong, Nguyen Xuan Phuc, Ha Phuong Thu (2016), "Folate attached, curcumin loaded Fe₃O₄ nanoparticles: A novel multifunctional drug delivery system for cancer treatment", *Mater. Chem. Phys.*, **172**, pp.98-104.

[24] Ha Phuong Thu, Le Thi Thu Huong, Hoang Thi My Nhung, Nguyen Thi Tham, Nguyen Dac Tu, Ha Thi Minh Thi, Pham Thi Bich Hanh, Tran Thi Minh Nguyet, Nguyen Thi Quy, Pham Hong Nam, Tran Dai Lam, Nguyen Xuan Phuc, Duong Tuan Quang (2011), "Fe₃O₄/o-Carboxymethyl Chitosan/Curcumin-based Nanodrug System for Chemotherapy and Fluorescence Imaging in HT29 Cancer Cell Line", *Chem. Lett.*, **40**, pp.1264-1266.

[25] Thi Thu Trang Mai, Thi Thu Thuy Nguyen, Quang Duong Le, Thi Ngoan Nguyen, Thi Cham Ba, Hai Binh Nguyen, Thi Bich Hoa Phan, Dai Lam Tran, Xuan Phuc Nguyen, Jun Seo Park (2012), "A novel nanofiber Cur-loaded polylactic acid constructed by electrospinning", *Adv. Nat. Sci.: Nanosci. Nanotechnol.*, **3**, 025014.

[26] Phuong Thu Ha, Mai Huong Le, Thi My Nhung Hoang, Thi Thu Huong Le, Tuan Quang Duong, Thi Hong Ha Tran, Dai Lam Tran, Xuan Phuc Nguyen (2012), "Preparation and anti-cancer activity of polymer-encapsulated curcumin nanoparticles", *Adv. Nat. Sci.: Nanosci. Nanotechnol.*, **3**, 035002.

[27] Thi Minh Phuc Le, Van Phuc Pham, Thi Minh Lua Dang, Thi Huyen La, Thi Hanh Le, Quang Huan Le (2013), "Preparation of curcumin-loaded pluronic F127/chitosan nanoparticles for cancer

therapy", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **4**, 025001.

[28] Thi Thuy Duong Le, Thi Huyen La, Thi Minh Phuc Le, Van Phuc Pham, Thi Minh Huyen Nguyen, Quang Huan Le (2013), "Docetaxel and curcumin-containing poly(ethylene glycol)-block-poly(ϵ -caprolactone) polymer micelles", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **4**, 025006.

[29] Dai Hai Nguyen, Ngoc Quyen Tran, Cuu Khoa Nguyen (2013), "Tetronic-grafted chitosan hydrogel as an injectable and biocompatible scaffold for biomedical applications", *J. Biomater. Sci. Polym. Ed*, **24**, pp.1636-1648.

[30] Thi Phuong Nguyen, Bach Hai Phuong Doan, Dinh Vu Dang, Cuu Khoa Nguyen, Ngoc Quyen Tran (2014), "Enzyme-mediated in situ preparation of biocompatible hydrogel composites from chitosan derivative and biphasic calcium phosphate nanoparticles for bone regeneration", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **5**, 015012.

[31] Dang Hoang Phuc, Nguyen Thi Hiep, Do Ngoc Phuc Chau, Nguyen Thi Thu Hoai, Huynh Chan Khon, Vo Van Toi, Nguyen Dai Hai, Bui Chi Bao (2016), "Fabrication of Hyaluronan-Poly(vinylphosphonic acid)-Chitosan Hydrogel for Wound Healing Application", *Int. J. Polym. Sci.*, Article ID 6723716.

[32] Thuy Duong Van, Ngoc Quyen Tran, Dai Hai Nguyen, Cuu Khoa Nguyen, Dai Lam Tran, Phuong Thi Nguyen (2016), "Injectable Hydrogel Composite Based Gelatin-PEG and Biphasic Calcium Phosphate Nanoparticles for Bone Regeneration", *J. Electro. Mater.*, **45**, pp.2415-2422.

[33] Le Huy Nguyen, Hai Binh Nguyen, Ngoc Thinh Nguyen, Tuan Dung Nguyen and Dai Lam Tran (2012), "Portable cholesterol detection with polyaniline-carbon nanotube film based interdigitated electrodes", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **3**, 015004.

[34] Quang Huy Tran, Anh Tuan Mai, Thanh Thuy Nguyen, Van Chung Pham, Thi Hong Hanh Nguyen (2012), "Towards the use of protein A-tagged gold nanoparticles for signal amplification of electrochemical immunosensors in virus detection", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **3**, 025013.

[35] Hai Binh Nguyen, Van Chuc Nguyen, Van Tu Nguyen, Thi Thanh Tam Ngo, Ngoc Thinh Nguyen, Thi Thu Huyen Dang, Dai Lam Tran, Phuc Quan Do, Xuan Nghia Nguyen, Xuan Phuc Nguyen, Hong Khoi Phan, Ngoc Minh Phan (2012), "Graphene patterned polyaniline-based biosensor for glucose detection", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **3**, 025011.

[36] Quoc Minh Le, Thu Huong Tran, Thanh Huong Nguyen, Thi Khuyen Hoang, Thanh Binh Nguyen, Khanh Tung Do, Kim Anh Tran, Dang

Hien Nguyen, Thi Luan Le, Thi Quy Nguyen, Mai Dung Dang, Nu Anh Thu Nguyen, Van Man Nguyen (2012), "Development of a fluorescent label tool based on lanthanide nanophosphors for viral biomedical application", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **3**, 035003.

[37] Minh Tan Pham, Thi Van Nguyen, Thuy Duong Vu Thi, Ha Lien Nghiem Thi, Kim Thuan Tong, Thanh Thuy Tran, Viet Ha Chu, Jean-Claude Brochon, Hong Nhung Tran (2012), "Synthesis, photophysical properties and application of dye doped water soluble silica-based nanoparticles to label bacteria *E. coli* O157:H7", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **3**, 045013.

[38] Hai Binh Nguyen, Van Chuc Nguyen, Van Tu Nguyen, Huu Doan Le, Van Quynh Nguyen, Thi Thanh Tam Ngo, Quan Phuc Do, Xuan Nghia Nguyen, Ngoc Minh Phan, Dai Lam Tran (2013), "Development of the layer-by-layer biosensor using graphene films: application for cholesterol determination", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **4**, 015013.

[39] Trong Huyen Le, Ngoc Thang Trinh, Le Huy Nguyen, Hai Binh Nguyen, Van Anh Nguyen, Dai Lam Tran, Tuan Dung Nguyen (2013), "Electrosynthesis of polyaniline-multilayered carbon nanotube nanocomposite films in the presence of sodium dodecyl sulfate for glucose biosensing", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **4**, 025014.

[40] Vo Ke Thanh Ngo, Dang Giang Nguyen, Hoang Phuong Uyen Nguyen, Van Man Tran, Thi Khoa My Nguyen, Trong Phat Huynh, Quang Vinh Lam, Thanh Dat Huynh, Thi Ngoc Lien Truong (2014), "Quartz crystal microbalance (QCM) as biosensor for the detecting of *Escherichia coli* O157:H7", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **5**, 045004.

[41] Hong Nhung Tran, Thi Ha Lien Nghiem, Thi Thuy Duong Vu, Viet Ha Chu, Quang Huan Le, Thi My Nhung Hoang, Lai Thanh Nguyen, Duc Minh Pham, Kim Thuan Tong, Quang Hoa Do, Duong Vu, Trong Nghia Nguyen, Minh Tan Pham, Cao Nguyen Duong, Thanh Thuy Tran, Van Son Vu, Thi Thuy Nguyen, Thi Bich Ngoc Nguyen, Anh Duc Tran, Thi Thuong Trinh, Thi Thai An Nguyen (2015), "Optical nanoparticles: synthesis and biomedical application", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **6**, 023002.

[42] Vo Ke Thanh Ngo, Hoang Phuong Uyen Nguyen, Trong Phat Huynh, Nguyen Nguyen Pham Tran, Quang Vinh Lam, Thanh Dat Huynh (2015), "Preparation of gold nanoparticles by microwave heating and application of spectroscopy to study conjugate of gold nanoparticles with antibody *E. coli* O157:H7", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **6**, 035015.

[43] Van Binh Pham, Xuan Thanh Tung Pham, Thanh Nhat Khoa Phan, Thi Thanh Tuyen Le, Mau

Chien Dang (2015), "Facile fabrication of a silicon nanowire sensor by two size reduction steps for detection of alpha-fetoprotein biomarker of liver cancer", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **6**, 045001.

[44] Thi Hanh Le, Van Phuc Pham, Thi Huyen La, Thi Binh Phan, Quang Huan Le (2016), "Electrochemical aptasensor for detecting tetracycline in milk", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **7**, 015008.

[45] Thi Ha Lien Nghiem, Thi Tuyen Nguyen, Emmanuel Fort, Thanh Phuong Nguyen, Thi My Nhung Hoang, Thi Quy Nguyen, Hong Nhung Tran (2012), "Capping and in vivo toxicity studies of gold nanoparticles", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **3**, 015002.

[46] Anh-Tuan Le, Thi Tam Le, Van Quy Nguyen, Huy Hoang Tran, Duc Anh Dang, Quang Huy Tran, Dinh Lam Vu (2012), "Powerful colloidal silver nanoparticles for the prevention of gastrointestinal bacterial infections", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **3**, 045007.

[47] Thanh Son Cu, Van Du Cao, Cuu Khoa Nguyen, Ngoc Quyen Tran (2014), "Preparation of silver core-chitosan shell nanoparticles using catechol-functionalized chitosan and antibacterial studies", *Macromol. Res*, **22**, pp.418-423.

[48] Ngoc Duong Trinh, Thi Thanh Binh Nguyen, Thanh Hai Nguyen (2015), "Preparation and characterization of silver chloride nanoparticles as an antibacterial agent", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **6**, 045011.

[49] Thi Thuy Duong, Thanh Son Le, Thi Thu Huong Tran, Trung Kien Nguyen, Cuong Tu Ho, Trong Hien Dao, Thi Phuong Quynh Le, Hoai Chau Nguyen, Dinh Kim Dang, Thi Thu Huong Le, Phuong Thu Ha (2016), "Inhibition effect of engineered silver nanoparticles to bloom forming cyanobacteria", *Adv. Nat. Sci.: Nanosci. Nanotechnol*, **7**, 035018.

[50] Nguyen Thi Hiep, Huynh Chan Khon, Vo Van Thanh Niem, Vo Van Toi, Tran Ngoc Quyen, Nguyen Dai Hai and Mai Ngoc Tuan Anh (2016), "Microwave-Assisted Synthesis of Chitosan/Polyvinyl Alcohol Silver Nanoparticles Gel for Wound Dressing Applications", *Int. J. Polym. Sci.*, Article ID 1584046.

[51] Phuong Phong Nguyen Thi, Minh Tien Nguyen, Dai Hai Nguyen (2016), "Role of Collagen Concentration in Stability of Star-Shaped Silver@Gold Nanoparticles", *J. Nano Res*, **40**, pp.113-119.

Estimating sea level rise for Vietnam East Sea

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Abstract:

Sea level rise for Vietnam East Sea in the 21st century was determined under both RCP 4.5 and RCP 8.5 scenarios. Changes in sea level of the Vietnam East Sea due to dynamic and thermosteric processes was estimated using results of different Atmosphere - Ocean General Circulation Model (AOGCMs) under the prescribed method in the IPCC's Fifth Assessment Report (AR5). Changes in sea level due to ice melting and land water storage was determined using a transfer function for global water balance based on the contribution of each sea level rise contributing component for different regions. Changes in sea level as a result of the vertical motion of the Earth's crust due to changes in the Earth's cryosphere was determined using the ICE5G models. The results showed that for the RCP 8.5 scenario, by the end of the 21st century, the average sea level rise is 76 cm, with estimated values varying between 52 cm and 106 cm at the 5% and 95% confidence intervals, respectively. For the RCP 4.5 scenario, the average sea level rise is 52 cm, with values of 33 cm and 75 cm at the 5% and 95% confidence interval, respectively. The sea level rise scenario determined for the Vietnam East Sea is slightly higher in comparison with the globally estimated results in AR5.

Keywords: climate change, sea level rise scenarios, Vietnam East Sea.

Classification number: 6.2

Introduction

Global average sea level has increased significantly between 1920 and 1950; especially after 1993 until now [1]. The significant increase after 1993 was also identified from the assessment of sea level using satellite data [2]. In Vietnam, tidal gauging data (between 1960 and 2013) showed an increase of sea level along the coast of Vietnam with levels of approximately 3 mm/year. On the other hand, satellite data (1993-2014) implied a sea level increase approximately 3.4

mm/year along the coast and 4.1 mm/year for the entire Vietnam East Sea [3]. The observed trend is slightly higher than the global average value for the same period.

Vietnam is assessed to be among the most severely impacted countries due to climate change and sea level rise. Estimating sea level rise in Vietnam is therefore, form scientific basis for climate change impacts assessment and adaptation measures.

There is a large number of approaches in determining sea level increase worldwide, especially after the publication of IPCC's Fourth Assessment Report (AR4) in 2007. The different studies have assessed the spatial distribution of the contributing components to sea level rise such as the thermosteric process, ice melts or changes in land water storage [1, 4, 5]. Estimated the increase in sea level in each region by assessing the different contributions under 3 emissions scenarios (B1, A1B, and A2) [4]. The thermosteric component was modelled based on CMIP3 while glacier melt component was determined based on the volume approach, and the ice in Greenland and Antarctica was determined based on the estimates from AR4. When accounting for the glacial isostatic adjustment (GIA) from the ICE-5G (VM2) model [6], it was determined that the thermosteric component and glacier melt contributed the most to overall sea level rise, with the thermosteric component being highly variable spatially. Using a different approach, Church came to the conclusion that the difference between sea level rise at the regional and global scale is due to the dynamical changes in the different regions as a result of water advection, temperature, salinity and wind circulation [1]. Slangen extended the research for the other contributing components using outputs of CMIP5 models [5]. In particular, the effects of the atmospheric loading (due to

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changes in the atmospheric circulation and changes in the column-integrated atmospheric moisture content) was estimated using the method proposed by Stammer & Huttermann [7]. The glacier melt component was determined using simulated temperature and precipitation data. The surface mass balance component of ice in Greenland and Antarctica was determined based on its relationship with the projected CMIP5 global mean surface temperature change using two total least squared fits [8]. The land water storage component was determined using data from Wada, et al [9], based on the difference between groundwater extractions and recharge using two different socio-economic projections in combination with population change. The method developed by Church and Slagen has been widely adopted for a number of nations in developing their own sea level rise scenarios [1, 5]. This includes Australia [10], Singapore [11], and the Netherlands [12].

This study applies the aforementioned approaches as well as results from IPCC's AR5 to estimate the sea level rise in Vietnam East Sea. The estimated sea level rise results were compared with observed data including data from tidal gauges and satellite data to assess reliability. Uncertainty in the total sea level rise estimation was also determined through determining uncertainties of each individual contributions.

Methodology

Estimating sea level rise contributing components

The method to determine sea level rise for Vietnam was developed based on IPCC's AR [1, 5], and sea level rise scenarios from Australia, the Netherlands and Singapore. The increase in sea level was determined as a sum of the contributing components in the region, this includes: sea level rise due to (i) thermosteric processes, (ii) melting of glaciers, (iii) ice mass balance in Greenland (GSMB), (iv) ice

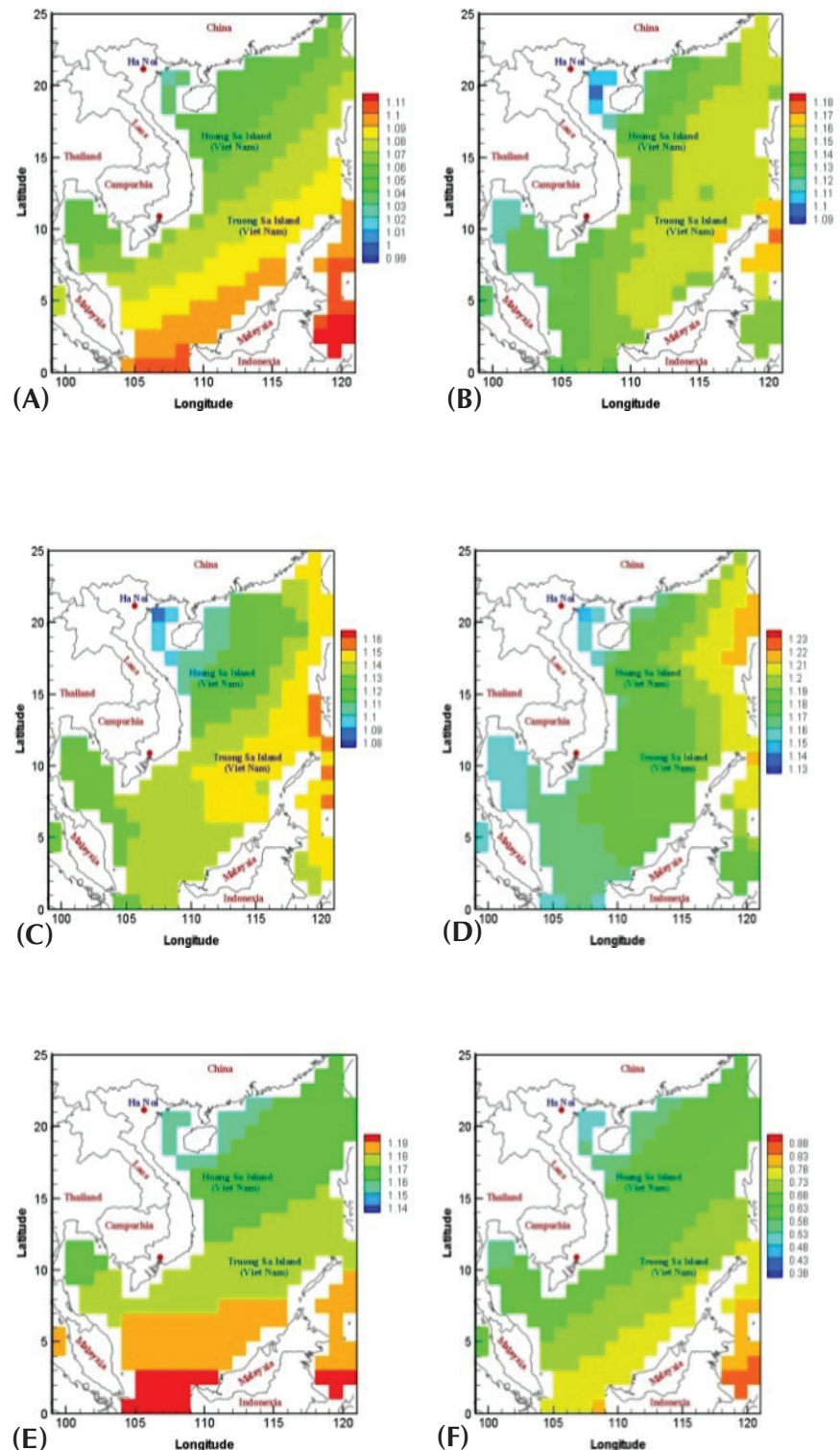


Fig.1. Spatial fingerprints of changes in: (A) Glaciers; (B) Surface mass balance in Greenland; (C) Surface mass balance in Antarctica; (D) Ice sheet dynamic in Greenland; (E) Ice sheet dynamic in Antarctica and (F) Land water storage.

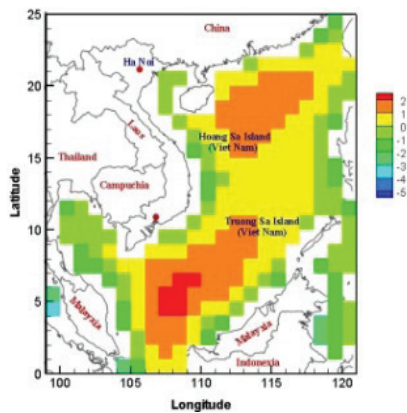


Fig. 2. The estimates of glacial isostatic adjustment from ICE5G model.

mass balance in Antarctica (ASMB), (v) ice sheet dynamic in Greenland (GDIS), (vi) ice sheet dynamic in Antarctica (ADIS), (vii) land water storage, and (viii) glacial isostatic adjustment (GIA).

Sea level rise due to dynamic and thermosteric components were determined using outputs from 21 Atmosphere- Ocean General Circulation Model (AOGCMs) published by IPCC. Both of these data were downloaded at monthly resolution and on the native model grids.

Other components such as glaciers, surface mass balance in Greenland and Antarctica; ice sheet dynamic in Greenland and Antarctica; land water storage; and glacial isostatic adjustment were determined based on the global mean time series published in IPCC's AR5 [13] and downscaled to the spatial fingerprint according to Slangen (Fig. 1A, 1B, 1C, 1D, 1E and 1F) [5].

Sea level change due to changes in the vertical motion of the Earth's crust in response to changes in the cryosphere were determined from the ICE5G models by Peltier [6] (Fig. 2).

Combining uncertainty of sea level rise

Level of uncertainty of the total sea level rise was determined based on the sum of the uncertainties of each individual component. For the dynamic and thermosteric components,

uncertainty was determined based on the models utilized. For the changes in surface mass balance, it is assumed that the component is heavily influenced by the magnitude of climate change. For the glaciers, uncertainty was determined based on IPCC [12].

Level of uncertainty of each component (except for the glacial isostatic adjustment) has a central estimate (median), an upper and lower estimates which are indicative of the 5th and 95th percentiles of the distribution and/or the likely range assessed in the IPCC's AR5 [12]. A sum of the estimates of the uncertainty of each component was determined so that a total value of the possible variation of the sea level rise for Vietnam could be calculated.

ice sheet in Antarctica; and dynamic ice sheet in Greenland respectively.

Results

Comparing the results with observed data

Figure 3 depicts the time series of sea level rise for the standard deviation of the average sea level in 14 tidal gauging stations (Cua Ong, Co To, Bai Chay, Hon Dau, Con Co, Son Tra, Quy Nhon, Phu Quy, Vung Tau, DK12, Con Dao, Tho Chu, and Phu Quoc) along the coast and islands of Vietnam, satellite data, and historical simulations of AOGCMs. It can be seen that for the period 1986-2013, computed trend of changing sea level in the Vietnam East Sea is in line with both observed data

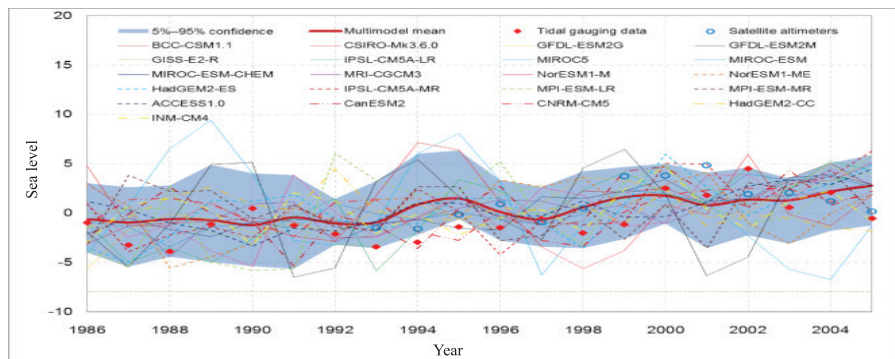


Fig. 3. Comparing the ensemble mean sea level with observed data for the period 1986-2005.

Level of uncertainty in the calculation of the total sea level rise was determined assuming that all contributions have a strong correlation with global air temperature and are correlated uncertainties; therefore can be added linearly as follows [1]:

$$\sigma_{\text{tot}}^2 = (\sigma_{\text{steric/dynamic}}^2 + \sigma_{\text{smb}_a}^2 + \sigma_{\text{smb}_g}^2) + \sigma_{\text{glac}}^2 + \sigma_{\text{LW}}^2 + \sigma_{\text{dyn}_a}^2 + \sigma_{\text{dyn}_g}^2$$

In which: σ_{tot} is the total uncertainty of sea level; $\sigma_{\text{steric/dynamic}}$, σ_{smb_a} , σ_{smb_g} , σ_{glac} , σ_{LW} , σ_{dyn_a} , σ_{dyn_g} are the uncertainties of the thermosteric, dynamic sea level, surface mass balance in Antarctica, surface mass balance in Greenland, glaciers, land water storage, dynamic

from the gauging stations and satellite. The rate of sea level change observed from the gauges is approximately 2.8 mm/year, slightly higher than computed results (approximately 2.4 mm/year). In general, for most of the analyzed period, average sea water level at the gauging stations as well as satellite data are within the 5-95% confidence levels of the modelled results.

The correlation coefficient of the average historical sea level data at the gauges and from the ensemble mean of the models (between 1986-2014) is 0.76; while the correlation coefficient of the satellite data and ensemble mean

of the models between 1993 and 2006 is 0.8 (Fig. 4A, 4B). The high level of agreement between simulation and observation data implies a high reliability level of the model in estimating sea level in the future for the Vietnam East Sea.

Estimating sea level rise for the Vietnam East Sea

Sea level rise in late 20th century is a result of global warming due to climate change [1]. Although the increasing trend of global air temperature in the beginning of the 21st century has slightly

diminished, the trend of sea level rise continues due to thermosteric and ice melting processes.

Figure 5A shows the estimated regional sea level rise for Vietnam East Sea. The estimated results imply that on both global and Vietnam East Sea regional scale, the rate of sea level rise in the 21st century is higher than the 20th century due to the increase in radiative forcing from increased greenhouse gas emissions. In the first decades of the 21st century, the rate of sea level rise

for the RCP 4.5 and RCP 8.5 scenarios are similar. However, this similarity no longer holds after 2040 with sea level for the two scenarios differing greatly. For the RCP 8.5 scenario, the regional sea level rise of Vietnam East Sea is 76 cm, with an upper estimate (95% quantile) of 106 cm and lower estimates (5% quantile) of 52 cm. For the RCP 4.5 scenario, at the end of the 21st century, the total sea level rise is 55 cm, with an upper estimate (95% quantile) of 81 cm and lower estimate (5% quantile) of 34 cm (Fig. 4A, Table 1).

In late 21st century, for the RCP 8.5 scenario, dynamic and thermosteric processes contributes most significantly to sea level rise, corresponding to a value of 33 cm, up to 44% of the total sea level rise. This is followed by sea level rise due to glaciers of 19 cm, up to 26% of the total. Similarly, ice melt in Greenland (both surface mass balance and dynamic ice sheet) accounts for 17 cm of sea level rise, equivalent to 23% of the total rise. Sea level rise due to ice in Antarctica contributes 5 cm, accounting for 6% of the total sea level rise. Surface land storage changes contribute an increase of 3 cm, approximately 4% of the total sea level rise. The total sea level rise in Vietnam

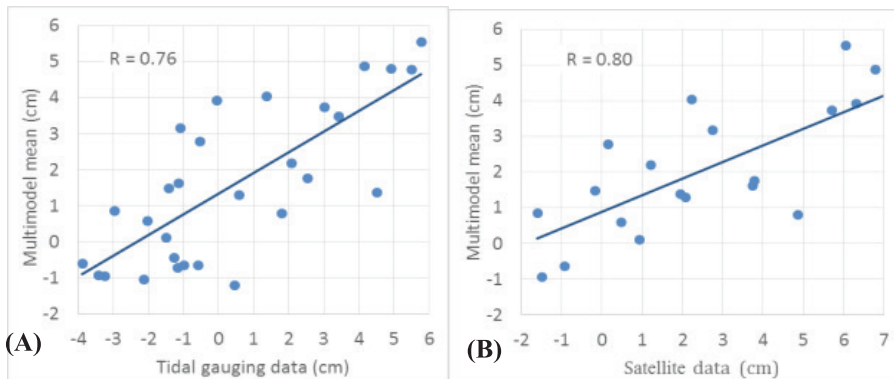


Fig. 4. Correlation between ensemble mean sea level of models and observed data from (A) tidal gauging stations in the Vietnam East Sea for the period of 1986-2014 and (B) satellite data for the period 1993-2006.

Note: Tidal gauging data (red diamond shaped), satellite altimeters (blue circle), historical simulations of AOGCMs (dotted lines), multimodel mean (red bold line), confidence interval 5-95% (grey shaded area).

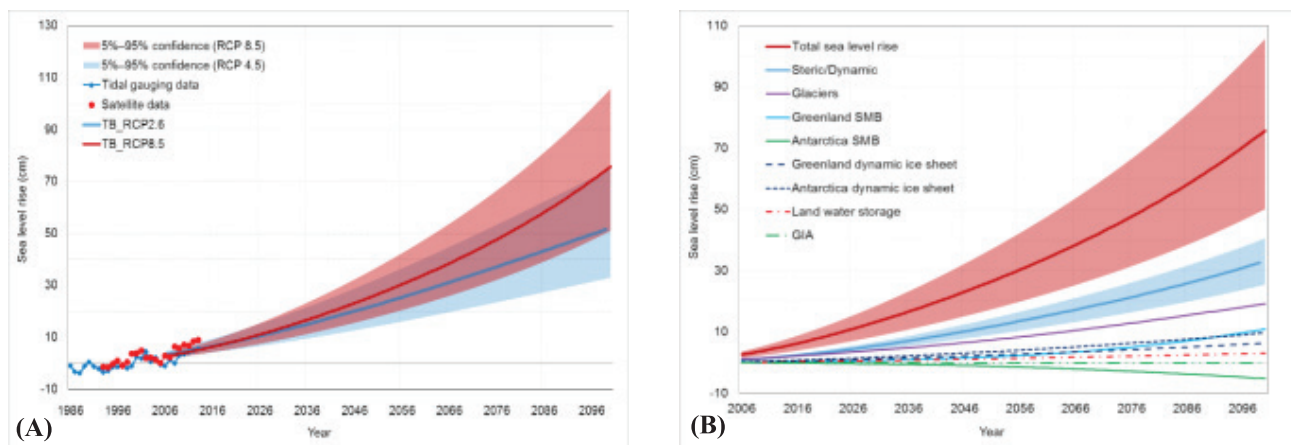


Fig. 5. Observed sea level data (red diamond shaped), estimated sea level rise under RCP 4.5 with likely range (blue) and RCP 8.5 with likely range (red) relative to the 1986-2005 period (A), and the contributions of sea level rise under RCP8.5 (B) in Vietnam East Sea.

Table 1. Estimated sea level rise and its contributions with likely ranges in the late 21st century with respect to a baseline period of 1986-2005 in Vietnam East Sea and globally (according to Table 13.5 from AR5, [1])

Component	RCP 4.5		RCP 8.5	
	Vietnam	Global	Vietnam	Global
Total sea level rise	52 [33÷75]	53 [36÷71]	76 [52÷106]	71 [52÷98]
Dynamic/ Thermosteric	21 [15÷34]	19 [14÷23]	33 [25 ÷ 40]	28 [21÷33]
Glaciers	14 [8÷20]	12 [6÷19]	19 [8÷25]	16 [9÷23]
Greenland Surface mass balance	5 [2÷10]	4 [1÷9]	11 [7÷20]	10 [3÷16]
Greenland Dynamic Ice sheet	5 [2÷7]	4 [1÷6]	7 [4÷10]	5 [2÷7]
Antarctic Surface mass balance	-3 [-4÷0]	-2 [-5÷-1]	-5 [-8÷-2]	-4 [-7÷-1]
Antarctic Ice sheet dynamic	10 [3÷18]	7 [-1÷16]	10 [3÷19]	8 [-1÷16]
Land water storage	3 [0÷8]	4 [-1÷9]	3 [0÷8]	4 [-1÷9]
GIA	-0.1	N/A	-0.2	N/A

East Sea and the separate contributions are similar in value yet slightly higher when compared to the global mean sea level rise. In particular, global mean sea level rise and its individual contributing component value of glaciers, ice melt in Greenland, ice melt in Antarctica and changes in land water storage are: 71 cm, 28 cm, 15 cm, 4 cm, and 4 cm respectively. Lastly, the glacial isostatic adjustment component contributes negatively to the increase in Vietnam East Sea (-0.2 cm) (Fig. 5B, Table 1).

The spatial distribution of sea level rise in late 21st century with respect to a baseline period of 1986-2005 for the RCP 4.5 and RCP 8.5 scenarios are depicted

in Fig. 5. Unsurprisingly, sea level rise for the RCP 8.5 scenario is higher than RCP 4.5 scenario. For both scenarios, in the central part of the Vietnam East Sea including Hoang Sa (Parcel) and Truong Sa (Spartly) islands, the sea level rise is significantly higher when compared to other areas. This is followed by the southern part of Vietnam East Sea. The area with lowest level of rise is the Northern Gulf (a.k.a. Gulf of Tonkin) and northern Vietnam East Sea. When only the coast of Vietnam is considered, increase in sea level in southern provinces from Da Nang southward is higher than that of the north. This result is compatible with the prognosis of sea level change based on the historical data

from gauging stations in this region [5].

Conclusions

Sea level rise in Vietnam was estimated in the 21st century for the RCP 4.5 and RCP 8.5 scenarios. The data and method used was based on data and method recommended by IPCC's AR5 [1]. Global sea level rise estimates were downscaled for Vietnam's coast through estimating the spatial distribution of the sea level rise contributions of ice melt and land water storage [5]. The changes in regional sea level due to dynamic and thermosteric processes were determined from 21 AOGCMs. Changes in sea level due to the glacial isostatic adjustment were determined based on ICE5G data (Peltier, 2004). The results showed:

- Estimated sea level rise in Vietnam by the late 21st century is slightly higher than global values determined in IPCC's AR5 (Fig. 6 A and Fig. 6B).

- In the first decades (up to 2040), there is no considerable difference between estimated sea level for the RCP 4.5 and RCP 8.5 scenarios. Therefore, up to this time period, the uncertainty of the estimated sea level rise does not depend on the greenhouse gas concentration scenario but only on the method of determining sea level rise.

- At the end of the century, there is a significant difference in estimated sea level rises for the RCP 4.5 and RCP 8.5 scenarios. Therefore, the uncertainty of the estimation depends both on the Representative Concentration Pathways and the method to determine sea level rise.

- The average sea level in the 21st century will consequently increase the extremities of sea level in Vietnam. This leads to an increased risk of natural disasters such as flooding due to storm surges, tidal activity.

- Sea level rise due to geological subsidence processes was not included in this study. Therefore, future research in determining regional sea level rise should also estimate this contribution.

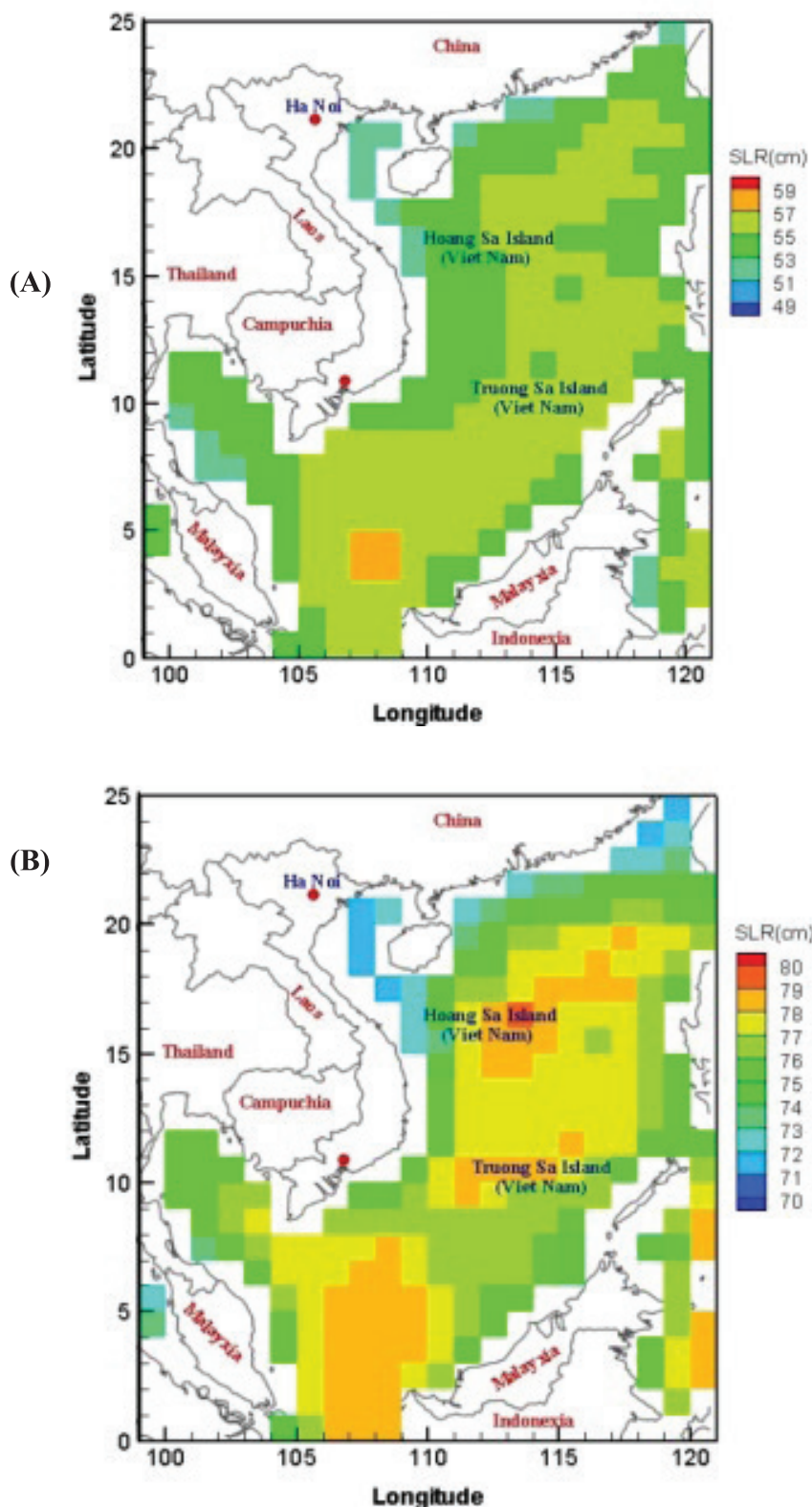


Fig. 6. Spatial distribution of sea level rise in the Vietnam East Sea in the late 21st century relative to the 1986-2005 period for the RCP 4.5 (A) and RCP 8.5 (B).

REFERENCES

- [1] J.A. Church, et al. (2013), "Sea Level Change", In: *Climate Change 2013: The Physical Science Basis*, Contribution of Working Group I to the AR5 of IPCC, Cambridge University Press, Cambridge, United Kingdom and New York, NY, USA.
- [2] S. Jevrejeva, J.C. Moore, A. Grinsted (2012), "Potential for bias in 21st century semiempirical sea level projections", *J. Geophys. Res.*, **117**, D20116.
- [3] T. Tran, X.H. Nguyen, Q.H. Le, T.T.H. Doan (2015), "Updated trend of change of sea level of the East Sea, Vietnam", *Scientific and Technical Hydro - Meteorological Journal*, **657**, pp.25-30 (in Vietnamese).
- [4] A.B.A. Slangen, C.A. Katsman, R.S.W. Van de Wal, L.L.A. Vermeersen, R.E.M. Riva (2012), "Towards regional projections of twenty-first century sea-level change based on IPCC SRES scenarios", *Climate Dynamics*, **38**(5-6), pp.1191-1209, doi: 10.1007/s00382-011-1057-6.
- [5] A.B.A. Slangen, M. Carson, C.A. Katsman, R.S.W. Van de Wal, A. Koehl, L.L.A. Vermeersen, D. Stammer (2014), "Projecting twenty-first century regional sea-level changes", *Climatic Change*, doi: 10.1007/s10584-014-1080-9.
- [6] W.R. Peltier (2004), "Global Glacial Isostasy and the Surface of the Ice-Age Earth: The ICE-5G (VM2) Model and GRACE", *Ann. Rev. Earth and Planet. Sci.*, **32**, pp.111-149.
- [7] D. Stammer and S. Hüttemann (2008), "Response of Regional Sea Level to Atmospheric Pressure Loading in a Climate Change Scenario", *J. Climate*, **21**, pp.2093-2101.
- [8] X. Fettweis, B. Franco, M. Tedesco, J.H. Van Angelen, J.T.M. Lenaerts, M.R. Van den Broeke, H. Galée (2013), "Estimating Greenland ice sheet surface mass balance contribution to future sea level rise using the regional atmospheric model MAR", *Cryosphere*, **7**, pp.469-489.
- [9] Y. Wada, L.P.H. Beek, F.C. Sperna Weiland (2012), "Past and future contribution of global groundwater depletion to sea level rise", *Geophysical Research Letters*, **39**, L09402, doi:10.1029/2012GL051230.
- [10] CSIRO and Bureau of Meteorology (2015), *Climate Change in Australia Information for Australia's Natural Resource Management Regions: Technical Report*, CSIRO and Bureau of Meteorology, Australia.
- [11] M. Palmer, K. McInnes, M. Chattopadhyay (2014), "Key factors for sea level rise in the Singapore region", *Met Office V2 Stage 5 Science Report*, 23pp.
- [12] B. Van den Hurk, B. Siegmund, A.K. Tank (2014), *Climate Change scenarios for the 21st Century - A Netherlands perspective*, Scientific Report WR2014-01, KNMI, De Bilt, The Netherlands.
- [13] IPCC (2013), *The Physical Science Basis*, Contribution of Working Group I to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change, Cambridge University Press, Cambridge, United Kingdom and New York, NY, USA, 1535 pp, doi:10.1017/CBO9781107415324.

Changes in climate extremes in Vietnam

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Abstract:

This study represents the observed and projected changes in climate extremes in the context of climate change. A linear regression method was used to identify trends and variations of climate extremes in the past, while projected changes in climate extremes were detected based on dynamical downscaling and compared with the baseline period (1986-2005). The results show that daily maximum and minimum surface air temperatures (T_{xx}, T_{nn}) increased considerably with the highest value of about 0.9°C/decade during the period of 1961-2014. The number of hot days increased across most observed stations, especially in Central Vietnam. Trends of extreme precipitation varied among the regions: decreasing across most stations in the Northwest, Northeast and Red River Delta; and increasing at other stations. In Vietnam, over the period 1959-2015, there were no obvious changes in the frequency of tropical cyclones causing landfall events, including typhoons and tropical depressions. However, the rate of occurrence of the very strongest typhoons are currently on the increase. In recent years, typhoon seasons tend to end later than in the past, and typhoons occur more frequently in Southern regions. Predicted results of climate extremes in the future for the periods 2046-2065 and 2080-2099, compared with the baseline period of 1986-2005 under the medium and high scenario (RCP 4.5 and RCP 8.5) show that temperature extremes will likely increase considerably in the future. The number of hot days will likely increase in both frequency and intensity, while the number of extreme cold days will likely decrease at most stations in the North. A maximum 1-day rainfall will also likely increase across all regions in Vietnam. Results from models show that the number of strong typhoons will likely increase in the mid- and late-century.

Keywords: *climate change, climate extreme.*

Classification number: 6.2

Introduction

Vietnam is one of the countries most affected by natural disasters and climate change. Storms and floods are the most frequent of severe natural disasters affecting Vietnam. Annually, extreme disasters cause negative effects on the natural environment, habitat and socio-economic development of Vietnam. Recent studies show that climate extreme events are likely adding more complexity to future issues of climate change [e.g. 1-5]. Climate change is leading to increases in surface temperatures, causing the occurrence of unusual climate extreme events (e.g. increase in drought) [1, 6, 7]. In addition, climate change is one cause of altering climate variations, resulting in extreme events. For instance, the increased rainfall in the rainy season may cause heavy rainfalls.

It is difficult to observe the extreme events caused by changes in climate variations; therefore, these have been defined by their thresholds. The identity of thresholds for extreme events depends on the consequences of their changes; thus, the thresholds differentiate among their respective regions [8]. To identify and quantify extreme events, a climate extreme index (CEI) was introduced in the United States in 1996. Since then, the CEI has been adapted and used by various regions around the world, especially in tropical regions [7]. Besides that, in the IPCC's fourth assessment report (AR4-2007) and fifth assessment report (AR5-2013) [9], the special reports about the managing risks of extreme events and disasters in order to advance climate change adaptation (SREX-2012), showed that the CEI was applied to assess climate extreme events on a global scale [e.g. 5]. In 2009, the world meteorological organization (WMO) announced a guide document designed for use to analyze and evaluate climate extreme events. Based on this guide document, many countries have built climate extreme indexes which are consistent with local climatic conditions. In Vietnam, Nguyen Thi Binh Minh et al. 2015 has proposed climate extreme indexes for monitoring and assessing climate change in Vietnam [10].

A large number of studies of the changes in climate variations and climate extremes have been conducted of Vietnam [1, 2, 4, 6, 9]. In general, these studies have given details and shown the assessment of climate extreme events based on meteorological data gathered up to 2010. These studies exhibited the impacts of climate change on future climate extreme events based on special report on emission scenarios issued by intergovernmental panel on climate change (IPCC). In this study, we focus on the state-of-the-art assessment of recent changes in climate extremes in Vietnam for the period of 1961-2014, and future changes

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in some climate extremes in the context of global warming. The results from this study would benefit Vietnam to improve environment management, socio-economic development, and decision-making. This study has been a source of reliable information for the national report “*Updating on climate change and sea level rise scenarios for Vietnam*”.

Methodology

Data

In order to identify trends, long-term data is required for analysis and assessment. To analyze the climate extreme events occurring on short temporal and spatial scales, we generally need daily- or hourly-observed data, long term enough to detect any trends. In Vietnam, there are 174 meteorological observation stations; however, at a majority of those stations in the South, observed data is only available beginning in 1975 and is discontinuous. Therefore, we have only used observed data from stations which meet three criteria: (1) any data missing for a month cannot exceed five consecutive days; (2) across one year, all months must be completed as the first criterion; and (3) for a long-term series that is equal to or more than 65% of the time series, will be completed for years as the second criterion. After evaluating the observed data, 82 stations were chosen to submit data with time series from 1961 to 2014. In addition, the observed data for tropical cyclones derived from the national center for hydro-meteorological forecasting (NCHMF) until 2015 were also used for the assessment.

To assess the changes of climate extremes in the future, the simulated data from numerical model were used including: (i) the atmospheric general circulation (AGC) model of meteorological research institute (MRI) derived from the Japan meteorological agency (JMA), (ii) the providing regional climates for impact studies (PRECIS) model derived from the met office hadley centre - United Kingdom, (iii) the CCAM model derived from the cCommonwealth scientific and industrial research organization (CSIRO) - Australia, (iv) RegCM models derived from the international centre for theoretical physics (ICTP) - Italy and the cWRF model derived from the santander meteorology group - Spain.

Method

In this study, linear regression was used to identify the trends and variations of climate extremes over a month, season or year based on daily observed data. Linear regression of a prediction and (x) at time (t) can be described as follows:

$$x(t) = a_0 + a_1 t \quad (1)$$

$$a_0 = \bar{x} - a_1 \bar{t} \quad (2)$$

$$a_1 = r \frac{s_x}{s_t} \quad (3)$$

in which $\bar{x}$, $\bar{t}$ are means, and s_x , s_t are standard deviations of x and t , respectively; r is linear correlation coefficient between x and t . The increased and decreased trends of $x(t)$ are identified by the slope a_1 . Predictors were identified by the climate extreme indices as shown in Table 1.

Table 1. Climate extremes indices.

Indices	Definition	Unit
Number of very hot days (SU39)	Count of days with daily maximum temperature $\geq 39^\circ\text{C}$	days
Number of hot days (SU35)	Count of days with daily maximum temperature $\geq 35^\circ\text{C}$	days
Highest maximum temperature (Txx)	Maximum value of daily maximum temperature	$^\circ\text{C}$
Lowest minimum temperature (Tnn)	Minimum value of daily minimum temperature	$^\circ\text{C}$
Number of cold days (CD15)	Count of days with daily mean temperature $\leq 15^\circ\text{C}$	days
Number of extreme cold days (CD13)	Count of days with daily mean temperature $\leq 13^\circ\text{C}$	days
Number of heavy rainfall days (R100)	Count of days with daily precipitation > 100 mm	days
Maximum 1-day rainfall (Rx1day)	Maximum value of daily precipitation	mm
Maximum 5-day rainfall (Rx5day)	Maximum value of 5-day accumulated daily precipitation	mm

For the future, we have used simulated models to assess the changes of climate extremes. The changes of climate extremes were assessed by comparing the future trends and variations of climate variables (2046-2065, 2080-2099) with the trends and the variations in the reference period (1986-2005) (referred to as baseline).

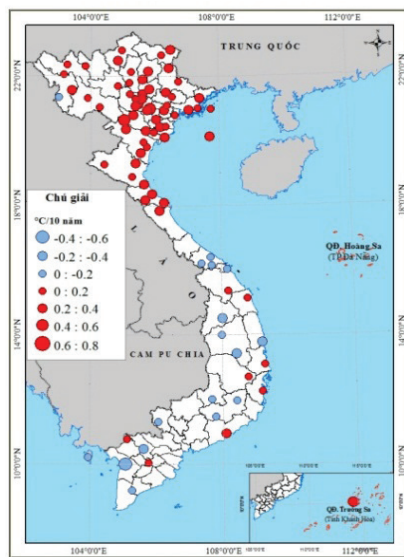
Results and discussion

Observation

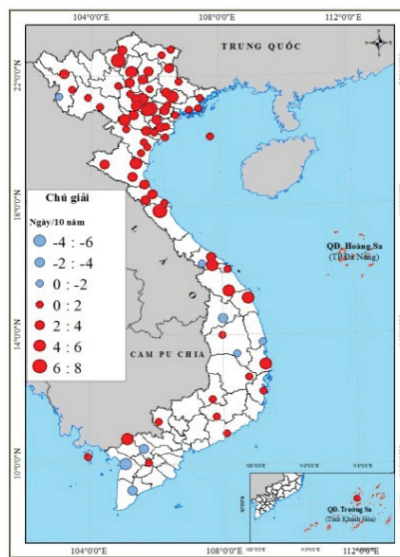
Temperature extremes:

In the past half-century (1961-2014), there was an increasing trend in the highest maximum temperature (Txx) at most stations in the North and a decreasing trend in most stations in the South. The highest increasing rates of about $0.9^\circ\text{C}/\text{decade}$ (Fig. 1A) were observed in some stations in Northwestern and Northeastern Vietnam. The highest decreasing rates of about $0.8^\circ\text{C}/\text{decade}$ were found in some stations in the North Central Vietnam. The increasing trends of SU35 were observed in most stations of Northern Vietnam (North, North Central Coast, and Mid Central Coast) with a regular increase of about 2-6 days/decade. Whereas, the decreasing trends were found in most stations of the Southern Vietnam (South Central Coast, Central Highlands and Mekong River Delta) with a regular decrease of about 2-4 days/decade (Fig. 1B). In most stations in Northern Vietnam (Northwest, Northeast, Red River Delta and North Central Coast), SU39 had increasing trends with regular increases of about 0.2-0.6 days/decade. Decreasing trends were found in most stations of Southern Vietnam with a regular decrease of about 0.4-0.8 days/decade (Fig. 1C).

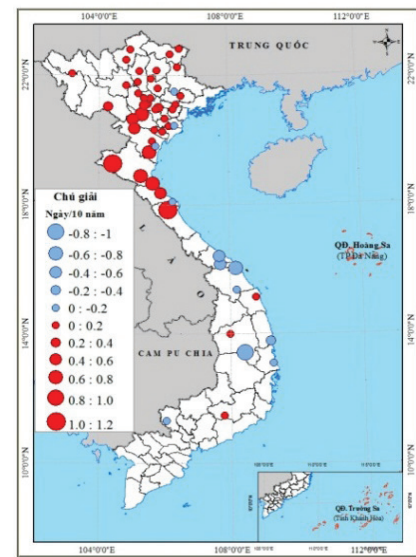
The trend of the lowest minimum temperature (Tnn)



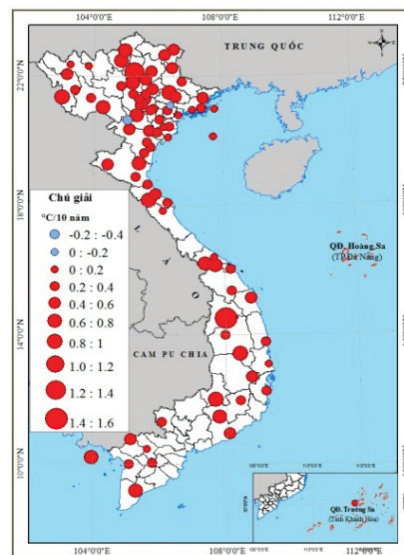
(A) Txx



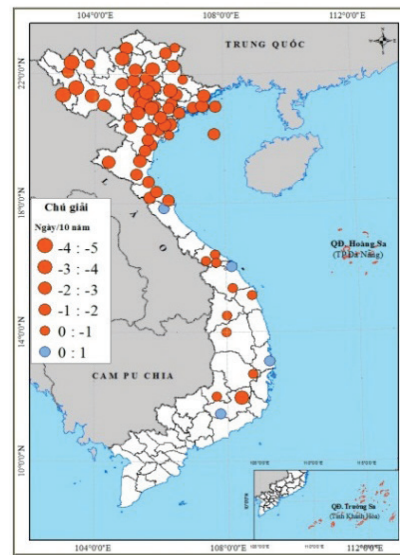
(B) SU35



(C) SU39



(D) Tnn



(E) CD15

Fig. 1. Observed trends of climate extreme variables during the period of 1961-2014.

increases in most stations over the country, except Chi Linh, Mai Chau station. A regular increase was in a range of 0.4 to 0.8°C/decade. An increase of about 1.2°C occurred in some stations North of Thanh Hoa Province and the Central Highlands (Fig. 1D). In general, the increasing rate of Tnn was faster and more significant than that of Txx. The number of cold days (CD15) had an obviously decreasing trend at the stations in Northern Vietnam, and the Central Highlands had regular decreases of about 2-4 days/decade. The number of cold days over four days was observed at some stations of Northwest (Fig. 1E).

Rainfall extremes:

Over the past 54 years, rainfall extremes had contradictory trends between regions. However, the observed data exhibited an obvious relation of these trends within a climate region. In general, the trends of the Rx1day, Rx5day and R100 were decreasing at most stations in Northern Vietnam, especially at the Red River Delta; and increasing in most stations in Central Vietnam (Fig. 2).

Storms and tropical depressions:

Over the past half-century (1959-2015), trends of tropical

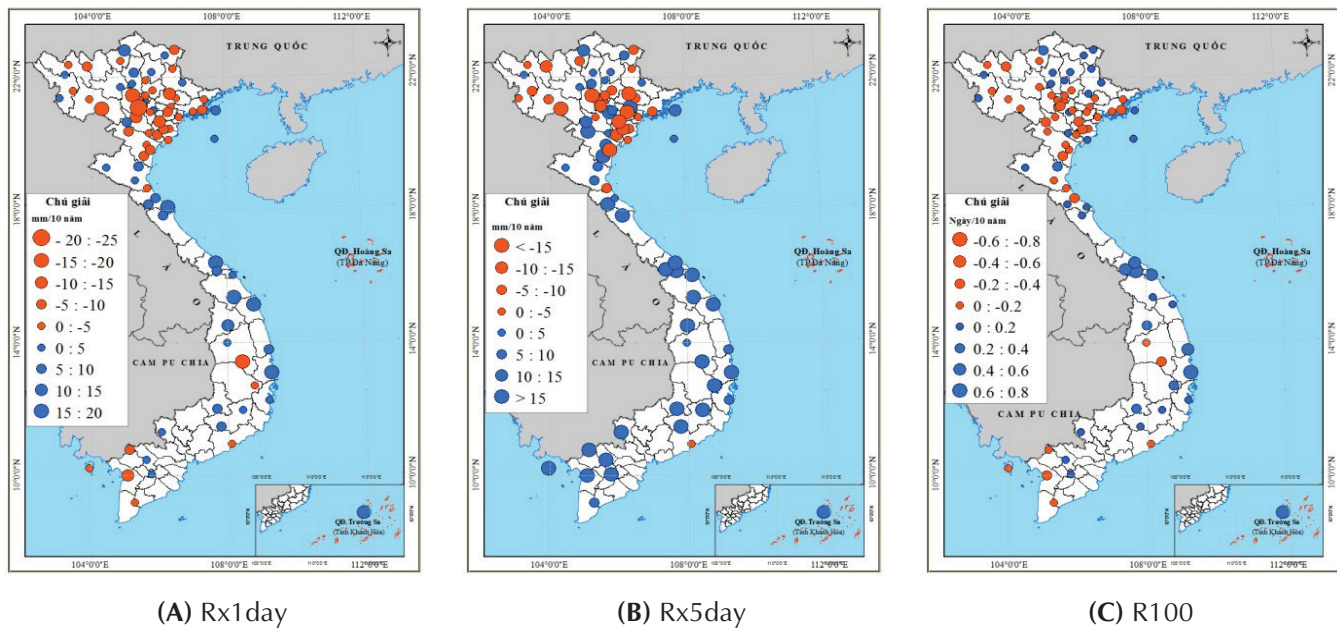


Fig. 2. Changes in extreme events related to rainfall during the period of 1961-2014.

cyclones affecting and occurring in Vietnam had no significant changes (Fig. 3A). However, the number of strong typhoons (over level 12) had a slightly increasing trend in recent years (1990-2015) (Fig. 3B).

Prediction

Temperature extremes:

Under the RCP4.5 scenario, changes in the multi-model mean maximum temperature (Fig. 4A) shows increases of $1.7 \div 2.7^\circ\text{C}$ by the end of the century, with the greatest increases of mean maximum temperatures to be in the Northeast and Northern Delta region of Vietnam, and with the largest increases at over 2.5°C . The smallest increases will be about 1.4°C , observed in the South and South Central Vietnam. The changes of multi-model mean minimum temperature (Fig. 4B) shows increases of $1.8 \div 2.2^\circ\text{C}$ by the end of the century. Similar to maximum temperatures, there will be the greatest increases of mean minimum temperatures in the Northeast and Northern Delta region of Vietnam. Under the RCP8.5 scenario (not shown), mean maximum temperature will increase at $3.0 \div 4.8^\circ\text{C}$ and mean minimum temperature will increase at $3.0 \div 4.0^\circ\text{C}$ by the end of the century.

Heat waves will likely increase in the future when compared to the baseline. SU35 will increase by about $25 \div 35$ days for the RCP4.5 scenario and $35 \div 45$ days for the RCP8.5 scenario (Fig. 5 and Fig. 6). By the end of the 21st

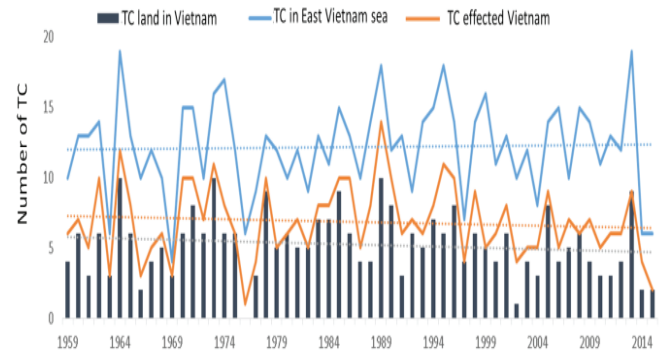


Fig. 3A. The number of tropical cyclones in the period of 1959-2014.

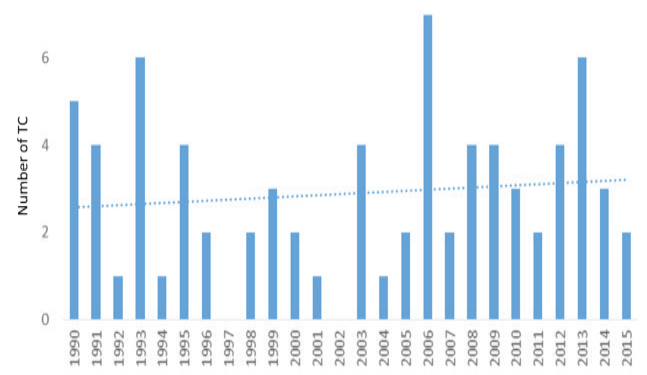
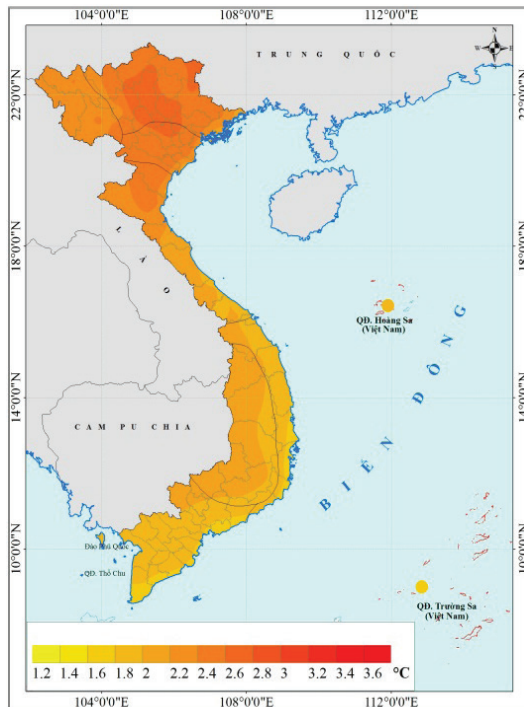


Fig. 3B. The number of typhoons over level 12 in the East Sea in the period of 1990-2015.



(A) Maximum temperature



(B) Minimum temperature

Fig. 4. Predicted changes in annual mean maximum temperature (A) and minimum temperature (B) at the end of the 21st century compared to the baseline period under the RCP4.5 scenario from an ensemble of models.

century, according to the RCP4.5 scenario, the largest increase in SU35 will likely be above 50 days in Central Vietnam, and the smallest increase of SU35 will likely be in the Central Highlands and Southern Vietnam (Fig. 5B). According to the RCP8.5 scenario, the largest increase of SU35 will likely be above 100 days in the Northeast, South Central and Southern Vietnam (Fig. 6B).

According to the RCP4.5 scenario, by the mid-21st century, trends from the CD15 and the CD13 tend to decrease by about 5÷10 days across most provinces in the North when compared to the baseline. The highest decrease will likely be above 15 days in the Northwest and Northeast; the lowest decrease (under five days) will likely be in North Central Vietnam. By the end of the 21st century, the number of extreme cold days and dangerously cold days tends to decrease from 10 to 20 days, with the highest decrease likely being at some stations in the Northwest and Northeast (above 20 days), and the lowest decrease will likely be less than 10 days in North Central Vietnam (Table 2 and Table 3).

Table 2. Changes of the CD15 compared with the baseline.

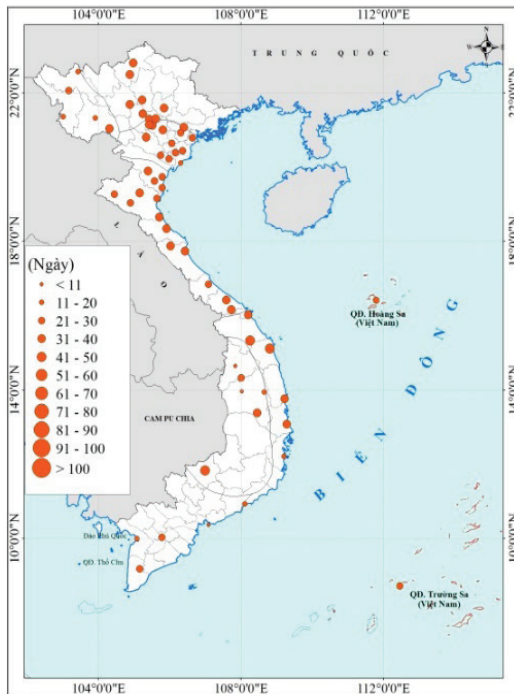
Region	RCP4.5 scenario			RCP8.5 scenario		
	2016-2035	2046-2065	2080-2099	2016-2035	2046-2065	2080-2099
Northwest	-13.1 ÷ -1.8	-30.9 ÷ -2.6	-38.7 ÷ -2.8	-20.4 ÷ -2.3	-37.1 ÷ -3.0	-61.0 ÷ -3.2
Northeast	-13.2 ÷ -1.2	-28.3 ÷ -2.1	-35.1 ÷ -2.7	-18.9 ÷ -1.6	-34.6 ÷ -2.5	-58.1 ÷ -3.1
Red River Delta	-3 ÷ -1.9	-7.1 ÷ -5.2	-10.0 ÷ -7.2	-5.2 ÷ -3.5	-9.0 ÷ -6.3	-11.2 ÷ -7.9
North Central Coast	-2.0 ÷ -0.1	-4.1 ÷ -0.1	-5.2 ÷ -0.1	-3.2 ÷ -0.1	-4.9 ÷ -0.1	-5.7 ÷ -0.1

Table 3. Changes of the CD13 compared with the baseline.

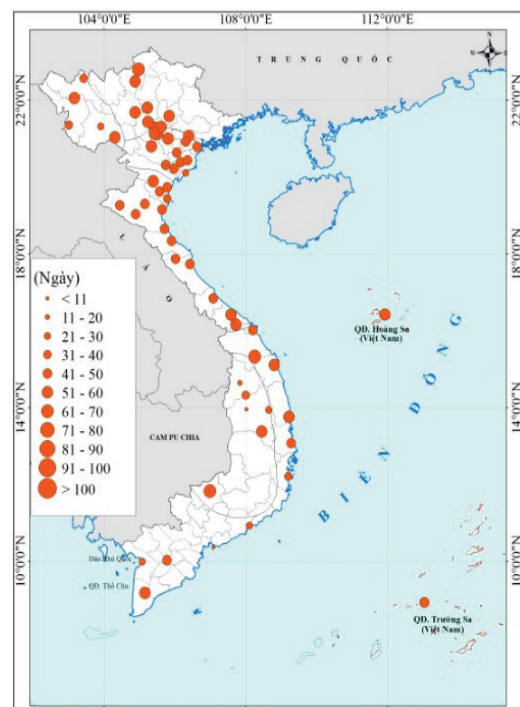
Region	RCP4.5 scenario			RCP8.5 scenario		
	2016-2035	2046-2065	2080-2099	2016-2035	2046-2065	2080-2099
Northwest	-14.0 ÷ -5.2	-32.6 ÷ -8.3	-42.8 ÷ -10.3	-22.5 ÷ -7.0	-40.6 ÷ -9.8	-71.1 ÷ -12.3
Northeast	-14.2 ÷ -2.4	-31.6 ÷ -4.5	-40.3 ÷ -6.5	-20.9 ÷ -3.6	-39.3 ÷ -5.5	-66.4 ÷ -7.8
Red River Delta	-5 ÷ -3.2	-13.1 ÷ -9.5	-17.9 ÷ -13.2	-10.5 ÷ -7.1	-16.5 ÷ -11.9	-23.9 ÷ -17.3
North Central Coast	-4.4 ÷ -0.7	-9.8 ÷ -0.9	-13.5 ÷ -1.1	-7.7 ÷ -0.6	-12.1 ÷ -1.2	-16.9 ÷ -1.5

Rainfall extremes:

According to the RCP4.5 and the RCP8.5 scenario, maximum 1-day Rainfall (Rx1day) tends to increase within a range of 10 to 70% over the country in the middle of the 21st

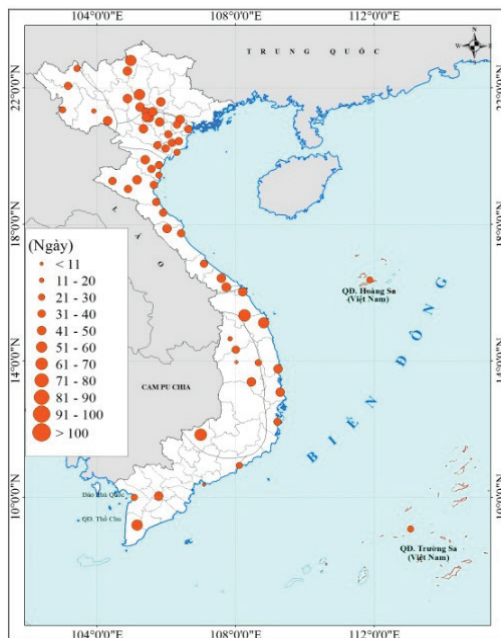


(A) The mid-21st century

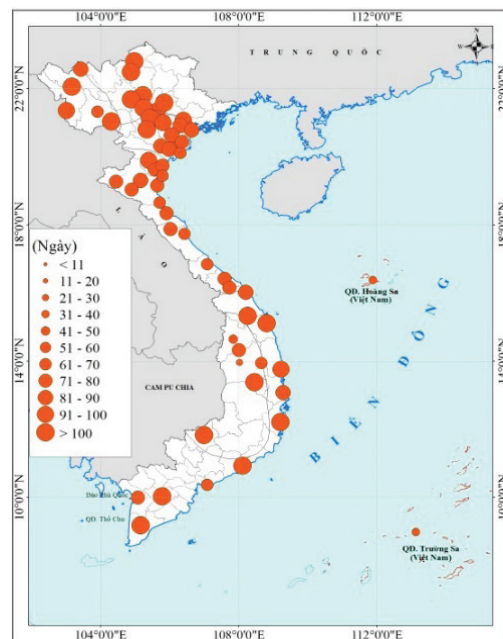


(B) The end of the 21st century

Fig. 5. Predicted changes in SU35 for the middle (A) and the end (B) of the 21st century compared to the baseline period according to the RCP4.5 scenario from an ensemble of models.



(A) The mid-21st century



(B) The end of the 21st century

Fig. 6. Predicted changes in the number of SU35 for the middle (A) and the end (B) of the 21st century compared to the baseline period according to the RCP8.5 scenario from an ensemble of models.

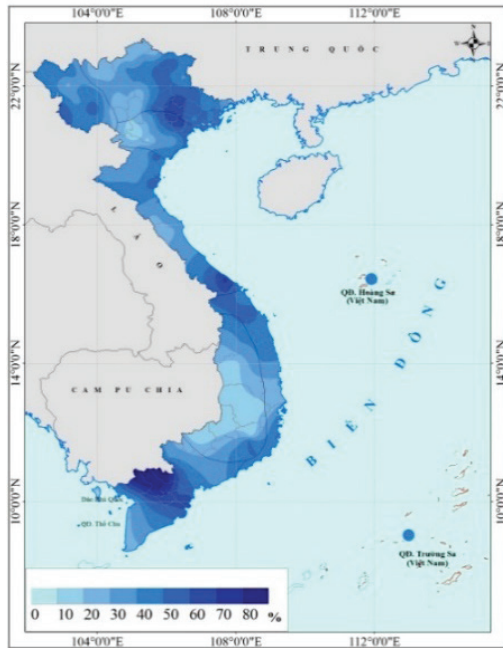
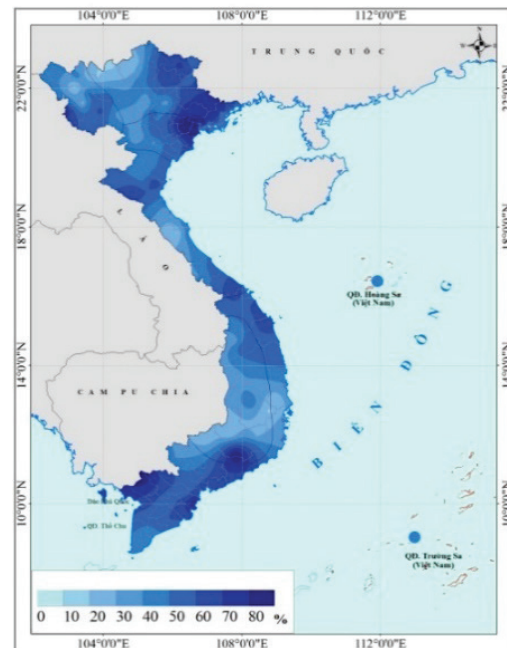
(A) The mid-21st century(B) The end of the 21st century

Fig. 7. Predicted changes in the Rx1day (mm) by the middle (A) and the end (B) of the 21st century compared to the baseline period according to the RCP4.5 scenario.

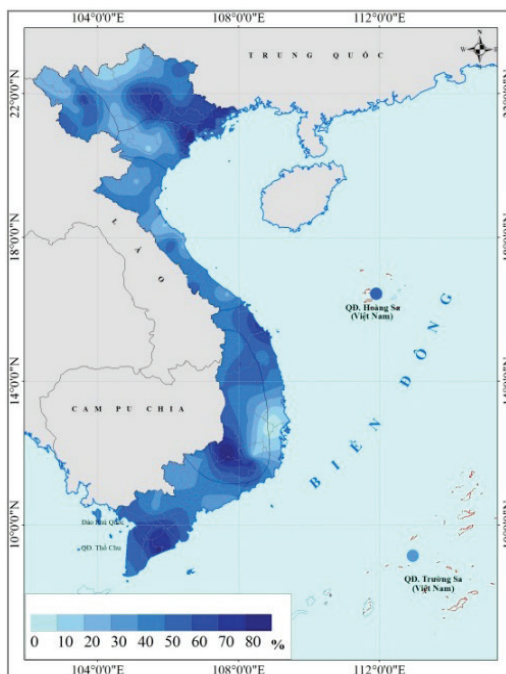
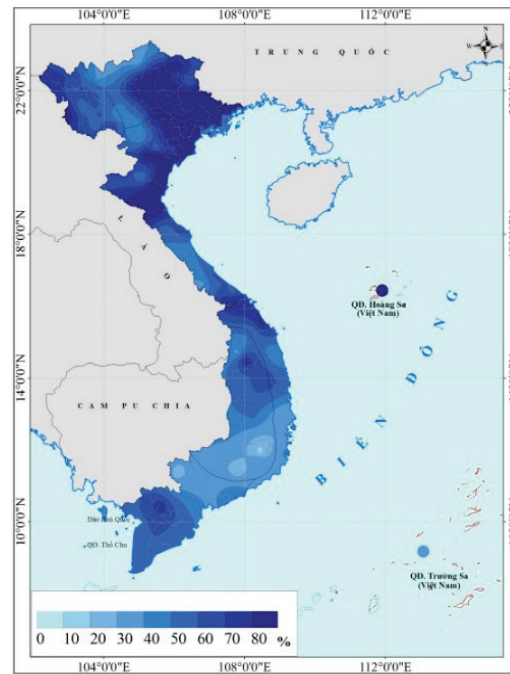
(A) The mid-21st century(B) The end of the 21st century

Fig. 8. Predicted changes in the Rx1day (mm) by the middle (A) and the end (B) of the 21st century compared to the baseline period according to the RCP8.5 scenario.

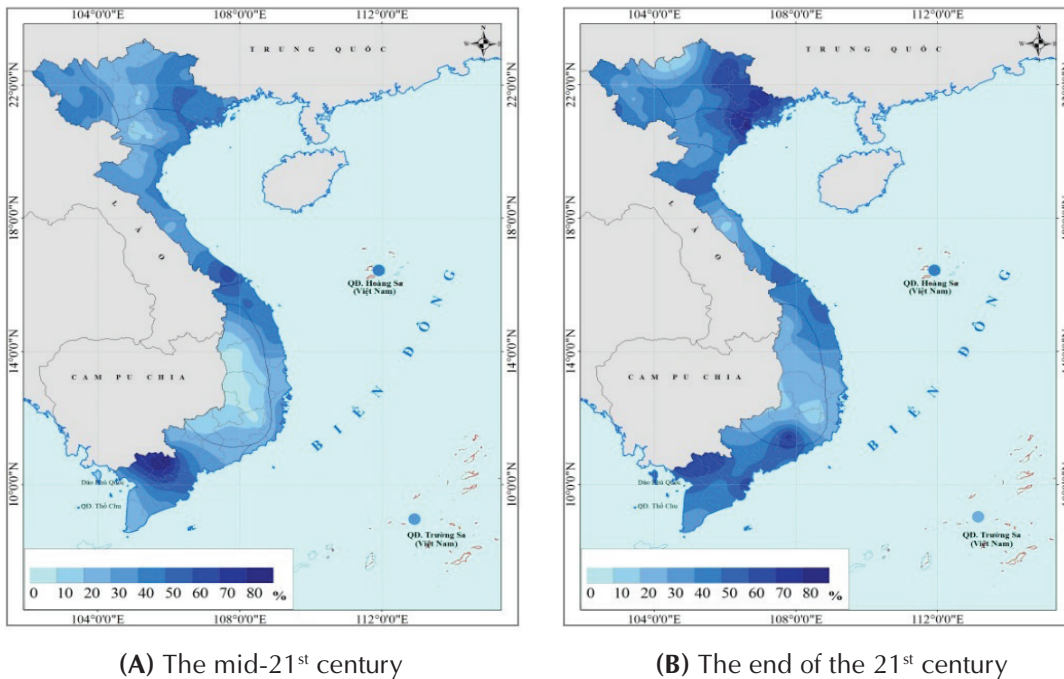


Fig. 9. Predicted changes in the Rx5day (mm) by the middle (A) and the end (B) of the 21st century compared to the baseline period according to the RCP4.5 scenario.

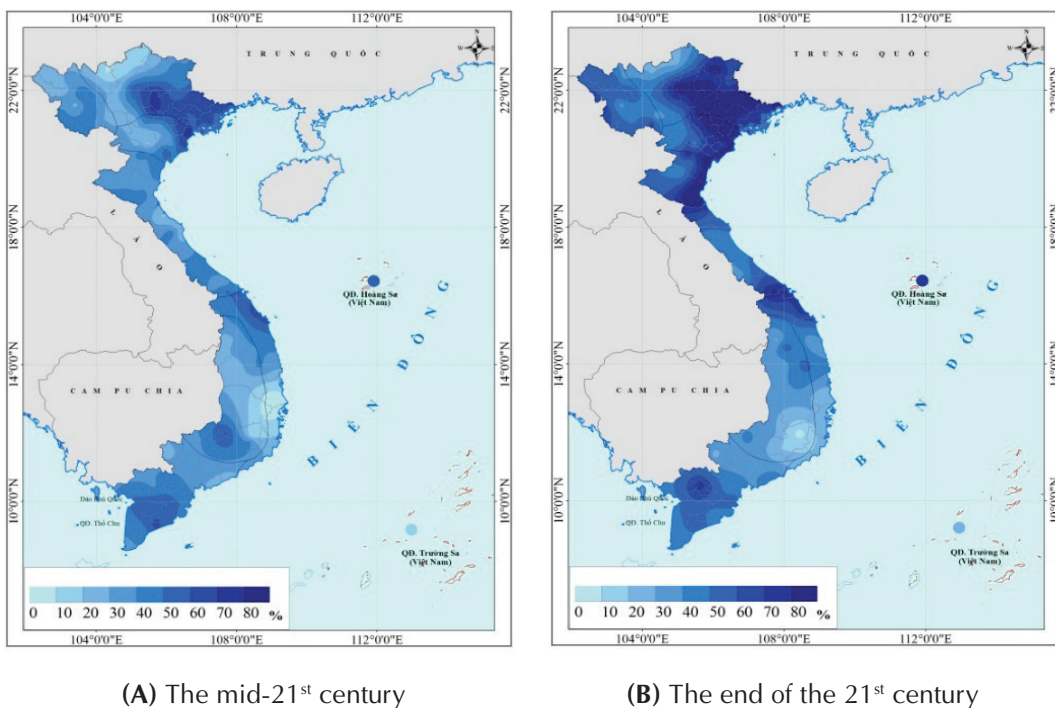


Fig. 10. Predicted changes in the Rx5day (mm) by the middle (A) and the end (B) of the 21st century compared to the baseline period according to the RCP8.5 scenario.

century, when compared to the baseline. By the end of the 21st century, the increasing trend of the Rx1day will be higher with similar patterns as compared to the trend observed in the mid-21st century (Fig. 7 and Fig. 8).

According to the RCP4.5 scenario, by the mid-21st century, the Rx5day tends to increase within a range of 10 to 50% across the country when compared to the baseline. The highest increase of about 80% will likely occur in the East of Southern

Vietnam. By the end of the 21st century, the increasing trend will be higher with similar patterns than compared to the trend observed in the mid-21st century (Fig. 9). As shown through the RCP8.5 scenario, the Rx5day tends to increase within a range of 10 to 60% all over the country happening at the middle and the end of the 21st century. The highest increase of about 80% will likely be in the Northeast and North Central Coast at the end of the 21st century (Fig. 10).

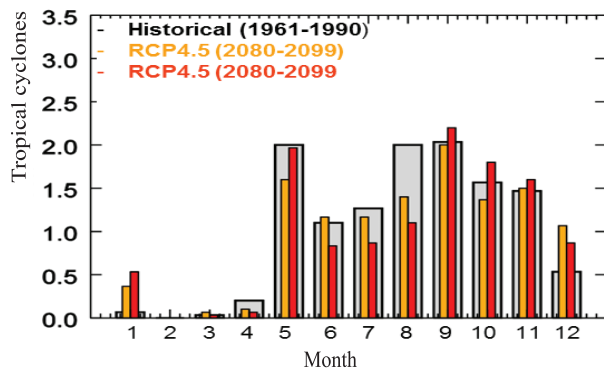


Fig. 11. The number of tropical cyclones at the end of the 21st century (PRECIS model).

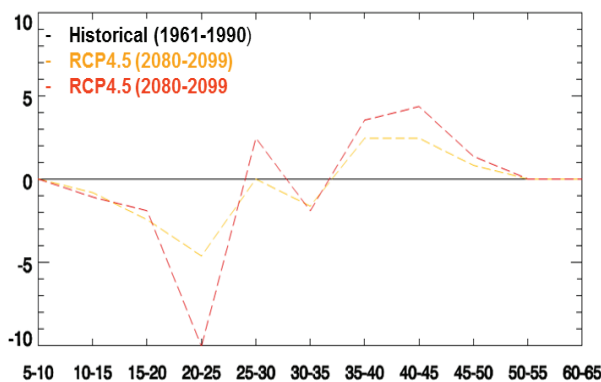


Fig. 12. The changes of tropical cyclones with different intensity at the end of the 21st century when compared with the baseline (PRECIS model).

Tropical cyclone:

According to the simulations derived from the PRECIS model, tropical cyclone activities tend to decrease early in the typhoon season (Jun-August) in the East Sea for both RCP4.5 and RCP8.5 scenarios. However, it is likely that tropical cyclone activities increased in the last typhoon season, especially based on the RCP8.5 scenario (Fig. 11). It can be seen that tropical cyclone activities will shift to the end of the typhoon season, which is the period at which typhoons occur mainly in the South. Figure 12 indicates that the number of weak and normal typhoons will decrease, while the number of strong typhoons will increase significantly by the end of the 21st century.

Conclusion

We investigate long-term changes of climate extremes over Vietnam for the period of 1961-2014 and future changes of some climate extremes in the context of global climate change. The resulting evidence shows obvious decreasing and increasing climate extreme trends across all regions of Vietnam.

Over the past half-century (1961-2014), the highest

maximum temperatures had an increasing trend at most stations in the North and a decreasing trend at most stations in the South. The trend for lowest minimum temperatures was clearly decreasing across the whole country. The number of cold days had a decreasing trend at stations in the North and at the Central Highlands. The trends of the maximum 1-day and 5-days rainfall were decreasing at most stations in the North, whereas the trends were increasing at stations in the Central and the South. There was no obvious change in the frequency of tropical cyclones, including typhoons and tropical depressions causing landfalls. However, the rate of very strongest typhoons is on the increase. The typhoon season, at present, tends to end later than in the past, and typhoons occur more frequently in Southern regions.

Presented figures clearly show the predictions of changes in climate extremes across the country. By the end of the 21st century, the number of hot days will increase significantly for both scenarios (RCP4.5 and RCP8.5), according to simulated models. The number of cold days and extremely cold days will decrease across most provinces in the North and for the North Central Coast. The trends for the maximum 1-day and 5-days rainfalls will increase across the whole country. In general, other trends observed at the middle and the end of the century will stay at the same levels. However, any increasing trends observed at the end of the century will be more significant in values and patterns. Projected result show the number of tropical cyclones in the East Sea and their impacts on Vietnam do not show a clear trend and it is uncertain, but the number of strong typhoons will likely increase in the future.

REFERENCES

- [1] Ministry of Natural Resources and Environment (2012), *Updated scenarios of climate change and sea level rise for Vietnam*, Agricultural Publishing.
- [2] Nguyen Thi Binh Minh, et al. (2015), "Proposal of extreme climate indices related to temperature and precipitation in service monitoring and evaluation", *Journal of Natural Resources and Environment*, 5.
- [3] Phan Van Tan, et al. (2010), "Research on the impact of global climate change to the elements and extreme climate events in Vietnam, predictability and strategic solutions to cope", *Report a summary of scientific and technological topics state level under the program KC08.13/06-10*, Hanoi.
- [4] L.V. Alexander (2006), "Global observed changes in daily climate extremes of temperature and precipitation", *J. Geophys. Res.*, **111** (D05109), DOI:10.1029/2005JD006290.
- [5] A.M.G. Klein Tank, F.W. Zwiers, X. Zhang (2009), "Guidelines on analysis of extremes in a changing climate in support of informed decisions for adaptation, Climate data and monitoring", *WCDMP-No.72, WMO-TD No.1500*, 56p.
- [6] Institute of Meteorology, Hydrology and Climate Change (2016), "Updated scenarios of climate change and sea level rise for Vietnam".
- [7] T.C. Peterson, and M.J. Manton (2008), "Monitoring changes in climate extremes - A tale of international collaboration", *BAMS*, DOI:10.1175/2008BAMS2501.1.
- [8] T.R. Karl, N. Nicholls, A. Ghazi (1999), "CLIVAR/GCOS/WMO Workshop on Indices and Indicators for Climate Extremes: Workshop Summary", *Climatic Change*, **42**(1), pp.3-7.
- [9] IPCC (2013), "IPCC fifth assessment report: climate change 2013 - The physical science basis", *Cambridge University Press*, Cambridge, UK, 1535 p.
- [10] Nguyen Van Thang, et al. (2015), *Changes in Climate Extremes and Impacts on the Natural Physical Environment*, Viet nam Publishing House of Natural Resources, Environment and Cartography, Hanoi, Vietnam, pp.84-139.

Impacts of climate change on wave regimes in the East Sea

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Abstract:

The study applied the PRECIS and SWAN modelling packages to simulate wind and wave regimes under climate change in the Vietnam East Sea. The results indicated that under RCP4.5 climate change scenario, by the end of the century, there are significant changes in both wave height and wave period in summer and winter months. In the East Sea during July, wave height is expected to increase 11.5% while wave period expected to increase 3.3%. On the other hand, wave height in January is projected to decrease approximately 7% while wave period in the same month is projected to decrease 4.4%. There are no significant changes in wave direction.

Keywords: climate change, climate change scenario, PRECIS, SWAN.

Classification number: 6.2

Introduction

Climate change causes global warming and consequently, changes meteorological, coastal, and wave conditions, ocean currents, and sea level. There is a large number of studies within the last few years assessing the impacts of climate change on sea wave regimes. The study by Seneviratne, et al. (2012), based on a large number of data sources such as data from monitoring stations, satellite image and wave hindcasting, concluded that average wave height have increased in the Pacific, and Northern Atlantic within the last 50 years and at the southern parts of global oceans in the 1980s [1]. Other studies such as Woolf, et al. (2002), Allan & Komar (2006), Adams, et al. (2008), Menendez, et al. (2008), Izaguirre, et al. (2011) also based on different data sources, determined the linkages between changes in the wave-wind regime and the changes in climate such as ENSO [2-6]. Other studies on the impacts of climate change on oceanic wave regime include Wang & Swail (2006), Hermer, et al. (2013), Mori,

et al. (2013), also showed an increase in average significant wave height, wave period and wave direction in the oceans. The region with largest change occurs in the southern part of global oceans with an increase in average significant wave height between 5 and 10% as compared to now [7-9]. Graham, et al. (2013), using several models (for the SRES A2 scenario), predicted a decrease in average significant wave height in winter in the Northern Hemisphere in the mid latitudes in the Pacific by the end of the 21st century [10]. Hemer, et al. (2012) applied various simulation models (for SRES A2 and B1 scenarios) have also projected a decrease in average significant wave height in the South Eastern coastal area of Australia by the end of the 21st Century as compared to now [11].

In the East Sea region, the wave regime is strictly governed by the monsoon wind system. Under climate change, however, the East Sea monsoon is expected to be altered in both intensity and timing [12], thus leading to changes in the wave regimes in the East Sea.

Methodology

PRECIS model

Providing Regional Climates for Impacts Studies (PRECIS) model is a PC based regional dynamical climate model developed by the Met Office Hadley Center. The model is designed to generate detailed climate change scenarios for small regions of the world. The basis of the PRECIS model is the HadRM3P model developed in 1991 to project climate change. The PRECIS model has been widely used globally to generate regional and national climate change scenarios. For a more detail description of the PRECIS model, relevant documents could be referred to [13].

SWAN model

Simulating Waves Near shore (SWAN) model is a third generation wave simulation model which simulates the 2 dimensional wave spectral through solving for the spectral action balance equation. SWAN allows the simulation of wave characteristics in the coastal zones close to land, in lakes and estuaries from input variables such as wind, bed surface and current conditions. Detailed description of the SWAN model could be referred to in relevant documents [14].

Simulation conditions

PRECIS model:

In this study, the PRECIS model was used in the bounded grid region between 95°E - 135°E; and 10°S - 30°N, with a resolution of 1/8 longitude/latitude degree, and 19 horizontal levels. Boundary and initial conditions are updated from output predictions of the third generation atmosphere-ocean coupled model HadCM3Q0 of the Hadley Center, United Kingdom. Five different runs were performed on PRECIS with a large scale boundary condition from the HadCM3Q0 global model. The five runs include: HadCM3Q0, HadCM3Q3, HadCM3Q10, HadCM3Q11 and HadCM3Q13. In which: (i) HadCM3Q0: is the base model, run under moderate emissions. The remaining HadCM3Qx scenario are dynamically and physically

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adjusted from the base scenario; (ii) HadCM3Q3: Small temperature amplitude changes calibrated; (iii) HadCM3Q10: Dry skew prediction calibrated; (iv) HadCM3Q11: Wet skew prediction calibrated; (v) HadCM3Q13: Large temperature amplitude changes calibrated.

SWAN model:

SWAN model was applied for the entire East Sea region between 1°N-23°N and 99°E-121°E with a grid size of 1/8 longitude/latitude degree. The boundary conditions of the model are long term wave characteristics determined from global hindcasting data [15].

The topography of the study area was generated from the Gebco database with a resolution of 30 second. Fig. 1 depicts the topography of the study area that was used in the SWAN model.

Wind input data of the model is the output of the PRECIS simulation from above.

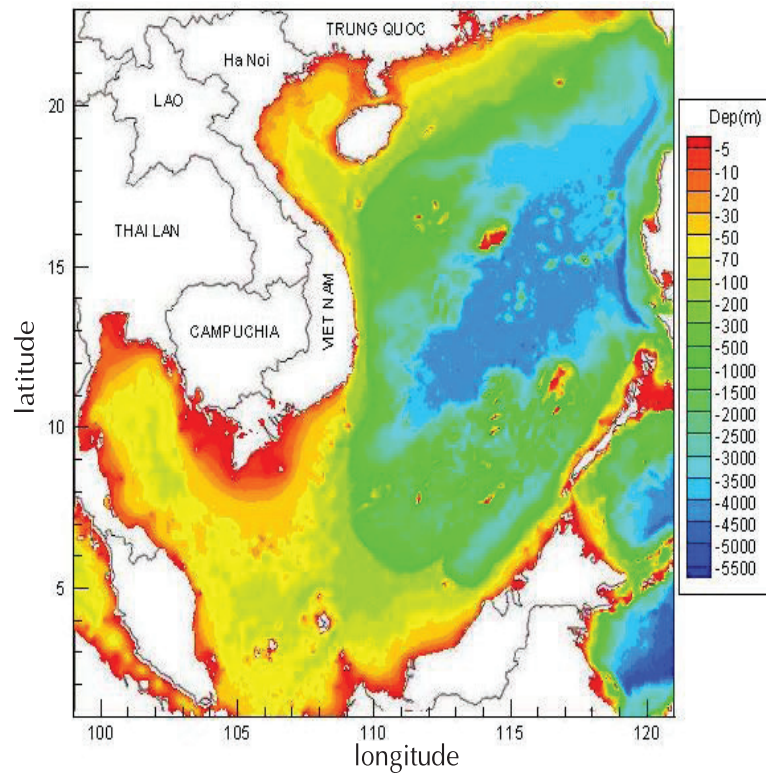


Fig. 1. Topography of the study area.

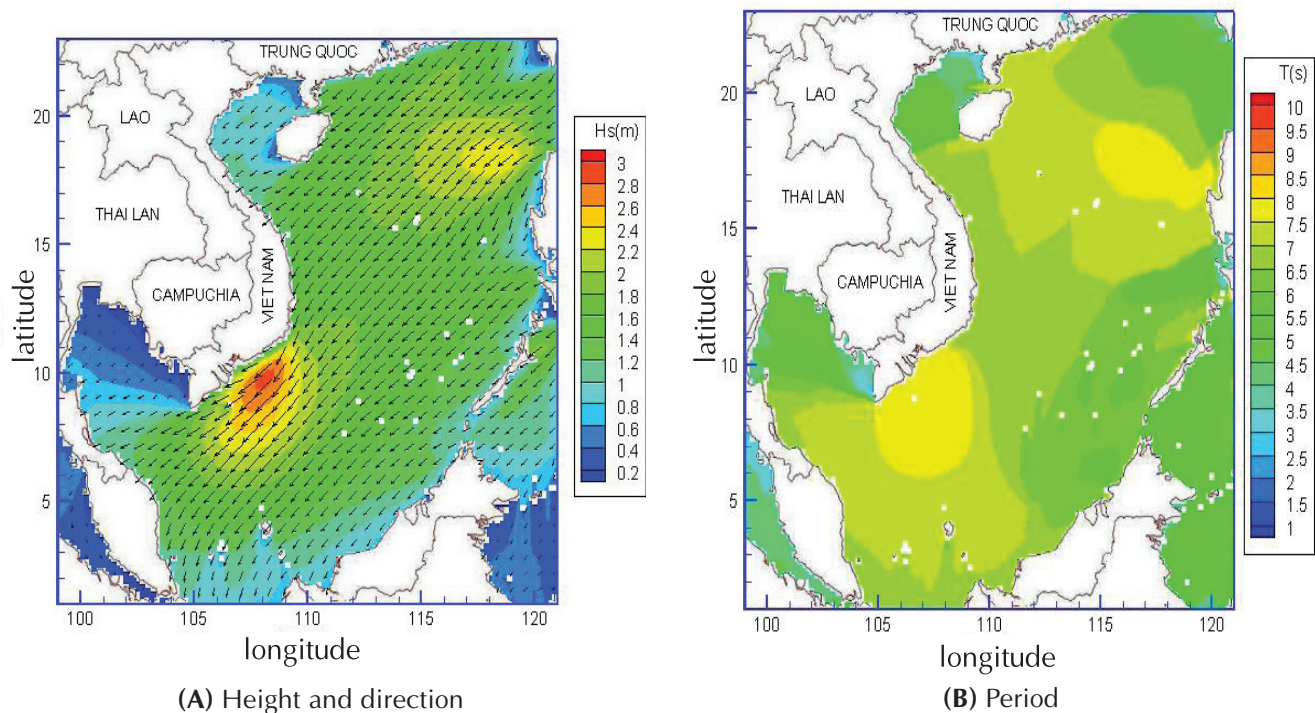


Fig. 2. Average wave characteristics for January in the East Sea based on average wind data for the period of 1980-2000.

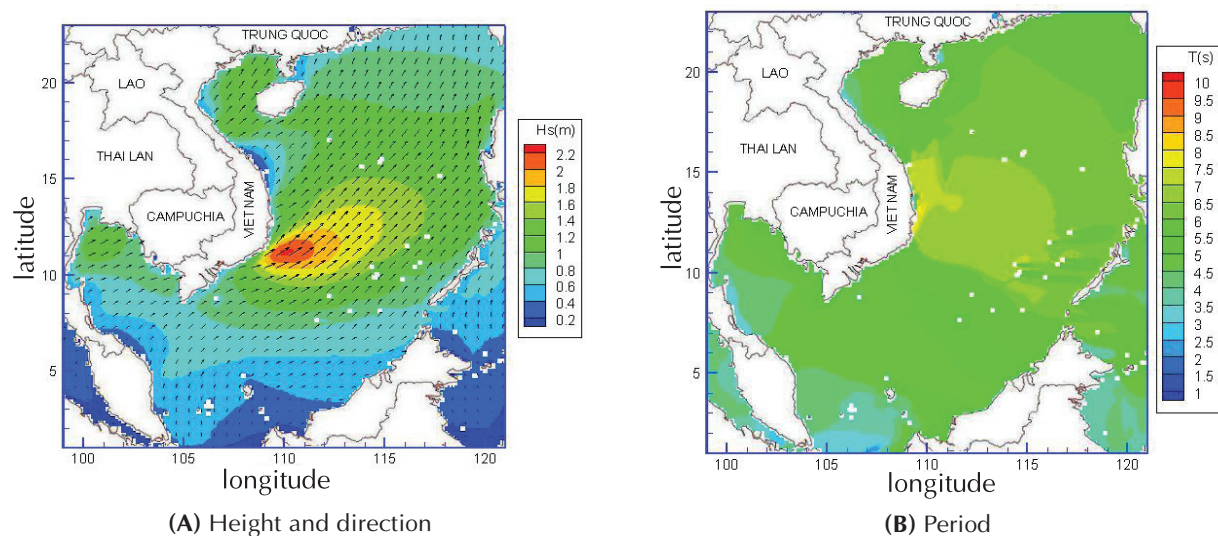


Fig. 3. Average wave characteristics for July in the East Sea based on average wind data for the period of 1980-2000.

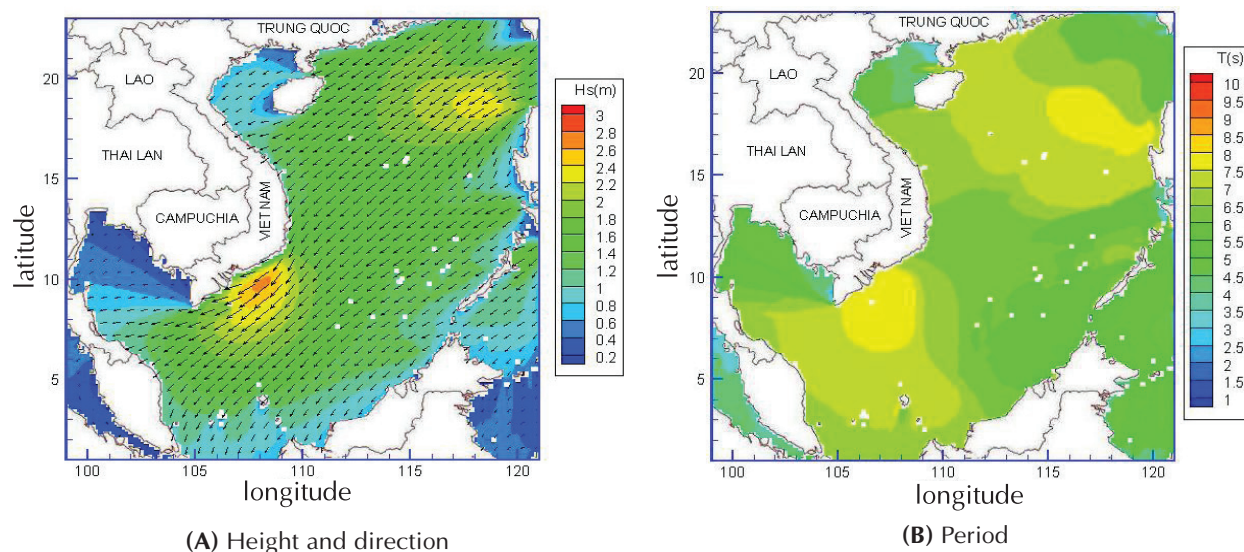


Fig. 4. Average wave characteristics for January in the East Sea based on average wind data for the period of 2080-2099.

Simulation results

Scenarios and assumptions

To determine the impacts of climate change on wave regimes in the East Seas, 2 wind system scenarios were used: (i) a status quo scenario (wind values were determined from hindcasting in the period between 1980-2000; (ii) a climate change scenario (wind was determined from PRECIS under RCP4.5 scenario for the period of 2080-2099).

Results and discussion

The simulated results showed that under the status quo scenario, in winter months, wave direction in the East Sea is predominantly

North-East. Largest wave height occurs in the middle of the East Sea, along the North East-South West axis from the Bashi Channel region to the Mekong River estuary region with an average wave height of 2-3 m.

In the coastal zone of Vietnam, the largest wave height occurs offshore South Eastern Vietnam with average wave height between 3-3.5 m, wave in the Northern coastal zone is less in height and lies between 0.5 to 1 m while wave heights in the Central coastal area is around 1.5 to 2 m. Common wave period is in between 5 to 7.5 seconds; with a maximum reaching up to 8s in the North Eastern part of the East Sea near the Philippines and offshore South Eastern Vietnam (Fig. 2). In

the summer months, wave direction in the East Sea is predominantly South-West, with largest wave height up to 2-2.5 m, occurring in the middle of the East Sea. For the coastal zone of Vietnam, largest wave height occurs offshore South Central Vietnam with height above 2 m. In the sea of the northern part of Vietnam, wave heights are between 1.2 to 1.5 m, while in the south, wave only reaches 1m in height. Wave period in the East Sea fluctuates between 4 to 7 seconds, reaching a maximum of 7.5 seconds in the seas of the South Central Vietnam between Binh Dinh and Ninh Thuan provinces (Fig. 3). The results agree well with studies from Nguyen Manh Hung (2005) [15].

Under climate change scenario RCP4.5,

wave simulation shows that in comparison to the 1980-2000 period (baseline), in the 2080-2099 period, spatial distribution of wave height and period changes significantly, while wave direction remains mostly unchanged.

In winter months, wave height and wave period mostly decrease in the East Sea, leading to a reduced regional spatial distribution of wave height (Fig. 2A and 3A) and wave period (Fig. 2B and 3B) compared to the baseline scenario.

The changes in wave regimes under climate change is further assessed at 8 locations through comparing the simulated wave height and period at 8 representative points in the East Sea (refer to Table 1).

Table 1. Data point location.

Data point	Coordinates	
	Longitude	Latitude
Bach Long Vi	107.750	20.125
Con Co	107.375	17.125
Cu Lao Cham	108.500	16.000
Hoang Sa	111.625	16.500
Phu Quy	109.000	10.500
Truong Sa	111.875	8.625
Con Dao	106.625	8.625
Gulf of Thailand	101.875	9.750

Results comparison for January - representing winter (Table 2), indicated that on average, wave height and wave period in the East Sea decreases approximately 7% and 4.4% respectively. Wave height reduction in the Bach Long Vi Island in the Northern Gulf of Tonkin is 13.1% and 15.4% respectively. In Con Co Island, lowest wave height reduction is at 5.6%, while lowest wave period reduction is 0.4% at Con Dao Island. At Cu Lao Cham, Hoang Sa, Phu Quy, and Truong Sa Islands, wave height decreases between 7.7% and 8.9% while wave period decreases between 1.3% and 3.9%. On the contrary, wave height in the Gulf of Thailand increases 1.9% while wave period decreases 1.7%.

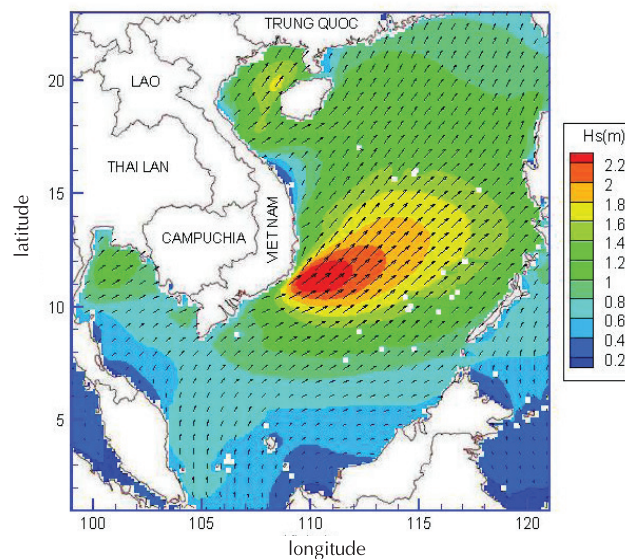
It can therefore be seen that changes in wave height and period in the East Sea is spatially variable. More specifically the changing trend of wave height in the middle of the Gulf of Thailand is in contradiction with the changes in other regions.

In contrast to winter months, wave height and wave period in summer mostly increase in the East Sea, leading to an increase in spatial distribution of wave height (Fig. 4A and 5A) and wave period (Fig. 4B and 5B) as

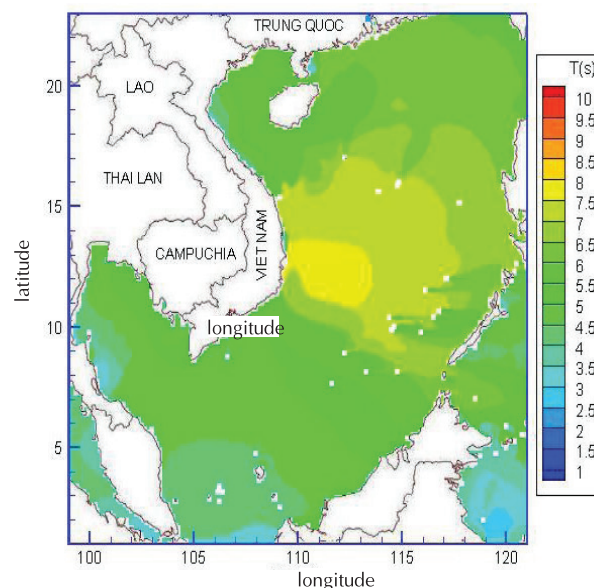
Table 2. Wave height and period in January comparison for selected locations in the East Sea for the baseline period and under climate change scenario.

Location	Wave height (m)		Change (%)	Wave period (s)		Change (%)
	Baseline	CC		Baseline	CC	
Bach Long Vi	0.99	0.86	-13.1	5	4.23	-15.4
Con Co	1.08	1.02	-5.6	6.89	6.62	-3.9
Cu Lao Cham	1.26	1.16	-7.9	6.82	6.68	-2.1
Hoang Sa	1.68	1.55	-7.7	7.15	7.06	-1.3
Phu Quy	2.54	2.34	-7.9	7.08	6.83	-3.5
Truong Sa	1.68	1.53	-8.9	6.59	6.13	-7.0
Con Dao	1.97	1.84	-6.6	7.72	7.69	-0.4
Gulf of Thailand	0.54	0.55	1.9	5.97	5.87	-1.7

Note: the “-” sign indicates a reduction in either wave height or wave period.



(A) Height and direction



(B) Period

Fig. 5. Average wave characteristics for July in the East Sea, results based on average wind data for the period of 2080-2099.

Table 3. Wave height and wave period in July comparison in selected locations in the East Sea for the baseline period and under climate change scenario.

Location	Wave height (m)		Change (%)	Wave period (s)		Change (%)
	Baseline	CC		Baseline	CC	
Bach Long Vy	1.22	1.48	21.3	5.92	5.94	0.3
Con Co	0.91	1.1	20.9	4.06	4.08	0.5
Cu Lao Cham	0.21	0.26	23.8	5.54	5.73	3.4
Hoang Sa	1.03	1.16	12.6	6.46	6.69	3.6
Phu Quy	1.73	1.86	7.5	5.97	6.01	0.7
Truong Sa	1.12	1.24	10.7	5.73	5.89	2.8
Con Dao	0.77	0.79	2.6	4.93	4.94	0.2
Gulf of Thailand	0.79	0.73	-7.6	4.34	4.97	14.5

Note: the “-” sign indicates a reduction in either wave height or wave period.

compared to the baseline period.

Results comparison for July -representing summer and results in the baseline period is depicted in Fig. 5. The results showed that average wave height increases 11.5% while average wave period increases 3.3%. The region with the largest and smallest increase in wave height as compared to the baseline is Cu Lao Cham Island and Con Dao Island with a 23.8% and 2.6% increase respectively. Wave height in Bach Long Vi and Con Co Islands increase significantly as compared to the baseline period with an increase of 21.3% and 20.9% respectively. Wave period increases most significantly in the middle of the Gulf of Thailand at roughly 14.5%. Increase in wave period in Bach Long Vi, Con Co, Phu Quy, and Con Dao Island is slightly lower, with values of 0.3%, 0.5%, 0.7%, 0.2% respectively.

Similar to the North-East monsoon months, wave height during the South-East monsoon period in the middle of the Gulf of Thailand exhibit a decreasing trend, contrasting the trend in the remaining areas in the East Sea. Wave height decrease in the area is approximately 7.6% (Table 3).

Overall, changes in wave height and period in July in the East Sea is highly variable yet the absolute change in wave height in July (summer) is greater than in January (winter) while the contrary is true for wave period, i.e. the absolute change in wave period in July is less than January.

There is also a degree of uncertainty in the assessment of changes in wave regimes in the East Sea under climate change. The uncertainties in the study is closely related to uncertainties in climate change scenarios and of climate change simulation models and wave simulation models.

Conclusion

Under RCP4.5 scenario, climate change significantly affects the wave regime in the East Sea, the impact is highly variable depending on the region and the season assessed.

In January, wave height in the East Sea decreases on average 7% while wave period in the East Sea decreases on average 4.4%. Wave height and wave period decreases the most at Bach Long Vi Island with predicted values of 13.1% and 15.4% respectively.

In the middle of the Gulf of Thailand, the trend of wave height change is reversed with the trend in other regions, with an increase of 1.9% while wave period follows the similar trend in other regions with corresponding value of 1.7%.

In July, wave height increases on average 11.5%, wave period increase on average 3.3%. The region with the highest increase in wave height as compared to the baseline period is Cu Lao Cham Island at approximately 23.8%. The lowest increase in wave height projected is in Con Dao Island at approximately 2.6%. Wave period increases most significantly in the middle of the Gulf of Thailand, at approximately 14.5%, and least significantly at Con Dao Island at 0.2%. Wave height in the middle of the Gulf of Thailand decreases 7.6%, contradicting the general trend in the East Sea.

Average absolute changes of wave height in July in the East Sea is greater than that in January. On the contrary, average absolute change of wave period in July is less than that in January.

The study provides the assessment of climate change impacts on wave regimes in the East Sea for January and July, the two

time period representing winter and summer in the region. There is a degree of uncertainty related to the study, this mainly spurs from the uncertainties in climate change scenario and simulation models. Further detailed assessment of climate change impacts on wave regimes in the East Sea in the future is needed.

REFERENCES

- [1] Seneviratne, et al. (2012), “Changes in climate extremes and their impacts on the natural physical environment”, *A Special Report of Working Groups I and II of the Intergovernmental Panel on Climate Change (IPCC)*, Cambridge University Press, Cambridge, UK, and New York, NY, USA, pp.109-230.
- [2] D.K. Woolf, P.G. Challenor, P.D. Cotton (2002), “Variability and predictability of the North Atlantic wave climate”, *J. Geophys. Res. Oceans*, **107**, C103145.
- [3] J.C. Allan, and P.D. Komar (2006), “Climate controls on US West Coast erosion processes”, *J. Coast. Res.*, **22**, pp.511-529.
- [4] P.N. Adams, D.L. Inman, N.E. Graham (2008), “Southern California deep-water wave climate: Characterization and application to coastal processes”, *J. Coast. Res.*, **24**, pp.1022-1035.
- [5] M. Menéndez, P.L. Woodworth (2010), “Changes in extreme high water levels based on a quasi-global tide-gauge data set”, *J. Geophys. Res. Oceans*, **115**, C10011.
- [6] C. Izaguirre, F.J. Méndez, M. Menéndez, I.J. Losada (2011), “Global extreme wave height variability based on satellite data”, *Geophys. Res. Lett.*, **38**, L10607.
- [7] X.L. Wang, V.R. Swail (2006), “Climate change signal and uncertainty in projections of ocean wave heights”, *Clim. Dyn.*, **26**, pp.109-126.
- [8] N. Mori, T. Shimura, T. Yasuda, H. Mase (2013), “Multi-model climate projections of ocean surface variables under different climate scenarios - Future change of waves, sea level, and wind”, *Ocean Eng.*, **71**, pp.122-129.
- [9] M.A. Hemer, Y. Fan, N. Mori, A. Semedo, X.L. Wang (2013), “Projected future changes in wind-wave climate in a multi-model ensemble”, *Nature Clim. Change*, **3**, pp.471-476.
- [10] N.E. Graham, D.R. Cayan, P. Bromirski, R. Flick (2013), “Multi-model projections of 21st century North Pacific winter wave climate under the IPCC A2 scenario”, *Clim. Dyn.*, **40**, pp.1335-1360.
- [11] M.A. Hemer, K.L. McInnes, R. Ranasinghe (2012), “Projections of climate change driven variations in the offshore wave climate off southeastern Australia”, *Int. J. Climatol.*, **33**, pp.1615-1632.
- [12] IMHEN (2014), *Applying Norwegian earth system model for Climate Change scenario development for Vietnam, monsoon and climate extreme studies*, Final Report, Hanoi.
- [13] J.R. Pope, K.M. Willett, Osborn, P. Thorne (2014), “Investigation and quality assessment of the Past Weather Code from the integrated Surface Database”, *Hadley Centre Technical Note 97*.
- [14] Delft University of Technology (2014), *SWAN - Scientific and Technical Documentation, Environmental Fluid Mechanics Section*.
- [15] Nguyen Manh Hung (2005), *Wave regimes in the East Sea*, Special issue on the East Sea, Ha Noi, pp.285-318.

Historic drought and salinity intrusion in the Mekong Delta in 2016: Lessons learned and response solutions

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Abstract:

During the dry season of 2015-2016, the Mekong Delta had suffered the worst historic drought and salinity intrusion occurrence on record, causing heavy damages to nine coastal provinces (in total 13 provinces) of the Mekong River Delta. Just after the drought and salinity intrusion occurred, the media offered some different opinions suggesting possible solution which offer effective responses and stable development to coastal regions. The author suggests that in order to have sustainable development for the Mekong Delta in general and for the coastal zones in particular, Vietnam needs to have some basic short-term and long-term solutions, for each region as well as the whole delta, including drought-salinity intrusion and flooding programs, structural and non-structural works, and coverage for both the Mekong Delta and the whole Mekong River Basin.

Keywords: historic drought, Mekong Delta, salinity intrusion.

Classification number: 6.2

Historic salinity intrusion 2015-2016 in the Mekong Delta

Salinity intrusion is a natural phenomenon that occurs annually in the Mekong Delta and is dependent on the following factors: low-flow from upstream of the Mekong River; water storage capacity during the end of the flooding season in the Mekong Delta; coastal water level happenings; and water use situation in the Mekong Delta. Each year, salinity intrusion often occurs at the Mekong Delta from December to May, with coverage at its peak in late April or early May.

According to water level statistics at Tan Chau (Mekong River) from 1926 to the present, the peak flow and total volume of water in the 2015 flood is the lowest in 90 years for the Mekong Delta, which is

to occur at 99% frequency, or once every 100 years. The total water for the overall flood season in 2015 was about 220 billion m³, approximately half of the largest floods on record (400-440 billion m³) and 60% of recorded medium floods (350-370 billions m³). The total temporary water flood storage in the whole Mekong Delta flood zone was shortly below 2 billion m³ in 2015, just behind that, half of the medium floods (4 billion m³) and 40% of the largest floods (6 billion m³). Since the 2015 flood was too weak, the flow into the Mekong Delta during the 2015-2016 dry season was also too low. Discharges at Tan Chau (on the Mekong River) and Chau Doc (on the Bassac River) from December 2015 to March 2016 were only 57-85% of the annual average. The main reason was due to the Mekong upstream flood flow into

the Great Lake (Cambodia) decreasing by 33% from its average, leading up to the amount of water input for the low flow into the Mekong Delta (beside of the Mekong upstream flow) from November 2015 to the end of March 2016 decreasing to 53%. If counting the amount of water used along the river, the flow sent to the Mekong river mouth during the same time in 2016 was only about 65-70% of the average, from 1,300-1,500 m³/s. This shows that the salinity intrusion level in 2016 was more serious than was in 1998 [1].

With the flow conditions described above, salinity intrusion during the 2016 dry season had occurred worse up to now. From the beginning of November 2015, saline water began entering the coastal areas and estuaries, about 1.5 months earlier than usual. Until February 2016, the saline boundaries were approximate with its highest boundary as the average year and from this time, the salinity intrusion are up higher. Until the end of March 2016, saline boundaries of 4 g/l reached the peak of the year, exceeding annual average 20-25 km, even some places over 30 km (Vam Co Tay River). In specific: On the Vam Co Tay River, saline water deeply intruded to 135 km (from the river mouth), passed the Tuyen Nhon 25 km; On the Mekong River, 79 km, near to Binh Thanh island, far from 3-5 km downstream of Mekong and Ham Luong River confluence; On the Ham Luong River, 78 km, passed 25 km from the Ben Tre River mouth (near the town of Cho Lach district); On the Co Chien River, 81 km, passed 2-3 km from Mang Thit River mouth; On the Bassac River, 70 km, passed 2 km from An Lac Thon and far 7 km to downstream from Cai Cui Port. In the Ca Mau Peninsula, saline water intruded to Nga Nam town on the Quan Lo-Phung Hiep canal and the middle of Nang Ren-Cai Trau-Phu Loc canal, adjoining with saline water from Cai Lon-Cai Be river, that forms the pincer surrounded the central area of Ca Mau Peninsula.

Until the end of the 2015-2016 drought-salinity intrusion spell (May 2016), drought had affected all 13 provinces of the Mekong Delta, while salinity intrusion affecting nine coastal provinces (Fig. 1). The total damage across all fields can be calculated up to 360 million USD. In that,

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Fig. 1. Much of the area of rice production in the Mekong Delta were withered due to the effects of salinity intrusion.

according to a report of the Ministry of Agriculture and Rural Development and local authorities, the total damages to agriculture and aquaculture is more than 300 million USD. The damaged areas: For rice, 238,276 hectares (130,280 hectares in 2015 and 107,996 hectares in 2016); For fruit trees, 29,277 hectares; For vegetables, 6,575 hectares; For brackish water shrimp, 79,000 hectares. In addition, the total number of households suffering from the lack of clean water is 211,261 (with over 1,000,000 inhabitants), the estimated cost of implementing the temporary solutions for water supply is more than 22.5 million USD. Other damages are approximately 45.0 million USD, primarily due to additional works to dredge canals and repair and reinforce embankments, cattle and poultry died due to lack of drinking water, epidemics caused by a lack of clean water [2].

Lessons learned from drought and salinity intrusion during 2015-2016

When considering all collected data, an analysis of the causes, impacts, and responses from the historic drought-salinity intrusion during 2015-2016 in the Mekong Delta shows the following:

A need to focus on implementation and to improve the effectiveness of long-term hydro-meteorological forecasts: Problems

with the hydro-meteorological forecast, particularly for the long-term, is extremely important. Due to many reasons, so far, Vietnam focuses primarily on short-term forecasts (1-3 days) and medium-term forecasts (3-10 days), and has yet to fully consider long-term forecasts (1-6 months), and have especially neglected very long-term forecasts (3-5 years). From this, we can assume that the prevention of natural disasters has been very passive, even considering drought only, and not yet hurricanes, floods, and other natural disasters.

Long-term and very long-term forecasts hardly require highly accurate data, and often only need to identify a general trend. From this, we must remove the warnings and recommendations to and from the ministries and local authorities to consistently arrange seasonal calendars, cultivated area maps, and prevention and response plans for natural disasters. Instead, we need to instill the point of view that "forecasts are requisite, and warnings are sufficient". The fact that the drought-salinity intrusion happenings from 2016 in the Mekong Delta show that if the forecasts and early warning activities had been heeded at the end of the 2015 flood, then surely the damage would be decreased more than what actually happened. For efficient long-term forecasts, Vietnam

can propose to China, Laos, and Thailand to operate flushing activities sooner for the hydro-power reservoirs than at the beginning of the dry season in 2016, which will help to significantly reduce drought-salinity intrusion issues in the next months.

Direct activities to prevent and respond to drought-salinity intrusion: When drought-salinity intrusion occurs, authorities from the local government, central government, and local people try to prevent and overcome resulting damage, but so far, damages caused by drought-salinity intrusion have been extremely large, causing no small hardship for the socio-economic development of the whole Mekong Delta, both in general, and particularly for the lives of millions of inhabitants living in the influenced areas. Considering these damages, it must be said that there are many lessons of which the direct activities to prevent and respond to the drought and salinity intrusion of the authority levels can be used to learn. That is, the central authorities have not yet implemented initiative actions for forecasting and early warning of drought-salinity intrusion situations for local authorities, although the rain and flood happenings in 2015 gave noteworthy information to help study the historic drought and salinity intrusion in the dry season of 2016, and although the drought and salinity intrusion situation happened right from the end of the year 2015, locals did not take initiative, nor did they take actions to direct people to arrange and shift the seasonal calendar, cultivated areas, and other activities. When the process of drought and salinity intrusion occurs, coordination and direction between the central and local authorities are also limited, and should not keep up the drought and salinity intrusion happenings to promptly warn local authorities and local people; using an agreement among Vietnam, China and Laos to flush water using hydro-power reservoirs to reach anti-drought and salinity intrusion is necessary, but if Vietnam takes the initiative to propose these contracts sooner, the issues caused by the dry season of 2015-2016 would be significantly reduced.

A need to consider the overall water discharge by hydro-power reservoirs from China and Laos: The Chinese hydro-power reservoirs operate using a mechanism for water storage from melting ice, Spring

floods, mainly occurring between February and April, with a high reached in March, and flooding due to rains from June to September. During Spring-Summer 2016, temperatures trended higher than average, and the snow melted sooner and bigger in the Tibet region than past years. Thus, the floods suffered by China from the middle of March to the middle of April in 2016 are easy to understand, because of the time when the floods occurred. It should be noted that after the upstream hydro-power reservoirs were built by China, besides mostly discharging a negligible flow through turbines, more water may be discharged through spillways in case there is too much snow melt. Due to the non-members of the Mekong River Commission, China carries almost no binding responsibility to flush water downstream. If the Mekong Delta continues facing severely droughts and salinity intrusion as in 2016, and while the amount of snow melt is limited, China also may find it hard to discharge more water downstream.

In addition to China, Laos is an official member of the Mekong River Commission. Therefore, the country should have a higher binding mechanisms to cooperation with Laos, and Thailand, to discharge water from hydro-power reservoirs downstream to help solve drought and salinity intrusion according to the mechanism of the 1995 Agreement for sustainable development of the Mekong River Basin. However, due to the reservoirs in Laos, both Thailand and the Highlands of Vietnam have modest capacity, and should also be hard can help significantly improve the drought and salinity intrusion situation as in 2016.

Learning from the lessons above, Vietnam should not be too eager to expect water discharged from upstream hydro-power reservoirs, which is considered only as a band-aid measure, and that need to have proactive solutions for effective prevention and response to the drought and salinity intrusion phenomena in the future.

Proposed response and adaptation solutions

To sustainably and effectively respond to natural disasters in general, and drought-salinity intrusion in particular, the Mekong Delta needs to closely apply structural and non-structural solutions. With that, and an understanding of each level of disaster, the Mekong Delta also needs the

structural and non-structural solutions to be at corresponding levels. The Mekong Delta cannot use low level solutions to be able to effectively deal with higher natural disasters levels.

Structural solutions

Immediate solutions: local authorities and people should actively repair and complete the sluice/culvert system and saline water preventive embankments, proactive water storage soon when drought and salinity intrusion occur. Every year, local people should have water storage measures implemented at the end of the rainy season (starting from November), decanting fresh water when the tides are high (stating from December) to allow more water to reach fields, according to a scale of agricultural households ensuring that the production of the Winter-Spring crop. In order to supply domestic water to urban areas along the coastal regions (such as My Tho, Ben Tre, Tra Vinh, Bac Lieu, Ca Mau, Rach Gia...), the retrieved water points can be temporarily shifted on the river or creek facing risk of salinity intrusion up to places of more stable fresh water. Temporary fresh water pipeline should also be added to towns and residential quarters. Vehicles should also be used to transport fresh water to hamlets, communes and households. More deep groundwater aquifers should be exploited where there is a stable source of water. Drought and salinity intrusion occurrences should be closely monitored, especially those in the fields, at coastal region and at estuaries to promptly alert and subsequently handle complex situations that may occur.

Medium solutions: The sea dike and sluice systems used for salinity intrusion control at self-contained, stable production areas must be perfected. Increase accessibility to fresh water source for coastal regions via intake canals and sluices from stable fresh water sources. Focus must be on completing water resource systems and projects, such as Can Duoc-Can Giuoc (Long An Province), Bao Dinh-Go Cong (Tien Giang Province), North Ben Tre (Ben Tre Province), South Mang Thit (Tra Vinh Province), O Mon-Xa No (Can Tho city, Hau Giang and Kien Giang Provinces), and other places. Perfect the sea dike system and build dike structures according to the "Water Resources Master Planning for the Mekong Delta under the

Context of Climate Changes and Sea Level Rise" document, which was approved by the Prime Minister in September, 2012 (1397/QD-TTg). Focus on constructing and completing the central domestic water supply systems for residential areas there. For coastal municipalities, consider shifting the withdrawn point of raw water to upstream, in order to ensure safety from drought and salinity intrusion. Plan a stable water supply for rural areas that face severe drought and salinity intrusion spells.

Long-term solutions: Consider a solution for large scale structures in the Mekong River estuaries (including sluices of Vam Co, Ham Luong, Co Chien, Cung Hau and Cai Lon-Cai Be) and be proactive with the storage, keeping, and distribution of fresh water while maintaining a stable, large volume of water during the dry season in the regional and inter-regional levels. From now until 2020, the government should quickly construct two sluices at Cai Lon and Cai Be. Following that, in order to proactively deal with drought and salinity intrusion that can continue to happen at intensities greater than was seen in 2016, the government should speed up plans to construct remaining four sluices soon after 2020 (approved to plan after 2030). It can be shown that when the large sluices are constructed at estuaries, the fresh water supply and storage capabilities for the entire Mekong Delta will be significantly improved. Fresh water will not only be stored at a mass of billions cubic meters, but will also be supplemented by about 40-50% to the Mekong river (Tieu and Dai mouths) and 10-20% to the Bassac river (Dinh An and Tran De mouths) than naturally occurs, which will help to keep the saline boundaries at a safe distance much more than at present. Also from there, fresh water sources could be more favorable in order to transfer water to any difficult water supply regions, such as Vam Co, Cai Lon-Cai Be, the Ca Mau peninsula, and the coastal areas of Ca Mau and Bac Lieu Provinces. Besides that, there is a need for upstream Mekong countries and the Mekong River Commission to establish operation regulations for upstream reservoir systems. These are the basic solutions for a long-term solution in order to respond most effectively to the instability of a flow from upstream and increased climate changes and sea level rises in the Mekong Delta (Fig. 2) [3].

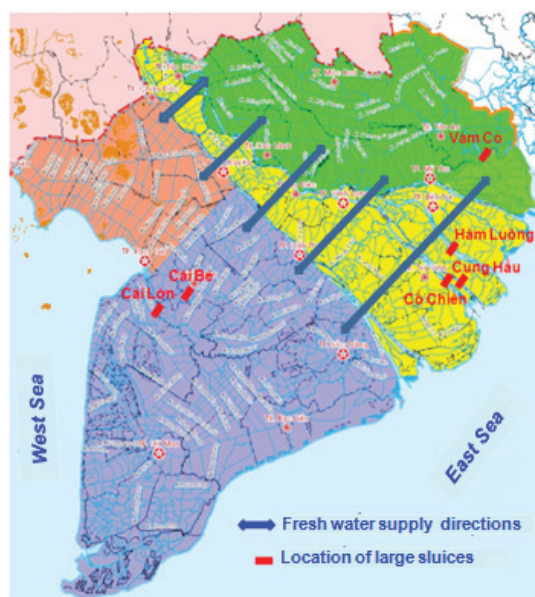


Fig. 2. The locations of six proposed, large sluices and fresh water supply directions from the central Mekong Delta.

General non-structural solutions

The basic point of view of non-structural solutions, is that all structural solutions available to respond to natural disasters cannot prevent all of the extreme values, especially for salinity intrusion at very high levels, exceeding the capabilities of the structural system. For all of the years of drought and salinity intrusion occurrences, should all efforts be responded to by structural solutions, it would not be rational for both economic and national resources. Thus, for inhabitants of the coastal region, they should gradually adapt to the saline environment, living with saline water, and at the same time, emphasizing proper control of industrial and agricultural developments in the coastal regions. In management of drought and salinity intrusion by structural solutions, development management and reasonable exploitation of saline region is extremely important, because this is the most basic foundation for subsequent activities in the natural disaster management by the non-structural solutions. Development management and reasonable exploitation of saline region is demonstrated in the following main activities:

First, the management of socio-economic development in the coastal strip

that deals with saline intrusion must not have adverse and negative effects on the environment. This can be done by trying to comply with the natural rules of the world, including the use of embankments, sluices, fresh water transfer canals, pumping stations, and other environmentally-friendly methods; transportation works including roads, waterways, and ports; natural disaster prevention works including dikes; and coastal works since this is the most powerful impact to the saline process.

Second, there must be a reasonable and wise use of saline water sources and products from estuaries and coastal areas for aquaculture and special progress of estuarine biodiversity. Management of the catch and use of natural aquatic resources must also be there.

Third, allowable limits must be enforced on crops, livestock and plant frames (especially rice crops and varieties) as progressing towards drought and salinity intrusion resistant crops. For example, in areas where locals producing two fairly stable rice crops, if severe salinity intrusion occurs and there is not enough water, the locals can switch to plant vegetables. In areas where locals produce two precarious rice crops which are often threatened by salinity intrusion, locals can switch to planting one rice crop and one vegetable crop, or one rice crop and one shrimp crop. In the case of unfavorable conditions, it may transfer to only aquaculture. The coastal regions should closely monitor annual occurrences of salinity intrusion to reduce the area used for early Winter-Spring rice crop in order to avoid concentrated water requirements on January and February, making the saline boundary higher. Also, reducing the later Winter-Spring and early Summer-Autumn rice crops to limits using too much fresh water during the lowest flow duration of year, particularly from the end of March to beginning of May, and switching to vegetable crops. However, to avoid causing large disorder and affecting other rice production areas, locals need to carefully plan and consider the implementation of transference on a large scale, do not make individual households to do not affect around and the whole region.

Fourth, organizing the relief, restoration and execution of drought and salinity intrusion damage insurance which will help carriers to share losses, and enhance the community's education

about natural disasters. Risk awareness programs, including community education, information dissemination, and awareness in order to reach the highest level for the community capable of self can immediately response with natural disasters without much support and intervention from outside.

Fifth, propagandizing and informing the community about important activities regarding awareness of the risks of damages caused by drought and salinity intrusion. The strategies used for media activities should change to suit each specific audience. Setting up an information system, through which, the relevant and accurate information about the natural disaster prevention and mitigation for drought and salinity intrusion should be frequently propagated through the appropriate media channels.

Sixth, management activities of non-structural solutions must include contingency plans that consider loss and damages caused by drought and salinity intrusion.

Conclusions

The Mekong Delta plays an important role in the National Food Security Program on an international scale, especially to the population and economy of the coastal region of the Mekong Delta. Therefore, when faced with natural disasters gradually trending towards extremely values, "masterful flow security" is available as an important national strategy, and policy for the present and the future of Vietnam in general, and the Mekong Delta in particular. Continued study into solutions for storage, keeping and provides stable low flow, initiative control of salinity intrusion, and responding effectively with the impacts from climate changes, sea level rise, and upstream activities, are extremely important in the development process of the Mekong Delta.

REFERENCES

- [1] Reports and data of the Mekong River Commission and Southern Institute for Water Resources Planning.
- [2] All information sources on internet, reports of the Mekong Delta local authorities and Ministry of Agriculture and Rural Development.
- [3] Institute for Water Resources Planning (2012), *Water resources master planning under the context of climate changes and sea level rise in the Mekong Delta*.

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[2] T. Binzoni, T.S. Leung, D. Boggett, D.T. Delpy (2003), “Non-invasive laser Doppler perfusion measurements of large tissue volumes and human skeletal muscle blood RMS velocity”, *Phys. Med. Biol.*, **48(1)**, pp.2527-2549.

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