# 2011 Yonsei-Nagoya University

Research Exchange Meetings In Health Sciences & Nursing

2011. 11. 3. - 11. 5.







Yonsei University Wonju Campus Wonju, Republic of Korea

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Preface

As Dean of College of Health Sciences and on behalf of Yonsei University at Wonju, it

is with great pleasure that I extend my heartfelt welcome to the delegates from Nagoya

University who have travelled long distances to take part in this joint symposium. I believe

that this joint symposium will be a unique forum to exchange ideas, discuss matters of mutual

interest and concerns, and share experiences among professors and students between the

two universities. It is my hope that this symposium jointly held by the two institutions will be

a long lasting one. This symposium is only just the beginning of our joint efforts. We've just

taken a first step toward building a greater cooperation and I am very excited to see what we

will be able to produce and accomplish through this joint symposium.

I also hope that your visit to our campus will provide you with a great opportunity to get

to know Korea and the Korean people as well as experience Korean culture in a fragrant fall

atmosphere. Now is the best time to see the very best and most beautiful autumn foliage. Fall

weather is something to enjoy here in Korea. Please don't miss it! I once again welcome all of

you here and I believe that your visit to our campus has just opened a new chapter of bilateral

cooperation and partnership between the two institutions to closely work together in the

years to come.

Thank you.

Tae Ue Kim, PhD

Dean

College of Health Sciences Yonsei University

Professor

Department of Biomedical Laboratory Science

Yonsei University

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Welcoming remarks

I welcome all of you to our Yonsei University Wonju campus.

At the beginning of last year the University of Nagoya and the Yonsei University agreed on

a collaboration that would include our professors as well as our graduate students in research.

In October 2010, Nagoya University hosted the first research project, and now the time has

come that our school to host the second research seminar, and we look forward to this great

opportunity.

I believe that it is an especially meaningful experience for our students and professors to

participate in this kind of an exchange program.

I believe that the opportunity, we have in this program, to share the customs and cultures

of our two neighboring countries, will enable us to be better prepared to face the challenges

of future patient care as we come to understand patient care from the perspective of another

country.

Thank you for all of your dedicated work in preparation so that our exchange programs will

flourish. We hope that we will all gain valuable experience from this research seminar.

Finally, even though your stay in Korea will be very short, I hope that your time here is

enjoyable and comfortable.

I welcome you again to our university, and on behalf of Yonsei University Wonju College of

Medicine, I thank you.

Joo Young Park, M.D., Ph.D.

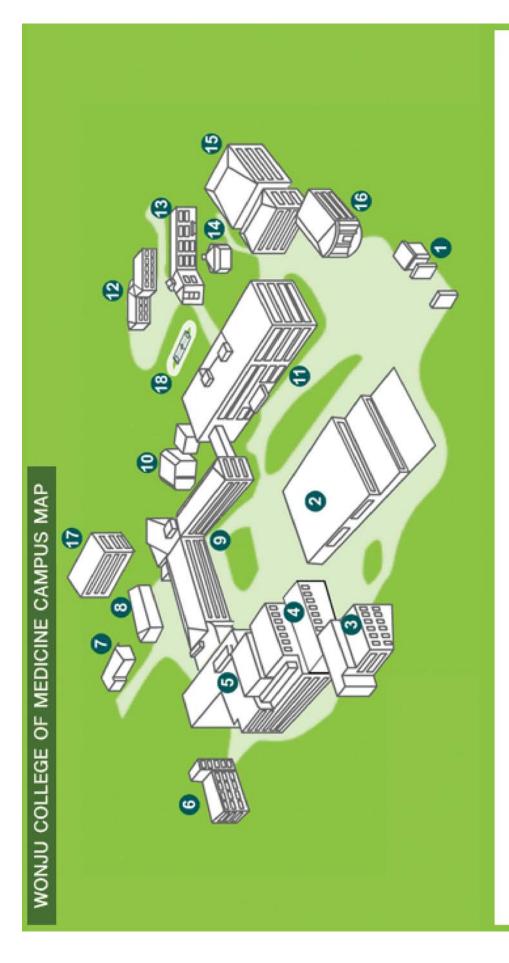
Dean

Yonsei University Wonju College of Medicine

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# Itinerary

Date	Time	Schedule	Other
	11:35 a.m.	Arrive at Incheon International Airport (KE752)	Greeted by Occupational Therapy Department/Bus provided.
	1:30 p.m.	Lunch at Deokpyeong Land	Korean food
	4 p.m.	Arrive at Inter-Burgo Hotel Wonju	Check-in $\sqrt{\text{Female students will check-in at}}$ Seyeon Dormitory following banquet
2011. 11. 3.	5:00 p.m	Leave for Yonsei University	
(Thursday)	5:00~5:40 p.m.	Brief Tour of University Campus / Check-in at Seyeon Women's Dormitory	Female students will check-in at Seyeon Women's Dormitory
	5:40~8:30 p.m.	Banquet	Banquet at Eco Little Theater, Student Union, Yonsei University
	8:30 p.m.	Move to Inter-Burgo Hote I/ Seyeon Women's Dormitory	
	8:00~9:30 a.m.	Breakfast and check-out at Inter-Burgo Hotel / Seyeon Dorminotry	Breakfast at Inter-Burgo Hotel or University Cafeteria for Female Students (Female Students Guided by Occupational Therapy Students)
	9:30 a.m.	Move to Conference Site	Yonsei University, Wonju Campus
	10~11 a.m.	Opening Ceremony	Marion E. Current Seminar Hall (Room 120) at Baekun Hall
	11 a.m.~1 p.m.	Departmental Presentations	Baekun Hall, Mirae Hall
2011. 11. 4. (Friday)	1~2 p.m.	Lunch	Hyonunjae, Yonsei University (Executive Committee Meeting in Room 103, Hyonunjae)
	2~5 p.m.	Departmental Presentations	Mirae Hall, Baekun Hall
	5~8 p.m.	Dinner	Arranged by each academic department
	8 p.m.	Depart for Seoul	Bus will depart in front of Medical Industry Techno Tower
	10 p.m.	Arrive at Grand Hilton Hotel	Check-in
	8:00~9:30 a.m.	Breakfast and check-out at Grand Hilton Hotel	
	9:30 a.m.	Move to Yonsei University Severance Hospital	Bus provided
2011. 11. 5. (Saturay)	10~11:30 a.m.	Tour of Severance Hospital	Meet in front of Information Desk on 3rdFloorofMainBuilding(BonKwan Building). 10 minutes of video and 50 minutes of hospital tour led by Ms. Jee-eun Ryu (010-5661-0124) and Ms. Sara Park (010-9920-3431)
	11:30 a.m.~ 4 p.m.	Lunch & Free time	Bus provided
	4 p.m.	Move to Incheon International Airport	Bus provided
	5:30 p.m.	Arrive at airport	Check-in
	7 p.m.	Leave for Nagoya	KE751



- 1 Main Gate
- 2 Husang-Gwan
- Regional Emergency Medical Center, Gastroenterology Center
  - 4 Health Promotion Center, Cancer Center
- 5 Judy Memorial hall (Clinic, Ward)
- 6 Dormitory(Nurse)

- Vocational Rehabilitation Center, Dormitory(Doctor)Worship room, Labor Union
- 9 Moon Chang Mo Memorial hall
- Compared to the compared to
- Euihak-Gwan (Main Building)
- Woneui-1-Haksa(Student Dormitory)

- (B) Woneui-2-Haksa(Student Dormitory)
- (4) Ilsan Historical Materials Pavilion(5) Jili-Gwan (Medical Library)
- 16 Luke Auditorium
  - T Funeral Hall
- (B) Playground



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4. 정의관 Jeongui Hall 5. 청송관 Cheorysong Hall 6. 청소관 Cheorysong Hall 7. 백운관 Baskun Hall 8. 미관관 Mirae Hall 9. 중앙도사관 Main Library 10. 학생회관 Student Union

### Organizing committee

신태민 (Tae Min Shin) Professor Department of Biomedical Engineering

신윤희 (Yun Hee Shin) Professor Department of Nursing

조효성 (Hyo Sung Cho) Professor Department of Radiological Science

한봉수 (Bong Soo Han) Professor Department of Radiological Science

유승현 (Sung Hyun You) Professor Department of Physical Therapy

박수현 (Soo Hyun Park) Assistant Professor Department of Occupational Therapy

이기종 (Ki-Jong Rhee) Assistant Professor Department of Biomedical Laboratory Science

### **Sponsors**

College of Health Sciences Yonsei University

Institute of Health Science Yonsei University

Yonsei University Wonju College of Medicine

Industry-Academic Cooperation Foundation (IACF), Yonsei University Wonju Campus

# Abstracts **Nursing**

## INVESTIGATION OF CRITERIA FOR OBESITY BASED ON INSULIN RESISTANCE IN JAPANESE COLLEGE ATHLETES

K. Aoishi, H. Sakakibara

Department of Nursing, Nagoya University Graduate School of Medicine

#### Introduction

Obesity is a morbid condition characterized by glucose intolerance, impaired lipid metabolism, and high blood pressure because of the accumulation of visceral fat or adipocyte abnormalities <sup>[1]</sup>. In Japan, obesity is defined as a BMI of  $\geq$ 25.0 kg/m² <sup>[2]</sup>. Waist circumstance (WC) is also included in the criteria for metabolic syndrome, and is  $\geq$ 85 cm for Japanese men <sup>[3]</sup>.

However, criteria for obesity in athletes are widely debated. Athletes with a high BMI may be healthy and not obese because they follow healthy lifestyles with regular physical activity. Meanwhile, in other studies that examined blood biochemistry in addition to BMI and body fat, obesity in athletes was associated with a high incidence of metabolic syndrome and cardiovascular disease [4-6]. But there is no published research that has included blood biochemical parameters that can indicate the presence of insulin resistance or glucose intolerance for young athletes.

Therefore, in this study, we investigated possible criteria for obesity in Japanese college student athletes by examining insulin resistance in athletes and non-athletes.

#### Methods

Design and sample: The present subjects were approximately 600 male students of the fourth grader from the first grader of a university in Aichi prefecture, Japan, to whom the purpose of this study was explained. Of these, 219 volunteered to participate in the study, including 119 athletes belonging to a sports team (mean age  $20.3 \pm 1.2$  years) and 100 who did not (non-athletes, mean age  $20.5 \pm 1.3$  years).

Measurements: The subjects were examined at an annual heath examination performed at the university. Information collected for each student included height, body weight, WC, blood glucose, HbA1c, insulin, personal and family health history, and nature and duration of physical activities on varsity and non-varsity sports teams. BMI was calculated as body weight (kg)/height (m)². Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as fasting blood glucose level (mg/dl) × fasting blood insulin level (μU/ml)/405.

*Data analysis:* BMI was classified into four groups in this study: <25.0,  $\ge25.0$  to <27.0,  $\ge27.0$  to <30.0 and  $\ge30.0$  kg/m<sup>2</sup>. WC was classified into four groups in this study: <85,  $\ge85$  to <90 and  $\ge90$  cm.

Data are presented as mean and standard deviation. Body composition and blood chemistry data were assessed using Student's t test with BMI <25.0 kg/m2 or WC <85 cm as a control, followed by Bonferroni correction for comparisons reaching statistical significance. The percentage of subjects with abnormal values was compared using  $\chi^2$  analysis. For all tests, the level of statistical significance was <0.05.

#### Results

Blood biochemistry data, including glucose profiles, according to each BMI group are shown in Table 1. Among non-athletes, the insulin level was significantly higher among the BMI  $\geq$ 25.0 to <27.0 kg/m² group (p < 0.01) and the BMI  $\geq$ 30.0 kg/m² group (p < 0.01) and non-significantly higher in the BMI  $\geq$ 27.0 to <30.0 kg/m² group compared with the BMI <25 kg/m² group. Similarly, HOMA-IR was significantly higher in BMI  $\geq$ 25.0 to

 $<27.0 \text{ kg/m}^2$  group (p < 0.05) and the BMI ≥30.0 kg/m² group (p < 0.05).

Among the athletes, the insulin level tended to be higher in the BMI  $\geq$ 27.0 to <30.0 kg/m² group (p < 0.10) compared with the BMI <25 kg/m² group and HOMA-IR was significantly higher in the BMI  $\geq$ 27.0 to <30.0 kg/m² group (p < 0.05). Fasting insulin and HOMA-IR were greater, although not significantly, in the BMI  $\geq$ 30.0 kg/m² group than in the BMI <25 kg/m² group.

The percentages of subjects with abnormal values are also shown in Table 1. The prevalence of HOMA-IR  $\geq\!\!2.5$  increased with increasing BMI and tended to be greater among non-athletes group than among athletes. About half (46%) of the non-athletes and 33% of athletes with BMI  $\geq\!\!30.0$  kg/m² had HOMA-IR  $\geq\!\!2.5$ .

As shown in Table 2, neither fasting blood glucose nor HbA1c increased with increasing WC. By contrast, fasting insulin was significantly higher in subjects with WC  $\geq$ 90 cm comparison with subjects with WC <85 cm in athletes (p < 0.01) and non-athletes (p < 0.001). HOMA-IR was also significantly higher in subjects with WC  $\geq$ 90 cm in both groups (p < 0.01). Among non-athletes, HOMA-IR value was also higher in subjects with WC of  $\geq$ 85 to <90 cm (p < 0.05).

Abnormal fasting insulin and HOMA-IR values were seen in athletes with WC  $\geq$ 90 cm. By contrast, among non-athletes, abnormal insulin and HOMA-IR values were found in subjects with WC of  $\geq$ 85 to <90 cm and in those with WC <85 cm. Elevated HOMA-IR was seen in 31% of non-athletes and 26% of athletes with WC  $\geq$ 90 cm.

#### Discussion

In the present study, none of the college student subjects was suspected of having diabetes mellitus based on fasting blood glucose and HbA1c, but elevated HOMA-IR ( $\geq 2.5$ ) corresponding to insulin resistance was seen in about 7% of the subjects. Most of the non-athletes with elevated HOMA-IR had BMI  $\geq 25.0~kg/m^2$  and WC  $\geq 85~cm$ , and almost all of the athletes with elevated HOMA-IR had BMI  $\geq 27.0~kg/m^2$  and WC  $\geq 90~cm$ . These findings in Japanese college students indicate that athletes are at risk for insulin resistance when BMI exceeds 27.0 kg/m² and WC exceeds 90 cm, or that obese athletes may have impaired glucose tolerance. For non-athletic students, their risk of insulin resistance is greater at BMI  $\geq 25.0~kg/m^2$  and WC  $\geq 85~cm$ .

In the present study, athletes were more insulin sensitive than non-athletes at the same BMI and WC, which could reflect the effects of regular physical activity on insulin resistance. However, when BMI exceeds 27.0 kg/m² and WC exceeds 90 cm, athletes are more likely to be at risk of insulin resistance.

Another study has suggested BMI  $\geq$ 27.9 kg/m<sup>2</sup> for athletes ( $\geq$ 34.1 kg/m<sup>2</sup> for American football players) and  $\geq$ 26.5 kg/m<sup>2</sup> for non-athletes <sup>[7]</sup>. Their proposal was based on the optimum BMI in terms of body fat in US individuals. The present criteria for Japanese college athletes were based on HOMA-IR or insulin resistance. Considering the criteria in our study, the sensitivity and specificity were calculated to be nearly 100% (or, more precisely, 80%) and 93.0% for athletes, and 90% and 70% for non-athletes, respectively.

Because the present study population was young and

healthy, the number of subjects with insulin resistance was insufficient to establish criteria for obesity based on BMI and WC. Further studies are needed by examining a larger number of subjects.

This manuscript has been published in the Obesity Research & Clinical Practice  $^{[8]}$ .

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#### Author address

E-mail: keiko\_ao@xa2.so-net.ne.jp

Table 1. Blood biochemical parameters and percentage of subjects with abnormal values according to categories of BMI

	BMI (kg/m <sup>2</sup> )	< 25.0	$\geq$ 25.0 to $<$ 27.0	$\geq$ 27.0 to < 30.0	≥ 30.0
	Athletes/non-athletes (n)	71/61	24/19	18/7	6/13
Fasting blood glucose	Athletes	$88.4 \pm 6.0$	$85.3 \pm 7.2$	$89.1 \pm 6.5$	$86.0 \pm 4.1$
(mg/dl)	Non-athletes	$90.1 \pm 6.8$	$86.5 \pm 7.7$	$85.4 \pm 6.6$	$90.1 \pm 6.8$
III- A 1 - (0/)	Athletes	$5.3\pm0.3$	$5.3\pm0.3$	$5.2\pm0.2$	$5.2\pm0.2$
HbA1c (%)	Non-athletes	$5.3 \pm 0.3$	$5.2\pm0.3$	$5.5\pm0.3$	$5.4 \pm 0.4$
F	Athletes	$3.7\pm1.5$	$4.7\pm3.2$	$6.4 \pm 4.1^{\dagger}$	$7.7 \pm 3.9$
Fasting insulin (μU/ml)	Non-athletes	$4.3\pm2.1$	$6.3 \pm 3.2**$	$8.2\pm3.7^{\dagger}$	$11.2 \pm 6.6**$
T10161 TD	Athletes	$0.8 \pm 0.3$	$1.0 \pm 0.7$	$1.4\pm0.9 *$	$1.7\pm0.9$
HOMA-IR	Non-athletes	$1.0\pm0.5$	$1.4\pm0.7\textcolor{white}{*}$	$1.8\pm0.9$	$2.5 \pm 1.6*$
Fasting blood glucose ≥ 110	Athletes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
mg/dl	Non-athletes	0(0.0)	0(0.0)	0(0.0)	0 (0.0)
$HbA1c \geq 5.9\%$	Athletes	0(0.0)	0 (0.0)	0 (0.0)	0(0.0)
H0A1C ≥ 3.9%	Non-athletes	1 (1.6)	0(0.0)	1 (14.3)	2 (15.4)
Fasting insulin $\geq 15.0~\mu U/ml$	Athletes	0(0.0)	0(0.0)	1 (5.6)	0(0.0)
	Non-athletes	0(0.0)	1 (5.3)	0 (0.0)	2 (15.4)
$HOMA-IR \ge 2.5$	Athletes	0(0.0)	1 (4.2)	2 (11.1)	2 (33.3)
помА-IR ≥ 2.3	Non-athletes	1 (1.6)	1 (5.3)	2 (28.6)	6 (46.2)

Note: values are means  $\pm$  standard deviation or n (%);  $^{\dagger}p < 0.10$ ,  $^{*}p < 0.05$ ,  $^{**}p < 0.01$  vs. BMI < 25 kg/m² (t test) Abbreviations: BMI, body mass index; HbA1c, hemoglobin A1c; HOMA-IR, homeostasis model assessment of insulin resistance.

Table 2. Blood biochemical parameters and percentage of subjects with abnormal values according to categories of WC

•	1 5		0 0	
	WC (cm)	< 85	≥ 85 to <90	≥ 90
	Athletes/non-athletes (n)	85/62	15/12	19/26
Easting blood always (mg/dl)	Athletes	$87.6 \pm 6.2$	$88.8 \pm 9.0$	$87.6 \pm 4.5$
Fasting blood glucose (mg/dl)	Non-athletes	$90.4 \pm 6.6$	$86.5 \pm 7.2$	$87.2 \pm 7.7$
III- A 1 - (0/)	Athletes	$5.3\pm0.3$	$5.2\pm0.2$	$5.3 \pm 0.3$
HbA1c (%)	Non-athletes	$5.3\pm0.3$	$5.2\pm0.3$	$5.4 \pm 0.4$
	Athletes	$3.8 \pm 1.9$	$4.8\pm1.8$	$7.6 \pm 4.4**$
Fasting insulin (μU/ml)	Non-athletes	$4.4\pm2.2$	$6.9 \pm 3.8^{\dagger}$	$8.9 \pm 5.6***$
HOMA-IR	Athletes	$0.8 \pm 0.4$	$1.0\pm0.4$	$1.7 \pm 1.0**$
	Non-athletes	$1.0\pm0.5$	$1.5\pm0.8*$	$2.0 \pm 1.4**$
Fasting blood glucose ≥ 110	Athletes	0 (0.0)	0 (0.0)	0 (0.0)
mg/dl	Non-athletes	0 (0.0)	0 (0.0)	0 (0.0)
HbA1c ≥ 5.9%	Athletes	0 (0.0)	0 (0.0)	0 (0.0)
$H0A10 \ge 3.9\%$	Non-athletes	1 (1.6)	0 (0.0)	3 (11.5)
E	Athletes	0 (0.0)	0 (0.0)	1 (5.3)
Fasting insulin $\geq 15.0 \mu U/ml$	Non-athletes	0 (0.0)	1 (8.3)	2 (7.7)
HOMA ID > 2.5	Athletes	0 (0.0)	0 (0.0)	5 (26.3)
$HOMA-IR \ge 2.5$	Non-athletes	1 (1.6)	1 (8.3)	8 (30.8)

Note: values are means  $\pm$ standard deviation or n (%);  $^{\dagger}p < 0.10$ ,  $^{*}p < 0.05$ ,  $^{**}p < 0.01$ ,  $^{**}p < 0.01$  vs. WC < 85 cm ( $^{t}$  test) Abbreviations: WC, waist circumference; HbA1c, hemoglobin A1c; HOMA-IR, homeostasis model assessment of insulin resistance.

#### FAMILY HEALTH MAINTENANCE IN A JAPANESE FAMILY WITH AN AUTISTIC TWIN

A. Furuzawa<sup>1)</sup>, M.Asano<sup>2)</sup>

- 1) Department of Nursing, Graduate School of Medicine, Nagoya University Nagoya, Japan
  - 2) Department of Nursing, School of Health Sciences, Nagoya University Nagoya, Japan

#### Introduction

Raising children with autism greatly impacts family functioning. In particular, mothers of adolescents with autism may experience feelings of anger towards their children that stems from continually having to care for them [1]. These mothers may also feel all-consumed by caring for their child, thus making intervention necessary. Friedman[2] considered the health care function to be particularly important. She suggests that this function can be examined by observing family health habits; specifically, it can be determined by observation at the level a nurse can provide. Furthermore, she states that family beliefs are important in promoting family health behavior and that they affect family functioning.

This study examined the chronological process of family health maintenance based on the case of a single family, which showed unique relationships between family health habits, health issues, and beliefs.

#### Methods

Research design: We chose the case study method because it is well suited to understanding a family case in all its depth and complexity and in its natural milieu, with a focus on relations and processes. Intensity sampling: A trusting relationship between the interviewer and family is crucial when selecting a family given the depth and frequency of the interviews. The family was chosen after much consideration. Data collection: The authors explained the purpose of the study to the family and the support group in both oral and written formats. They then contacted the family to arrange an interview and explained both the purpose of the study and ethical considerations. The interviewer conducted interviews during three visits to the family's home as well as during phone conversations between August 2009 and January 2010. We initially planned a visit once a month, but this was adjusted according to the family's situation. The interview content came from the "Interview Guide for Maintaining Family Health," but the interviews began with broad openended questions concerning, for example, the daily practices of the family related to family health, the respondent's thoughts on the health he or she desired for the family, and any beliefs he or she had related to health. Participants were allowed to determine the direction of the conversations and recall personal episodes during the interviews. Interviewer: The first author conducted the interview. Data analysis: We extracted and analyzed themes by looking at episodes related to (1) health issues, (2) health habits, (3) and beliefs.

#### **Ethical considerations**

This study was approved by the Ethics Committee of our institution (Approval number: 7-170). We informed the participants that they had the freedom to agree or decline to participate, data would be anonymous and stored securely, and that confidentiality would be maintained. We obtained consent from each family member for the interviews. Names of family members were changed to protect their identity.

#### Results

Family profile

The father of the family works as an official. The mother is a homemaker who developed depression while raising the children. Taro and Ken are 18-year-old twins, and Taro has autism.

Narratives of the three interview sessions with family members

The interviews were held in the family's living room. The mother did most of the talking, and the father mainly observed and nodded in agreement. The twins listened nearby and did not say much. The interview atmosphere was characterized by occasional laughter. There were three sessions, with an average session time of 63 minutes. The interviews began with the mother talking about the family's perception of the autistic twin's fixations. The mother explained that many of his behaviors were incomprehensible to her and she could not discern that they were part of his personality. Hospitalization of the non-autistic sibling for asthma led to poor psychological health in the mother, who subsequently suffered from depression. After the onset of depression, she became unable to prepare meals and carry out household chores. Prior to this, she had striven for perfection in the health habits of her family, but her own health problems prevented her from maintaining these habits. Of all the health habits, the mother spoke specifically of being unable to maintain the healthy eating habits of her family. She somehow managed to prepare meals while the children were still in pre-school, but her depressive state worsened once the children entered elementary school. She was unable to prepare meals for the family, even late in the evening. She did not cook rice and, before long, insects began to appear in the house. At that point, the father started purchasing pre-made meals to maintain the family's diet. However, his busy work schedule prevented him from sufficiently sharing daily household duties during the week. The mother and father both felt that the twins should go to the same elementary school. Unlike the situation at pre-school, the family now had no outward support, making dropping off and picking up the children a burden. The comments made by the children's teacher were painful for the mother to hear, perhaps because the teacher did not understand much about children with autism. During this time, the mother was hospitalized for a ligament injury, which resulted in the autistic child being sent to temporarily live at a facility.

At present, the twins are high school students, and the non-autistic sibling is preparing for college entrance examinations. There has been no change in the psychological state of the mother. Her sleep is shallow, and she is unable to escape the feeling that time is pressing upon her as she dreams. She is generally unable to prepare meals and carry out household chores. The father said that he once felt his wife was "lazy," but with a better understanding of her illness, he started to prepare meals. Seeing their father do this, the twins have begun to help

as well. There has been an observable change in how the family perceives their diet.

Turning points in the health maintenance of the family

The mother and interviewer charted the course of the family's health maintenance process from the twins' infancy to the present. Changes were observed, revealing the following prominent turning points in the health maintenance process: (1) the mother realized that her psychological health was at its worst during the twins' infancy, (2) The stage at which the mother strongly feels the presence of the family, and realizes that they must do everything possible to support one another, (3) the family began to take action in anticipation of the future during the twins' adolescence. These turning points occurred in the children at each developmental stage.

### Infancy stage: The mother realized that her psychological health was at its worst

We identified two themes associated with the mother's realization that her psychological health was at its worst during the twins' infancy: "Confusion about understanding a child with autism" "The mother sensed an abnormality in her condition that led to changes in family health habits"

#### Childhood stage: The stage at which the mother strongly feels the presence of the family, and realizes that they must do everything possible to support one another.

We found three themes from this stage: "The mother's depression influenced the family's health habits and psychological state" "Changes in the father's behavior led to changes in the twins' behavior" "A lack of understanding about raising children with autism by the general public (neighbors, school staff)"

### Adolescent stage: The stage at which the mother thinks about the child's future after the parents' death.

Themes identified from this turning point were: "Feelings of appreciation displayed among family members" "Thoughts on the independence of the children, affirmation of family beliefs, and the future of the family"

#### Discussion

This study focused on health issues, habits, and beliefs of a family with adolescent twins, one with autism. Turning points in the family's health maintenance were derived by examining the process temporally. Findings from the themes identified in these turning points are discussed below.

- 1. The child's health problems, such as one that results in hospitalization, places a great burden on the mother. These problems greatly affected the mother's health status and her ability to carry out household chores, ultimately influencing the family's health habits. If we were to surmise why this situation arose, it would likely be that the mother had already reached the limits of her ability to raise a child with autism. Furthermore, Ken's hospitalization pushed the mother beyond her limits, and she was thus unable to cope with the situation. The mother's plight was manifest in her inability to do housework.
- 2. Families with autistic children have trouble obtaining understanding from schools and others, starting from elementary school. The preschool had brought children from home to school in a bus, but when the children entered

elementary school, it became necessary to take the children to school by hand. This might appear at first to be no major challenge, but for a mother of an autistic child, it presents a very difficult situation. The mother was hurt by the school's inability to understand autistic children, and was unable to receive appropriate support from the school. Given these circumstances, mutual understanding among family members created positive changes in health habits, habits that are not easily reversed. This type of growth among family members is linked to thoughts on the future of the family.

3. In this study, the researcher visited the home of a family with an autistic child and conducted family interviews. The observations at the home allowed the researcher to understand that the family is working to maintain their day-to-day life to the best of their ability, and that a reversal of health habits that have undergone change is difficult. Furthermore, the family's efforts to maintain health habits were evident not merely in their words, but in the home environment as well.

In this sense, home nursing assistance can promote changes and is likely to become more necessary in the future. In order for this to occur, a major step will be to increase nurses' awareness of the importance of home visits. This, in turn, should lead to studies that promote family assistance skills among nurses.

#### Conclusion

Effective interventions by nursing professionals are regarded as important for the health care function of families. In particular, attention should be paid to the family's health habits. However, this family's health habits interacted with the mother's health issues, and changes that occurred in these habits became fixed and still remain. Although these are not ideal habits, bringing about a reversal of changes is difficult. However, both the parents and the adolescent children are thinking about the future and making preparations accordingly. In light of the actions of the family in anticipation of the future, it is important for family members to seek out and express both their family and personal beliefs.

#### **Strengths and Limitations**

A weakness of this case study is that it may not be representative of most cases of families in a similar situation. To better understand healthcare functions through family health issues, we selected a special family case in which one of the twins has autism, which although limiting the generalizability of the findings, did enable the family's experiences of the healthcare function to be explored.

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#### **Author address**

E-Mail: furuzawa.ayako@h.mbox.nagoya-u.ac.jp

# CARING FOR MOTHERS OF CHILDREN WITH AUTISTIC SPECTRUM -EFFECTS OF THE SKIP-MAMMA PROGRAM-

K.Niinomi<sup>1)</sup>, M.Asano<sup>1)</sup>, K.Yoshida<sup>1)</sup>, A.Kadoma<sup>4)</sup>, Y.Ohashi<sup>2,3)</sup>, A.Furuzawa<sup>2,5)</sup>, M.Yamamoto<sup>2)</sup>, A.Mori<sup>2)</sup>

- 1) Department of Nursing, School of Health Sciences, Nagoya University, Aichi, Japan 2) Graduate School of Medicine, Nagoya University, Aichi, Japan
- 3) Department of Nursing, College of Life and Health Sciences, Chubu University, Aichi, Japan 4) School of Nursing, Nagoya City University, Aichi, Japan
  - 5) Department of Nursing, Nagoya University School of Medicine, Aichi, Japan

#### Introduction

Recently, the number of children with autistic spectrum disorders (ASD) has been increasing. These children show unique behavior and ways of communication, therefore families often face difficulties in parenting. Improvement in a family's QOL cannot be achieved, when such families are not offered enough support to help reduce their anxiety and stress and to develop skills required for raising these children.

#### Aim

The purpose of this study was to examine the effects, mostly in QOL, of the Skip-Mamma program for mothers of children with ASD.

#### Methods

An intervention study was conducted. The Skip-Mamma program was designed to promote a mother's life-skills for childrearing and to refresh and heal her mind and body. Interventional effects were assessed using World Health Organization QOL-26 (QOL-26), Parenting Stress Index-Short Form (PSI-SF) and Family Assessment Inventory (FAI) at 3 time points during the program as follows: before the first session, at 3 months into the program, and after the program ended (6 months). Data were analysed by the Wilcoxon test using SPSS 13.0J software.

#### About The Skip-Mamma Program

Purpose of the Program: To improve the QOL of families who are raising a child with ASD, through promoting the parents life skills for childrearing, refreshing and healing their mind and body and identifying the family strength and functions.

Participants of the Program: Mothers of children older than 18 months who have or may have ASD. The program is conducted in a small group session, each including 4 to 8 participants.

Staff Background: Nurses (Including Public Health Nurses and Midwife).

*Idea of the Program*: Provide an Approach for Increasing Strength / Promote Self Care / Family System Approach / Promote Communication / Suffer-Solutions / Collaborate.

Outline of the Program (Figure 1): The program comprise 6 sessions, 1 conducted every month. Each session is for approximately 2 hours. Each session starts with a "warm-up" exercise with a balancing ball and mini-lessons are given each time with a different theme. The session is conducted either with a "relaxation" exercise performed with balancing ball or an aroma massage. Finally, a closing ceremony is held

in which certificates are awarded to all the participants. In the first half of the program, participants were given an opportunity to observe and learn about themselves, their children, and their families. In the latter half of the program, participants are given a chance to express what they consider an ideal family to be by learning about diversity through sessions and help from peers.

1st	2nd	3rd	4th	5th	6th	
		ara .	4th	501	otn	
15min Warming Up						
1st Survey Questionnaires	Balancing Ball	Balancing Ball	2nd Survey Questionnaires	Balancing Ball	Balancing Ball	
30min Mini-Lesso	on			'	Discussion	
ICE BREAKING Friend Searching BINGO! for Self Introduction	Barrier-Free for Children With ASD	"I'm OK, You're OK" Knowing About Self Basic Posture	"Small Box for Healing Oneself"	lesson for Peer Support 'Paper Plane ver."	Looking Back about Changing in Child-Rearing & Family	
15min Tea Break	Herb Teatime				Tea Party	
45min Work Shop						
Brain Storming What is Your	Discussion Family Values	Discussion Child Behavior	Discussion Daily Life of	Discussion Daily Life of		
Distress?			Parents	Family	Aroma Massage	
15min Relaxation					Ceremony	
Balancing Ball	Aroma	Aroma	Aroma	Aroma		
	Massage (hand)	Massage (hand)	Massage (foot)	Massage (foot)	3rd Survey Questionnaires	

Figure 1 Outline of Skip-Mamma Program

#### **Ethical Considerations**

The study was approved by the Nagoya University Ethics Committee.

#### **Results and Discussion**

The participants in this survey include 25 mothers  $\{39.4\pm4.3\ (Mean\pm SD)\ \text{years old}\}\$ from 5 session groups who completed the program and of 27 children  $\{83.2\pm33.6,\ 42\text{-}150\ (Mean\pm SD,\ Range)\$ months old $\}$  with ASD. There is a mild positive transition for every questionnaire, but there is no significant change (Table 1).

 Table 1
 Score Change 3 points in total process of the Skip

Mamma program			$N=27$ , Mean $\pm 3$	SD
	Before the	3 months into	after the	
	1st session	the program	program ended	p
QOL-26	$79.6 \pm 8.1$	$77.6 \pm 9.6$	$81.4 \pm 10.5$	ns
PSI-SF	$51.8 \pm 8.6$	$50.6 \pm 8.4$	$49.2 \pm 7.0$	ns
FAI	$115.8 \pm 13.5$	$116.0 \pm 14.6$	$117.8 \pm 20.0$	ns

Wilcoxon test

QOL-26: WHO QOL-26, PSI-SF: Parenting Stress Inventory-Short Form, FAI: Family Assessment Inventory

Next, detailed changes in QOL-26 were individually analyzed and three patterns were identified. There were classified into the QOL rising pattern group, descending pattern group or V-shaped pattern group. Most participants (n=15 / N=27) were classified into the QOL rising pattern group (Figure 2). This

increase in QOL through the program sessions observed in majority of the participants reflects the positive effect of the program.

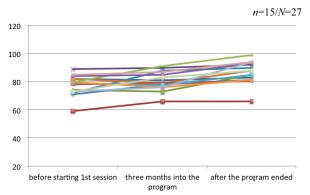
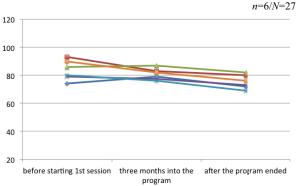


Figure 2 QOL-26 scores in each period of the Skip-Mamma Program [The QOL Rising Pattern]



**Figure3** QOL-26 scores in each period of the Skip-Mamma Program [The QOL Descending Pattern]

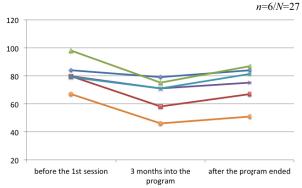


Figure4 QOL-26 scores in each period of the Skip-Mamma Program [The QOL V-Shaped Pattern]

We paid attention to the backgrounds of participants who showed the QOL descending pattern (n=6) and made observations as follow (Figure 3). In the descending group, there were participants who troubled by some physical symptoms or illnesses, and in one family, many of the members were in a poor condition. Every year in Japan, the months of March through April see events such as graduation, the first day of school, or promotions; such times are stressful for children with ASD, and their families are well aware of this majority of the families who participated in the program held during these months were classified in this descending pattern group. 6 participants were classified into the V-shaped pattern group (Figure 4). Before the program started,

a participant later classified under this pattern said "These days, I'm deeply depressed." and another said "Though I feel that I want to escape from reality, I got a chance to try and look after myself." As previously mentioned in the outline of the Skip-Mamma program, a part of the session in the first half of the program are composed of lessons and workshops that will help participants' observe and learn about their own mental state, and characteristics or problems of their family members. On the other hand, the latter half of the program is designed to promote a deeper understanding of what participants consider an ideal family to be by understanding group dynamics and taking help from peers. We found that the participants' increased understanding of themselves and their family is an important aspect, and the V-shaped pattern was expected to come out beforehand to be taken. For participants who completed the program, we held regular follow-up sessions to determine whether their QOL remained the same or showed improvement. We call this follow-up session a "Skip-Salon", and this salon started from request and hope by participants who complete the Skip-Mamma program.

#### Conclusion

The results suggest that the Skip-Mamma program is useful to the well-being of many mothers', and also pay attention to an individual's and family background as it is important for providing better care.

This work was support by Grant-in Aid for Scientific Research (C) (21592801).

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#### Author address

E-Mail: niinomi@met.nagoya-u.ac.jp

# CHANGES IN MENTAL STATUS FOLLOWING GASTROINTESTINAL SURGERY AND THEIR RELATIONSHIP WITH ADVERSE BEHAVIORS

S. Yamada<sup>1)</sup>

1) Department of Nursing, Graduate School of Medicine, Nagoya University, Nagoya, Japan

#### Introduction

More and more elderly and comorbid patients undergo surgical treatments in accordance with the advancement of medical technology. Changes in mental status are prevalent in such patients because the changes are enhanced by pulmonary and/or cardiovascular comorbidity, visual and/or hearing impairment, and nutrition status [1]. Altered mental status often leads to adverse behaviors such as pulling at tubes and falling from the bed. It is difficult to secure safety or comfort of those patients, and the patients' postsurgical recoveries are impeded. It is important to understand temporal pattern of mental alteration in order to prevent adverse behaviors.

The purpose of this study was to examine the relationship between mental status and adverse behaviors in patients after gastrointestinal surgery.

#### Methods

The subjects were patients of 65 years or older without dementia and/or psychosis who underwent gastrointestinal surgery. The data were collected from June to September 2005

Demographic data, primary diagnosis, type of surgery, and length of anesthesia were collected from hospital charts. Mental status was assessed using the Delirium Observation Screening Scale (DOSS) developed by Marieke [2]. It is a 25 item 4 point Likert type scale consisting of 8 subscales : [Consciousness] (3items), [Attention/concentration] (3items), [Thinking] (5items), [Memory/orientation] (3items), [Psychomotor activity] (4items), [Sleep/wake cycle] (3items), [Mood] (2items), and [Perception] (2items). Higher score indicates worse mental status. Adverse behavior was assessed for presence or absence of predetermined 13 behaviors including "Takes off oxygen mask" "Moves without caring of lines" "Moves restlessly" and "Suddenly gets up".

Data were collected at 6 points: preoperative period (stage I), immediately after surgery (stage II), night on the day of surgery (stage III), the next morning (stage IV), the afternoon (stage V), and the night of the day after surgery (stage VI).

Changes in mental status in the stages were determined using one-way repeated measures ANOVA, and the Dunnett test was employed for multiple comparisons. Student T-test was used to compare subscale scores of DOSS between the presence and absence of adverse behaviors at each stage. All values were two-tailed. A p<0.05 was considered statistically significant. Data were analyzed using SPSS 13.0J for Windows.

The Institutional Review Board approved the study and informed consent was obtained from the patients. When the subjects complained physical or mental fatigue due to the study, the data collection was discontinued.

#### Results

Twelve patients (4 males, 8 females) with age of  $71.3\pm5.8$  (mean  $\pm$  SD) years participated. Primary diagnosis of all subjects was colorectal carcinoma. Length of general anesthesia was 290.3  $\pm89.3$  minutes and mean blood loss was  $488.9 \pm 83.7$  ml. Sigmoid colotomy and low anterior resection were performed for four patients (33.3%) respectively, right side colotomy was for three (25%), and Miles' operation was for one (8.3%).

Changes in DOSS score are shown in Table 1. Postoperative data ware compared with stage I. Subscale scores except [Perception] were significantly higher than preoperative period in at least one stage. Subscales [Psychomotor activity], [Sleep/wake cycle] and [Mood] were significantly higher in all postoperative stages than preoperative period. High scores were found in items "Is sleepy/drowsy during the day" of [Sleep/wake cycle] and "Is apathetic/weary" of [Mood]. Postoperative [Attention/concentration] scores were significantly higher except stage V than preoperative period.

Adverse behaviors were observed in 4 patients (33.3%) of over seventy years old. Three patients exhibited such behaviors on stage III and one did on stage VI. Observed adverse behaviors were "Pulls at gastric tube", "Suddenly gets up", "Takes off oxygen mask" and " Moves restlessly". The DOSS scores were compared between subjects with adverse behaviors and without adverse behaviors. Significantly higher scores of DOSS were found in [Attention/concentration] on stage IV and V, [Thinking] from stage IV to VI, [Memory/orientation] from stage III to VI, and [Perception] on stage II and III in subjects with adverse behaviors (Table 2). Among those subscales, the item "Knows which part of the day it is" of [Memory/orientation] was the highest followed by "Is easily distracted stimuli from the environment" [Attention/concentration] and "Thinks to be somewhere else in" of [Memory/orientation].

#### Discussion

Postoperative changes in mental status were characterized by altered psychomotor activity, sleep-wake cycle, attention/concentration, and mood. Altered mental status sustained the next day of surgery. They were sleepy or drowsy during the daytime and fatigued. However, early ambulation is strongly recommended for postsurgical recovery [3]. It is necessary to incorporate rest as well as activities during the daytime.

The adverse behaviors were observed on the night of the surgery and the following day in this study. Although postoperative delirium has been thought to appear a few days after surgery [4], it is recommended to employ preventive measure from right after surgery. Adverse behaviors were concomitant to changes in perception, memory/orientation, attention/concentration, and thinking pattern. Use of psychometric scale may facilitate early recognition of changes in mental status.

#### Conclusions

In the current study, high scores in subscales [Psychomotor

activity], [Sleep-wake cycle], and [Mood] were sustained throughout the postoperative period. Adverse behaviors were observed in 4 patients (33.3%) aged 70 or over who exhibited significantly high scores for [Attention/concentration], [thinking], [Memory/orientation] and [Perception].

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#### **Author address**

E-Mail: shohkoy@yamanashi.ac.jp

Table 11. Changes in DOSS score before and after surgery						n=12	
Point of time	stage I	stage II	stage III	stage IV	stage V	stagVI	
subscales			Mean	± SD			
Consciousness	$1.0 \pm 0.1$	$2.1 \pm 0.7$	2.0±0.5	1.2±0.2	$1.2 \pm 0.4$	$1.1 \pm 0.4$	
Attention/concentration	$1.1 \pm 0.3$	$2.4 \pm 1.0$	$2.2 \pm 1.0$	$1.2 \pm 0.3$	$1.4 \pm 0.4$	$1.4 \pm 0.4$	
Thinking	$1.0 \pm 0.1$	$1.8 \pm 0.7$	$1.5 \pm 0.7$	$1.1 \pm 0.1$	$1.1 \pm 0.1$	$1.1\pm0.1$	
Memory/orientation	$1.0 \pm 0.0$	$2.7 \pm 1.0$	$2.3 \pm 1.1$	$1.5 \pm 0.7$	$1.2 \pm 0.5$	$1.4 \pm 0.7$	
Psychomotor activity	$1.0 \pm 0.1$	$1.7 \pm 0.4$	$1.5 \pm 0.3$	$1.3 \pm 0.3$	$1.2 \pm 0.3$	$1.3 \pm 0.3$	
Sleep/wake cycle	$1.0 \pm 0.0$	$2.0\pm0.2$	$1.9 \pm 0.3$	$1.6 \pm 0.4$	$1.7 \pm 0.5$	$1.6 \pm 0.6$	
Mood	$1.3 \pm 0.3$	$2.5 \pm 0.1$	$2.5 \pm 0.0$	$2.2 \pm 0.6$	$2.2 \pm 0.5$	$1.8 \pm 0.4$	
Perception	$1.0 \pm 0.0$	$1.1\pm0.3$	$1.1\pm0.2$	$1.0\pm0.1$	$1.1\pm0.3$	$1.2 \pm 0.3$	

Underlined score: p<0.05 significant from Stage I

Table 2. DOSS scores of patients with and without adverse behaviors n = 12Point of time stage I stage II stage III stage IV stage V stag VI (Number of patients) 8 subscales Mean±SD  $1.2\pm0.3$  $1.8 \pm 0.2$ Attention/ P(4)  $3.3\pm0.6$  $2.8\pm1.0$  $1.4 \pm 0.2$  $1.8\pm0.4$ Concentration  $1.1\pm0.2$  $1.2 \pm 0.4$ A(8) $1.1\pm0.2$  $2.0\pm0.9$  $2.0\pm0.8$  $1.3\pm0.3$  $1.1\pm0.1$  $2.0\pm0.6$  $1.9 \pm 0.7$  $1.2 \pm 0.0$ P(4)  $1.2 \pm 0.1$  $1.2 \pm 0.2$ Thinking  $1.0\pm0.0$  $1.8 \pm 0.7$  $1.0 \pm 0.0$ A(8) $1.4\pm0.6$  $1.0\pm0.0$  $1.0\pm0.1$ Memory/ P(4)  $1.0\pm0.0$  $3.4 \pm 0.3$  $2.2 \pm 0.8$  $1.6 \pm 0.8$  $1.9 \pm 0.9$  $3.3 \pm 0.7$ 2.3±1.0 Orientation A(8) $1.0\pm0.0$  $1.8 \pm 0.9$  $1.1 \pm 0.2$  $1.0\pm0.0$  $1.1 \pm 0.4$ P(4)  $1.0\pm0.0$  $1.4 \pm 0.5$  $1.1\pm0.3$  $1.3 \pm 0.5$  $1.3 \pm 0.3$  $1.3 \pm 0.3$ Perception

 $1.0\pm0.0$ 

 $1.0\pm0.0$ 

 $1.0\pm0.0$ 

 $1.0\pm0.0$ 

 $1.1\pm0.4$ 

 $1.0\pm0.0$ P: presence of adverse behaviors A: absence of adverse behaviors

Underlined score: p<0.05 significant between P and A

A(8)

# VALUABLE COMMUNICATION AND MEANING FOR MOTHER AND CHILD WITH AUTISM SPECTRUM DISORDERS (ASD): A CASE STUDY

M. Yamamoto<sup>1)</sup>, M. Asano<sup>2)</sup>

Department of Nursing, Graduate School of Medicine, Nagoya University, Nagoya, Japan
 School of Health Sciences, Nagoya University, Nagoya, Japan

#### Introduction

Autism spectrum disorders (ASD) is kown as a communication disorder. Children with ASD exhibit difficulties with social interaction and communication skills. Since 1999, research on ASD has been increasing in Japan. Communication methods with the autistic child have been researched in the fields of psychology, pedagogy, and therapy. However research with the focus on the mother-child relationship and the communications in daily life are very limited in Japan.

The mothers who are rearing child with ASD had the experience of connecting with child, and it was important for her. Therefore, I focused on the valuable communication whereby a mother is connected with a child.

#### Aim

The aim of this case study is to describe the communication between parent and ASD child. We explored what is mother's valuable communication, and what is meaning for them of the valuable communication.

#### Methods

#### Date Collection:

This study is a qualitative single case study. I used participant observation and interviews. Participant observation began in Aprl, 2010, and it was about two hours twice a week, at a support calss in which they were participating. I wrote the fieldnotes promptly after the support class. Interviews began July in 2010, it was about two and a half hours ever three or four monthes. Interviews were audio recorded and transcribed verbatim for analysis.

#### Data analysis:

I used qualitative methodology to analyze my data. After initil overviews, the fieldnotes and transcripts were read several times. The data were analyzed in terms of valuable communication and meaning.

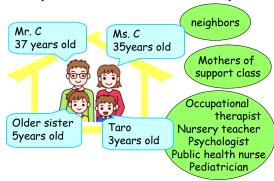
#### **Ethical Consideration:**

I received consent from Ms.C, the director of the support class and the nursery teacher. The study was approved by the University Ethics Committee.

#### Introduction of Ms.C and Taro:

Ms.C and Taro live with Taro's father and older sister. Taro was three years old. He struggles with verbal communication, likes to play alone, and has difficulty expressing feelings.Ms.C had the ability to talk about her idea and experience. Sometime, she talks about child rearing with other people. Frequently, Mr. C and Ms.C talk about child rearing. Some specialists are supporting the family.

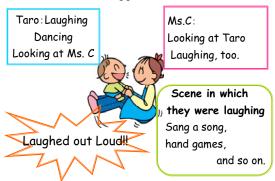
Family Members and human relationship



Taro was often playing alone in daliy life. At that time, he didn't change his expression and was repeating the same action. Ms.C desired to communicatie with Taro, but she didn't know what to do for him. She was confused. Around that time, she noticed Taro laughing when she singing and playing hand games. So, Ms.C thought that it was likely to be possible to communicate with Taro through play in which Taro laughs. Ms.C wanted to have the chance to communicate with Taro by singing and playing hand games.

The scene in witch Ms.C and Taro were laughing in the support class. Taro came to Ms.C with a smile. Ms. C began to sing, Taro was laughing, dancing, and looked at Ms.C. Ms.C looked at Taro who was laughing happily, and she was laughing,too. Their laughter reinforced mutually, and finally they laughed out loud.

One scene in the support class



#### Results

#### Valuable communication for Ms.C:

Ms. C said as follows about laughing together with Taro. "The happy time spent with Taro is when he is smiling, and laughing. I can laugh with Taro. I can enjoy time happily with Taro."

Ms. C often said that mutual laughter was the key to deepening relations with Taro. She wants to value the opportunities for Taro to express himself, because Taro has a delay in language development and difficulty expressing feelings. I asked Ms. C what is most enjoyable, she said laughing together. Therefore, I thought that the most valuable communication is "Laughing together", and this is based on the important idea that Ms. C wants to treasure Taro's happiness.

#### Meaning of "Laughing together" for Ms. C and Taro:

Ms. C talked about her feeling when she was laughing together with Taro in daily life.

"When I saw him laughing, I felt happy too, and I wanted even more for us to do things together."

"When Taro was singing a song, I remembered his song. I sang it together with him. My song affected him, and he laughed and danced. Ah! that's exactly what I thought. At that time, I felt connected to Taro."

Ms. C and Taro share feelings of happiness by *Laughing together*. They feel a desire to do things together. And *Laughing together* was a way of connecting Ms. C and Taro.

#### Conclusions

It might be difficult for a mother and autistic child to find the methods of mutual laughter. Ms. C hoped to treasure Taro's happiness and she produced the shared laughter using Taro's favorite thing. The value and meaning concerning communications are different in each parent and child. It is important that we learned the mother's values and sense of meaning.

It is necessary to connect the mother with a child who has ASD. Laughing together has developed feelings of connection between mother and child. We should pay attention to behavior connecting mother and child such as laughing together.

This study was a single case study. It is one side of the communication. Future studies should explore communication of plural pairs.

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This study subsidized by Japan Society of Nursing and Health Care.

#### Author address

E-Mail: yamamoto.mami@c.mbox.nagoya-u.ac.jp

#### Readability and Suitability of Printed Health Information Materials in Korean

Dong Eun Shin

MSN student, Graduate School, Yonsei University
Gangwon-do, Republic of Korea

**SIGNIFICANCE:** Health professionals use printed materials as primary teaching tools to give patients health information. Printed materials that require a high reading level may not be understandable by people with low literacy skills, or even cause unwanted consequences if individuals with low-literacy misinterpret the meaning of the materials. In addition to reading grade level, the suitability of printed materials, based on elements such as design and organization of content, can influence how much health information a reader absorbs. Not all health professionals are aware that printed materials requiring a high reading level or individuals with low literacy may present barriers to understanding printed health information.

**PURPOSE:** The purpose of this study was to review research studies on readability and suitability of printed health information materials in Korean.

**METHODS:** The databases PubMed, and electronic searches were searched for the terms printed health information materials, readability, and suitability in abstracts published from 2000 up to the present date in Korea. Data were extracted from 7 studies found to be eligible. The seven research studies were reviewed in terms of readability and suitability of the printed materials.

**RESULTS:** In the 7 studies evaluation was done of printed materials on hypertension, cancer, CT patient information, and diverse health information, which were developed by public healthcare institutions or the Korean Academy of Family Medicine. For readability, in all studies materials were evaluated using grade lexical items for teaching Korean (Kim, 2003). Results showed that the reading level of the materials was higher than a 6<sup>th</sup> grade reading level. For suitability, in all studies materials were evaluated using Suitability of Assessment of Materials – Korean Version (KSAM, Sung et al, 2004), which included content, literacy demand, graphics, layout and typography, learning stimulation and motivation, and cultural appropriateness. In the study by Lee et al (2011), 26% of hypertension information materials were evaluated as not suitable. In the study by Yoo (2001), 60% of CT patient information materials were evaluated as not suitable.

**CONCLUSIONS:** These findings suggest that as printed health information materials need to be readable and suitable for the patients and their families, it is essential to know how to evaluate readability and suitability of printed health information materials. In developing printed materials for patient teaching, appropriate readability and suitability levels must be achieved so they will be useful in enhancing understanding of health knowledge in individuals and their families.

#### A Mentoring Program for the Prevention of Sexual Violence among Korean Adolescents

Yang Heui Ahn, Young Mi Lim, Gi Yeon Kim, Ki Kyung Kim, Hee Young Song Department of Nursing, Nursing Center for Women Health Yonsei University, Wonju College of Medicine Gangwon-do, Republic of Korea

**INTRODUCTION:** In Korea, Ministry of Gender Equality and Family (2011) reported that 4% of Korean women suffer sexual assault in their lifetime. It is reported that the majority of sexually violent crimes are committed against adolescents and many offenders are youth themselves in Gang-Won province. One way to prevent sexual violence could be through a mentoring, which is structured and systematic intervention. This study was designed to develop and evaluate a mentoring program to enhance sexual self-efficacy and autonomy as well as sexual knowledge and attitude of adolescents. The purpose of this study, therefore, was to determine the effects of a mentoring intervention for the prevention of sexual violence among Korean adolescents.

METHODS: A nonequivalent control group pretest-posttest design with repeated measurement was conducted. Twenty five second-grade students of the middle school in the intervention group and 35 second-grade students in the control group participated. The mentoring intervention was performed by three trained nursing students as mentors. The intervention included formal 90-minute eight group sessions, and personal and informal contacts during the 4 week period. The instruments were Sexual Knowledge Scale, Sexual Attitude Scale, Sexual Self-Efficacy Scale, and Sexual Autonomy Scale. The instruments were measured in both the intervention and control group at baseline, post-intervention, and 8-week follow-up. For data analysis, t-test was used to homogeneity between the intervention and control group at baseline. Repeated measures analysis of variance was used to determine the effect of the intervention and the effect of time on the sexual knowledge, sexual attitude, sexual self-efficacy and sexual autonomy.

**RESULTS:** For homogeneity testing, there were no statistically significant differences in descriptive characteristics, and dependent variables between the intervention and control group at baseline measurement. For sexual knowledge, the interaction of time and group was significant as was the effect of time (p<.05). The between subject test of the effect of group was also significant (p<.05) in sexual knowledge. For sexual attitudes, there was not a statistically significant group effect (p<.05). For sexual self-efficacy, there was not a statistically significant group effect, time effect, and the interaction of time and group. For sexual autonomy, the effect of time was significant (p<.05) but the interaction of time and group was not a significant. In addition, the between subject test of the effect of group was also not significant.

**CONCLUSION:** The results show that sexual knowledge of adolescents was increased, indicating the effectiveness of the mentoring intervention for even a short period of time. The longitudinal research on a mentoring intervention needs to be further considered so that the teenagers could have the belief having the capability to control over adolescents' motivation and behavior in a sexual situation as well as the ability to make decisions about their own sexuality, which could result in decreasing victims and offenders of sexual violence.

#### Development of a simulation scenario of emergency care of dyspnea for use by nurses

Hye won Kang<sup>1</sup>, Hea kung Hur<sup>1</sup>, Hee young Song<sup>1</sup>, and Hyun Kim<sup>2</sup>
Department of nursing<sup>1</sup>, Department of emergency medicine<sup>2</sup>,
College of Medicine, Yonsei University, Gangwon-do, Republic of Korea

**INTRODUCTION:** Recently, the patients with dyspnea were increased by population aging. The causes of dyspnea are cardiac or pulmonary disease and potentially life threatening illness.

So it is essential to assess and stabilize the symptom rapidly through differential diagnosis. Many guidelines for emergency care of patient with dyspnea were suggested, but there were insufficient guidelines for nurses. And it is needed to develop the education for emergency care of dyspnea for nurses.

With development of patient simulation, simulation based education has been used in nursing education. Development of simulation scenario for emergency care of dyspnea for nurses will provide effective education and make the nurses to practice emergency care of dyspnea.

**METHODS**: The process for this study included the following stages. To construct the algorithm for dyspnea emergency care, a preliminary algorithm constructed based on a literature review and content validity and clinical validity were established. To develop simulation scenario, the simulation scenario template originally developed by Bay Area Simulation Collaborative(BASC) was modified and used. And to construct content validity, and clinical applicability was also established. To construct content validity, expert group consisted of 2 professors of nursing, a professor of emergency medicine, 3 nurses of emergency nursing, and a professor of a emergency medical technology wrote the translated and modified scenario validity check list which was suggested by Waxman(2010). And then collected expert's opinion, modified the scenario.

To establish clinical applicability 9 registered nurses were provided simulation scenario education used SimMan® in OSCE room of Y university. The skill performance, critical thinking, self-confidence, satisfaction which were suggested Jeffries's simulation model(2007) by open questionnaire. And then modified the scenario, confirmed the final scenario.

#### **RESULTS:** The results of this study are summarized as follows.

- 1. The algorithm for dyspnea emergency care consisted of 7 phases; initial assessment, immediate emergency care, reassessment of dyspnea, monitoring respiratory failure occurs, performing cardiopulmonary resuscitation if no pulse is present, or preparing for intubation if pulse is present, determining a differential diagnosis of cardiac origin, pulmonary origin or other causes based on additional assessment if dyspnea has improved.
- 2. Flow of the algorithm was unified into 5 paths; after the initial assessment and immediate emergency care, reassessment of current state of dyspnea requiring 3 paths were verified depending on origin of dyspnea as cardiac, pulmonary or other causes. The final 2 paths were, if dyspnea is aggravated, monitor for respiratory failure and check pulse and if no pulse, start cardiopulmonary resuscitation. If pulse is present, prepare for intubation.
- 3. The simulation scenario consisted of scenario overview, curricular integrity, and scenario script with case of aggravated dyspnea and another is improvement in dyspnea.

**CONCLUSION:** The results of this study suggest that the simulation scenario for emergency care of dyspnea provides guidelines of dyspnea emergency care for nurses and education utilizing the simulation scenario should improve nurse's knowledge, skill performance, and critical thinking.

Further studies are warranted to apply the simulation scenario to emergency care of dyspnea and to test its effectiveness.

# Relationship among depression, family support, and rehabilitation motive in patient with acute or subacute hemorrhagic stroke

Moon, Hak Hee<sup>1</sup>, Shin, Yun Hee<sup>1</sup>, Lim, Young mi<sup>1</sup>, Whang, kum<sup>2</sup> Department of Nursing The Graduate School Yonsei University<sup>1</sup>, Department of Neurosurgery Yonsei University College of Medicine<sup>2</sup> Gangwon-do, Republic of Korea

**INTRODUCTION:** After experiencing a stroke, it is possible to recover to one's normal life through rehabilitation (Madden, Hopman, Bagg, Verner & O'callaghan, 2006) Based on studies that indicate the sooner rehabilitation begins, the higher the chances are in recovery, it is recommended that patients who suffer a stroke start the rehabilitation process within 72hours of the stroke (Korean stroke society, 2009). This research aims to not only provide motives for early rehabilitation, but also to serve as a basis for development of rehabilitation nursing interventions by examining depression, family support, and rehabilitation motives in hospitalized patients with an acute or sub-acute hemorrhagic stroke.

**METHODS**: This is a descriptive correlational research to discover the influences that depression and family support have on rehabilitation motives. The participants were 78patients in 3general hospitals located in the Ganwon Province. The patients were between 1 to 21days since diagnosed with acue or subacute hemorrhagic stroke. The research scales consisted of 103 questions; questions regarding both general characteristics and characteristics related to strokes. The research instruments were below.

- 1) the Depression scale developed by Beck(1961) and revised by Kim Hyung-Sun(2009).
- 2)the Family support scale developed by Cobb(1976) and revised by Kang Heon-Sook(1984).
- 3) the Rehabilitation motive scale developed by hafen et al.(2001) and revised by Kweon Sam-Seok (2001).

Frequencies, percentages, means with standard deviation, t-test, ANOVA, Pearson correlation coefficients, and multiple regression analysis with the SPSS PC 12.0 for windows program were used for data analysis. Data collection was done on an one-on-one interview basis from March 15 to June 5th, 2010. 78of the 84 interviewed were valid.

**RESULTS:** 1. The research showed that the following factors influenced the amount of depression the participants felt: gender(t=2.809, p=.006), current marital status (F=3.211, p=.028), family living arrangements(F=6.618 p=.001), satisfaction with economic status(t=3.358, p=.040), main care-giver (F=3.683, p=.016), number of hospital days(F=3.176, p=.047), amount of hemorrhage(F=3.589, p=.018), affected side of the body(F=5.437, p=.006), and muscular strength on affected side(F=10.275, p=.000). There were significant differences in family support according to marital status (F=7.655, p=.001), family living arrangements (F=25.812, p=.001), satisfaction with economic status(F=7.364, p=.001), family's main care-giver (F=6.797, p=.000), and the amount of hemorrhage (F=2.595, p=.043). Significant differences were found in participants' rehabilitation motives related to marital status(F=3.787, p=.014), family living arrangements(F=10.922, p=.000), satisfaction with economic status(F=4.632, p=.013), main care-giver (F=4.746, p=.004), number of hospital days(F=7.154, p=.000), mount of hemorrhage(F=3.353, p=.023) and muscular strength on affected side (F=7.154, p=.000).

- 2. Depression in patients in the incipient stage of acute of sub-acute hemorrhagic stroke showed a negative correlation with family support [r=.631(p<.01)] and rehabilitation motive [r=.818(p<.01)]. Family support had a significant positive correlation with rehabilitation motive [r=.775(p<.01)].
- 3. Three variables; depression, family support, and number of hospital days, explained 77.9% of the variance for rehabilitation motive with the F-value being 86.719. Findings showed the higher the family support(B=.439, p<.001), the higher the rehabilitation motive, the higher the amount of depression(B=-.512, p<.001), the lower the rehabilitation motive, and the longer the period of hospitalization,(B=-.130, p<.05)the lower the rehabilitation motive.

**CONCLUSION:** The findings of this study indicate that lowered depression and greater family support or patients with acute or sub-acute hemorrhagic stroke could result in stronger rehabilitation motive and greater family support could lower depression. As the main factors affecting rehabilitation motive of patients with acue or sub-acute hemorrhagic stroke were found to be depression, family support and number of hospital days, the development of nursing interventions to improve rehabilitation motive should focus on preventing depression increasing family support and reducing the number of hospital days.

## Development of an Evidence-based Nursing Protocol after Neck Clipping Surgery for Patients with Cerebral Aneurysm in Intensive Care Units

# Jeon, Hee Jeong Department of Nursing Graduate School. Yonsei University Gangwon-do, Republic of Korea

**INTRODUCTION:** The purpose of this study was to develop an evidence-based nursing practice protocol for intensive care unit patients with neck clipping for a subarachnoid hemorrhage due to a ruptured aneurysm. In this study, a protocol was developed to improve clinical practice and to prevent complications and thereby, through the application of the protocol, reduce neurological deficits.

**METHODS**: A methodological design was used for this study. The study period was from September 1 to December 16, 2010. The protocol in the current study was developed based on the "Clinical Practice Guidelines Manual Version 1.0".

For the first step, a clinical guideline, 'Care of the Patient with Subarachnoid Hemorrhage [SAH]' for postoperative care by the AANN (American Association of Neuroscience Nurses) was compared to Korean clinical practice and used to construct preliminary items. More preliminary items were added through a literature review. Second, the preliminary items were evaluated for validity by a panel of 17 experts. Third, comprehensive literature search was done to identify evidence supporting each item and to confirm that the item was up-to-date. Fourth, each summary table for the evidence of the items was created based on the literatures and the quality of research for evidence was evaluated using SIGN (Scottish Intercollegiate Guideline Network) literature evaluation tools. Fifth, recommended items were formulated and evaluated for strength of each item using the NHS R & D (National Health Service Research & Development) Center for Evidence Based Medicine. Sixth, a preliminary nursing practice protocol was developed including the strength level of each item. Seventh, the preliminary protocol was assessed for appropriateness, applicability, and conformity with nursing care in intensive care units by a panel of 25 experts using a 9-point scale. Eighth, the final items were determined for the nursing practice protocol. Ninth, the nursing practice protocol was evaluated by a panel of 5 experts using AGREE (Appraisal of Guidelines Research and Evaluation).

Frequencies, percentages, means, and standard deviation of the applicability and appropriateness of each item were analyzed using SPSS PC 18.0 for Windows.

#### **RESULTS:** The results of this study are as follows.

- 1. According to the described procedure, a preliminary protocol was developed and evaluated for appropriateness and applicability of each item of the preliminary protocol. With the exception of two items, all items in Nursing Assessment received over 7.5 points. The 2 items were modified and included in the protocol. Of 10 items in Nursing Intervention with less than 7.5 points, two were modified and included and eight items were deleted. Of 19 items in Nursing Evaluation with less than 7.5 points, 4 items were included after modification and 15 items were deleted. Finally, all the items of the final protocol had appropriateness and feasibility scores of more than 7.5 points.
- 2. The final Nursing Practice Protocol had a total of 22 areas with 163 items including 6 areas with 52 items for Nursing Assessment, 14 areas with 94 items for Nursing Intervention,

and 2 areas with 17 items for Nursing Evaluation. The six areas for Nursing Assessment were (1) neurological examination (2) assess for vital signs (3) airway maintenance and oxygenation (4) assess for increased intracranial pressure (5) assess for laboratory tests (6) assess for cardiac complications. The 14 areas for Nursing Intervention were (7) prevention of vasospasm (8) management of cerebral edema (9) management of hydrocephalus (10) keep head of bed elevation (HOB) (11) fever control (12) administration of medications (13) prevention of deep vein thrombosis (DVT) (14) care for early rehabilitation (15) ventilator care (16) prevention of aspiration (17) mouth care (18) provision of adequate nutrition (19) skin care, and (20) hand washing to prevent infection. The two areas for Nursing Evaluation were (21) patient evaluation for the results after aneurysm ligation and (22) evaluation of the process of care.

- 3. In this study, the final 163 items were rated. For 121 items the rating was A, for 14 items, B, and for 28 items, C indicating the strength of each item according to criteria from the NHS R & D Center for Evidence Based Medicine. Although the 28 items for C were rated low, the experts were in consensus that the items were all clinically necessary and should be included.
- 4. The results by AGREE were that 'editorial independence' was found to be the highest at 100% and 'participation of stakeholders' the lowest at 73%.

Percentages for the scope and purpose, the rigor, the accuracy and expression were 82%, 89%, 85% respectfully, all over 80%.

**CONCLUSION:** The results suggest that this protocol for care after aneurysm neck clipping in patients admitted to the ICU for postoperative care is an evidence-based guideline. Adaptation of nursing practice protocols and guidelines will contribute to further improvement of nursing practice.

Key Word: subarachnoid hemorrhage, aneurysm neck clipping

# Pulmonary Rehabilitation of Korean Patients with Chronic Obstructive Pulmonary Disease (COPD)

<u>Ji Soo Jung</u>
MSN student, Graduate School, Yonsei University
Gangwon-do, Republic of Korea

**SIGNIFICANCE:** COPD has been increasing due to exacerbation of air pollution and increased rate of smoking, placing it in 5<sup>th</sup> place as a cause of death. COPD has the characteristics of chronic disease with gradual worsening and the experience of dyspnea when engaging in physical activity. The acceleration of symptoms such as fatigue, depression, anxiety, and sleep disorder cause difficulty in implementing treatment therapy and maintaining daily activity. Also, medical expenses due to COPD have been increasing. Therefore emphasis must be given to the importance of self-management to maintain patient's daily activity and decrease medical expenses, and to the importance of pulmonary rehabilitation at home for self-management.

**PURPOSE:** The purpose of this study was to review the intervention studies on pulmonary rehabilitation of Korean patients with COPD.

**METHODS:** The databases PubMed and electronic searches were used to search for the terms pulmonary rehabilitation, and COPD in abstracts published from 2000 up to the present. Data were extracted from 9 studies found to be eligible. Nine research studies were reviewed in terms of samples, interventions and outcome measurements.

**RESULTS:** In 5 of 9 studies, samples were reported as outpatients who were moderately severe. In 4 studies pulmonary rehabilitation was conducted, which included exercise programs, education, and breathing training. Outcomes from 2 studies showed significant changes but only in exercise programs (eg, multilevel exercise capacity test, maximum exercise oxygen level, 6-minute walk test, Borg scale), whereas in 3 other studies, outcomes that were more likely to show significant changes were in programs which including education, breathing training, exercise, and psychological interventions (eg, clinical tests, exercise capacity, dyspnea, health-related quality of life, socio-psychological measurement tool), suggesting that certain outcomes may be more difficult to maintain.

**CONCLUSIONS:** These findings indicate a need to further emphasize pulmonary rehabilitation, and to provide standardized protocols and home based pulmonary rehabilitation programs of Korean COPD patients.

# Abstracts Radiological Technology

#### Evaluation of radiation dose to infants in CT and other x-ray diagnostic radiology

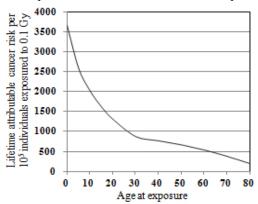
Naruto Sugimoto, Takahiko Aoyama, Shuji Koyama, Chiyo Yamauchi-Kawaura

Department of Radiological Sciences, Graduate School of Medicine, Nagoya University, Nagoya, Japan

#### Introduction

Recent technical innovation of diagnostic radiology conducted worldwide increase in the frequency of x-ray examinations, in particular of CT examinations, not only for adults but also for pediatric patients. Since the risk inducing cancer for infants has been estimated to be factors of 3-4 higher compared with that for adults (see Fig. 1 [1]), evaluation of exposure doses to infants would be important.

Although we extensively evaluated the doses for adults and for 6-years-old children [2,3], dose levels in CT and other x-ray diagnostic radiology for infants have not been investigated. In the present study, we examined organ and effective doses to newborn patients who underwent CT and other x-ray diagnostic radiology, based on in-phantom dose measurements, and compared the doses with those for adult patients.



**Fig. 1** Lifetime attributable risk of cancer incidence per 10<sup>5</sup> individuals exposed to 0.1 Gy as a function of age at exposure [1].

#### **Materials and Methods**

#### 1. In-phantom dosimetry system

Dose measurements were performed with a newborn anthropomorphic phantom, ATOM 703 (CIRS, Norfolk, VA), the scheme of which is shown in Fig. 2. The phantom represented a standard newborn baby, 3.5 kg in weight and 51 cm tall. Photodiode x-ray sensors were installed at the positions of various tissues and organs defined in the International Commission on Radiological Protection (ICRP) Publication 103 [4] to evaluate the effective dose, excepting lens. These positions and the number of photodiode sensors implanted in each tissue or organ are shown in Fig. 2. Radiation doses for small tissues and organs such as the thyroid and the bladder were measured with a sin-

gle sensor, and doses for large organs such as the brain and the colon were measured with several sensors.

	Brain	2	
		2	0.01
	Lens	1	-
	Salivary glands	1	0.01
	Thyroid	1	0.04
	Lung	1	0.12
3.2	Breast	1	0.12
	Esophagus	2	0.04
1/1/3	Liver	1	0.04
11-1-1	Stomach	1	0.12
	Colon	4	0.12
	Ovary	1	0.08
	Bladder	1	0.04
	Testis	1	0.08
	Bone surface	11	0.01
	Red bone marrow	10	0.12
9.0	Skin	2	0.01
	Remainder	9	0.12

**Fig. 2** The newborn phantom (CIRS, Norfolk, VA) used. Also shown are the numbers of photodiode sensors implanted in each position of tissues and organs and tissue weighting factors  $w_t$  listed in ICRP 103.

X-ray sensors used for the in-phantom dosimetry system were planer-type of silicon pin-photodiodes, Hamamatsu S8385-04, which were small sized but highly sensitive for diagnostic x rays. Since the sensitivity of a single photodiode of this type differed by the incidence direction of x-rays between front and back, two photodiodes were glued together back to back with epoxy cement, and were used as a single sensor with parallel connection. The sensor was wrapped up with  $11~\mu m$ -thick aluminum foil for electromagnetic shielding and connected to a pair of twisted carbon-fiber cables, which were tissue equivalent.

Signal current generated by x-ray incidence on a photodiode sensor was fed through the cables to a current integrator, and integrated to the total charge proportional to the dose absorbed by the photodiode sensor. Dose calibration of the photodiode dosimeters was performed against a Radcal 9015 with a 6 cm³ ion chamber. The values of exposure dose in the unit of coulomb per kilogram obtained with the ion chamber were converted to the values of absorbed dose for soft tissue by using the ratio of mass energy absorption coefficient of soft tissue to that of air at the effective energy of x rays used. Output signals from photodiode dosimeters were read out on a personal computer, from which organ and effective doses were computed according to guidelines published in ICRP Pub.103 [4].

#### 2. Dose measurements

Patient exposure dose in diagnostic radiography were measured for the typical examinations of head, chest, abdomen and hip-joint using various types of x-ray generators. All of the measurements were performed with patient-size dependent imaging protocols.

Doses in CT examinations were evaluated with four 64- and 16-detector row CT scanners from worldwide manufacturers, *i.e.* General Electric, Philips, Toshiba and Siemens. All of these scanners were operated with patient-size-dependent imaging protocols with and without automatic tube current modulation (ATCM). Dose measurements were performed with technical parameters clinically used in plain or non-contrast head CT, chest and cardiac CT, and abdomen including pelvis and abdomen with bolus tracking CT scans.

#### **Results and Discussion**

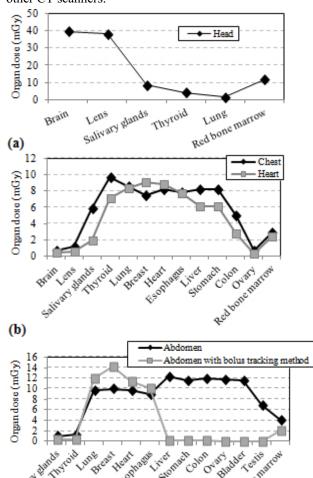
Figure 3(a) shows organ doses in head CT scans for newborn patients obtained with a 64-detector row CT scanner from Toshiba. Brain and lens doses, *i.e.* the doses for organs within the scan region, of 40 and 38 mGy were relatively high, though they were approximately 1-2 times lower than the doses of 42-71 mGy and 45-88 mGy observed for adult patients. On the other hand, though red-bone-marrow dose of 12 mGy was relatively low, it was approximately 2-4 times higher than that of 3-6 mGy for adults. The reason of which would mainly be due to a large weight-percentage of red bone marrow at the cranium for newborn babies than that for adults, e.g. 3 times larger weight-percentage for newborns than for adults.

Shown in Fig. 3(b) are organ doses in chest and heart CT scans for newborn patients obtained with the 64-detector row CT scanner from Toshiba. The doses for organs within the scan region as thyroid, lung, breast, heart, esophagus and liver, of 8-10 mGy in chest CT were approximately 2-4 times lower than those of 20-32 mGy for adults observed with the same scanner. On the other hand, doses for such organs located close to the scan region as colon and salivary gland were approximately 2-3 times higher for newborns than for adults because of small separations of these organs from the scan region for newborns.

Figure 3(c) shows organ doses in two types of abdominal CT scans for newborn patients obtained also with the 64-detector row CT scanner from Toshiba. Organ doses for organs within the scan region as liver, stomach, colon, ovary and bladder, of 12 mGy in abdomen including pelvis CT scans were approximately 2-3 times lower than those of 27-33 mGy in adult abdominopelvic CT scans observed with the same scanner. On the other hand, dose of 10 mGy for breast located close to the scan region was only 1.8 times lower than that for adults of 18 mGy.

Organ doses for newborn patients obtained with the Toshiba scanner were similar to those observed with

other CT scanners.



**Fig. 3** Organ doses in (a) head, (b) chest, heart and (c) two types of abdominal CT scans for newborn patients obtained with a 64-detector row CT scanner from Toshiba.

#### Reference

(c)

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#### Author address

E-Mail: <u>sugimoto.naruto@h.mbox.nagoya-u.ac.jp</u>

## ENERGY ESTIMATION IN A PHANTOM IN X-RAY CT : ANALYSIS USING MONTE CARLO METHOD

Shimpei Kondo<sup>1)</sup>, Shuji Koyama<sup>1)</sup>

1) Department of Radiological Sciences, Nagoya University Graduate School of Medicine, Nagoya, Japan

#### Introduction

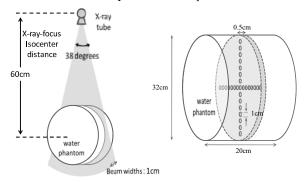
X-ray entered into a phantom is absorbed and scattered. In-phantom x-ray spectrum has the potential to differ from incident x-ray spectrum when continuous x-ray enters into object. We have small semiconductor dosimeters, which are very useful to measure doses in phantom. The semiconductor dosimeters have large energy dependence and, output values of them are influenced by changes in beam quality. It is important to measure x-ray energy spectrum and effective energy in phantom to know appropriate calibration factor, because calibration factor for the semiconductor dosimeters is required to estimate correct absorbed dose. It is, however, practically difficult to measure x-ray energy spectrum or half-value-layer in phantom. In this study, in-phantom x-ray energy spectrum and effective energy were analyzed by using Monte Carlo simulation which had the advantage of being able to calculate energy spectrum in difficult measurement situation.

#### **Materials and Methods**

X-ray energy spectrum and effective energy in a phantom undergoing x-ray CT scan were analyzed by Electron Gamma Shower 5 (EGS5) Monte Carlo simulation code.

#### 1. Monte Carlo Simulation Geometry

X-ray-focus isocenter distance was 60 cm. The cylindrical phantom consisted of water, 32 cm in diameter and 20 cm in length. Twenty five small water discs of 1 cm diameter were put inside the phantom, along horizontal and vertical axis of an axial plane at 0.2 cm intervals. Locations of each of four small discs nearest the phantom surface were placed at 0.7, 1.0, 1.3, and 1.6 cm from the phantom surface. **Fig.1** shows geometry of this calculation and the cylindrical water phantom.



**Fig.1** Geometry of this simulation undergoing x-ray CT and cylindrical water phantom

#### 2. Beam-shaping filter incorporated in simulation

X-ray CT is generally equipped with beam-shaping filter in front of the x-ray tube radiation window. By the beam-shaping filter, incident x-ray emitted from the target is adjusted to certain energy at CT detector after passing through phantom.

Before incident to the phantom, therefore, dose distribution and beam quality of x-rays originally emitted from the target are changed by the beam-shaping filter. For making x-ray CT simulation more concrete, the effect of beam-shaping filter that is contributed to x-ray attenuation and beam hardening, must be incorporated in incident fan beam. **Fig.2** shows effective energy and dose distribution based on measurement data from x-ray CT (TCT-300; Toshiba Medical, Tochigi, Japan), which were incorporated in incident fan beam of our simulation code.

To take into account the effect of beam-shaping filter, incident fan beam was divided into 7 parts (0-4, 4-5, 5-6, 6-7, 7-8, 8-9, and 9-18 degrees) on the half side of the fan beam and seven different spectrums were used in each part. Effective energy of the energy spectrums were 54, 57, 59, 62, 64, 72, and 73 keV from the center part to the outer part, respectively, and the number of photon corresponding to dose distribution data was used in each degree (0-18 degrees) of fan beam.

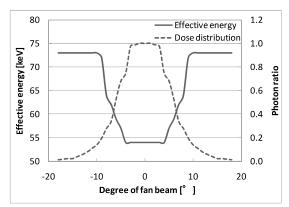


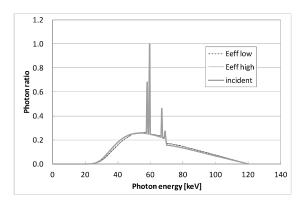
Fig.2 Effective energy and dose distribution data incorporated in this simulation

#### 3. Obtaining in-phantom spectrum and effective energy

The photons passing through the small disc inside the phantom were counted with respect to each energy bin, and those were used for calculating in-phantom energy spectrum and effective energy along x axis and y axis of an axial plane of the phantom. The total number of photon source was  $1.44 \times 10^9$ .

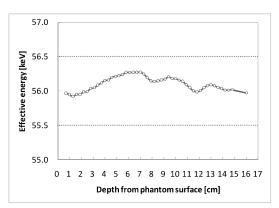
#### **Results and Discussions**

**Fig.3** shows two in-phantom x-ray spectrums with the lowest and highest effective energy (55.92 keV and 56.28 keV) and incident spectrum (effective energy:Eeff = 54 keV).



**Fig.3** Comparison of in-phantom x-ray spectrum with incident x-ray spectrum.

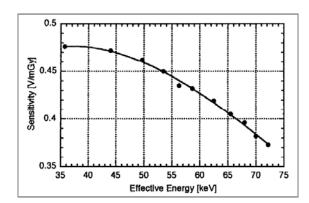
Change of effective energy in the phantom is shown in **Fig.4**. The in-phantom effective energy is 55.92 keV at the depth of 1 cm (raised by 3.61 % compared to effective energy of the incident x-rays), and 55.97 keV at the depth of 16 cm (raised by 3.65 %). The spread between the lowest and highest in-phantom effective energy is less than 1 keV.



**Fig.4** Change of in-phantom effective energy in each depth from the phantom surface

One would think that continuous x-ray entered in phantom is absorbed, and beam quality becomes just harder. That is true in looking at only primary x-ray, but not true with the scattered x-ray. In this research, little difference existed between incident and in-phantom effective energy. In the phantom, effective energy in each depth from the phantom surface also had little difference. At the point of each depth, low energy component of the x-ray spectrum was reduced by beam hardening effect. In contrast, low energy x-rays generated in another area by Compton scattering were absorbed to the point, and they were contributed to low energy component of the spectrum. The proportion between beam hardening and Compton scattering is important component of changing process of effective energy. Thus, in-phantom beam quality which contains scattered x-ray is not just harder.

Fig.5 shows the energy dependence of small semiconductor dosimeter owned Nagoya University. The difference of sensitivity of semiconductor dosimeter between incident and in-phantom effective energy is shown in Table 1. Relatively small changing of effective energy in phantom had little effect on calibration factor for the semi-conductor dosimeter.



**Fig.5** Energy dependence of small semiconductor dosimeter (made by T Aoyama; Nagoya University 2002) [1].

Table 1 Difference of sensitivity of small semiconductor dosimeter for effective energy

	Effective energy	Sensitivity	Difference for	incident Eeff
	[keV]	[V/mGy]	[V/mGy]	[%]
incident	54.00	0.448	-	-
in phontom	55.92(low)	0.440	-0.008	-1.79
in-phantom -	56.28(high)	0.441	-0.007	-1.56

#### Conclusions

In-phantom x-ray spectrum and effective energy were analyzed by using Monte Carlo simulation (EGS5). Little difference exists between incident and in-phantom effective energy.

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#### Author addres

E-Mail: kondo.shimpei@e.mbox.nagoya-u.ac.jp

#### APPLICATION OF THE NEW CT TECHNIQUE USING THE MONTE CARLO SIMULATION

Daiki Hayashi<sup>1)</sup>, Shuji Koyama<sup>1)</sup>

1) Department of Radiological Sciences, Nagoya University Graduate School of Medicine, Nagoya, Japan

#### Introduction

Recent years, tremendous advances in computed tomography (CT) scan technology and applications have been increased in clinical utilization. Among them, we focused on dual energy CT (DECT) and CT-auto exposure control (CT-AEC). In DECT, computed tomography dose index (CTDI) for DECT is measured using same method as the measurement method of SECT and used as reference of human dose. From this reason, we calculated the relationship between CTDI and human dose for SECT and DECT and compared between those two relationships. CT-AEC is the technique aiming at dose reduction and image quality optimization. CT-AEC is divided into the angular (x-y axis) and longitudinal (z-axis) tube current modulation (TCM). In order to incorporate CT-AEC into the simulation for accurate CT dose evaluation, we calculated TCM data. In this study, all simulations were performed using the Electron Gamma Shower ver.5 (EGS5) which is one of the Monte Carlo simulation codes.

#### **Materials and Methods**

#### 1. Accuracy validation of dose evaluation for DECT

Fig.1 shows simulation geometry for DECT. The geometric condition of a non-helical x-ray CT unit TCT-300 (Toshiba Medical Systems, Tochigi, JAPAN) was used. X-ray tube voltages were 80kV, 140kV (for DECT) and 120kV (for SECT). Three incident energy spectra were calculated using Tucker's formula [1]. In DECT, dose allocation between 80kV and 140kV was calculated by simulation to equalize the photon number of 80kV and 140kV reaching detector. As a result, the dose allocation was 80kV:140kV=69.4%:30.6%. Furthermore, we investigated the effect of varying the dose allocation from 80kV:140kV=59.4%:40.6% to 79.4%:20.6% at intervals of 5%. Two cylindrical phantoms (16 cm in diameter and 15 cm thick) were used. One of these phantoms was made from polymethylmethacrylate (PMMA). PMMA phantom is equivalent to the phantom for CTDI measurement. Another phantom was made from water. We assumed that water phantom is equivalent to human body. To calculate the relationship between CTDI and human dose, the absorbed dose ratio (Rad) was defined as

$$R_{ad} = \frac{D_w}{D_p}$$

where  $D_W$  was absorbed dose in water phantom.  $D_P$  was absorbed dose in PMMA phantom.  $R_{ad}$  was calculated at five (center and four peripheral) positions for SECT and DECT, respectively. Human dose can be estimated by multiplying CTDI by  $R_{ad}$ .

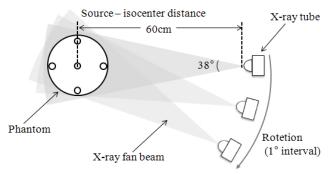


Fig.1 Simulation geometry for DECT

#### 2. Calculating longitudinal (z-axis) TCM data

Fig.2 shows simulation geometry for longitudinal (z-axis) TCM. The geometric condition of multi-slice CT unit Aquilion64 (Toshiba Medical Systems, Tochigi, JAPAN) was used. X-ray tube voltages were 120kV calculated using Tucker's formula [1] and x-ray beam which had width equal to the phantom and thickness of 1cm was used. CTU-41 (Kyoto Kagaku, Kyoto, Japan) voxel phantom was used in this simulation. The voxel phantom is made by assigning each material (soft tissue, bone, lung and air) into each voxel read from DICOM images taken by CT. This makes it possible to simulate anthropomorphic phantom which has complicated structure. In this study, we calculated the longitudinal (z-axis) TCM data. X-ray tube was moved in steps of 1.0cm along z axis direction and the number of photons reaching CT detectors was counted. Then the number of incident photons at each slice was calculated to equalize the photon number reaching detector. Longitudinal (z-axis) TCM data which equalize the image standard deviation (SD) of each slice was obtained. The calculated data was compared with the TCM data represented on CTU-41 image made by Aquilion64.

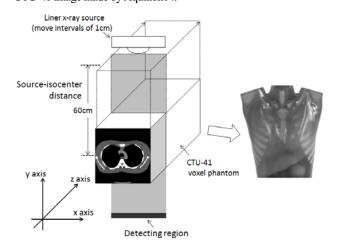
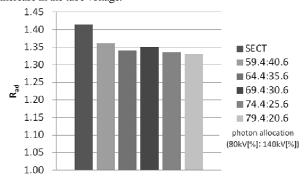


Fig.2 Simulation geometry for longitudinal (z-axis) TCM

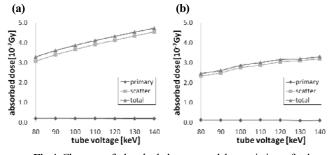
#### Results and discussion

#### 1. Accuracy validation of dose evaluation for DECT

Fig.3 shows Rad of SECT and DECT at each dose allocation in the center position of phantom. The  $R_{ad}$  of SECT (=1.414) was higher than that of DECT (=1.351). As the dose of 80kV increased, Rad of DECT decreased from 1.362 to 1.331. If the human dose was estimated from Rad of SECT, the human dose in DECT was overestimated by 4.5%. In the peripheral position, averages of  $R_{ad}$  for both CT were about the same ( $R_{ad}$  of SECT=1.367  $R_{ad}$  of DECT=1.371). As the dose of 80kV increased, Rad increased slightly from 1.356 to 1.377. In order to discuss the reason of these results, absorbed dose in the center position of the phantom for a variety of tube voltage was simulated. Tube voltage was increased from 80kV to 140kV at intervals of 10kV. The spectrum for each tube voltage was calculated using Tucker's formula [1]. For more detailed discussion, the absorption dose was divided primary x-ray component and scattering x-ray component. The changes of absorbed dose for a variety of tube voltage in the water phantom are shown in fig.4 (a) and in the PMMA phantom are shown in fig.4 (b). In the both phantoms, total absorbed dose was increased with increasing the tube voltage and the scattering x-ray component contributed largely to the increase in absorbed dose. But the increasing range of the total absorption dose differed between water phantom and PMMA phantom. In the water phantom, the total absorbed dose varied from 3.29 (100%) to 4.74 (144%). As for the PMMA phantom, the total absorbed dose varied from 2.46 (100%) to 3.30 (134%). Thus, the changes of R<sub>ad</sub> in Fig.3 were caused by difference of the increasing range of absorbed dose between water and PMMA phantom with increase in the tube voltage.



 $\label{eq:Fig.3} \textbf{Fig.3} \textbf{ Changes of } R_{ad} \textbf{ by a variance of dose allocation at center position in the cylindrical phantom}$ 



**Fig.4** Changes of absorbed dose caused by variation of tube voltage (a) Water phantom. (b) PMMA phantom.

#### 2. Calculating longitudinal (z-axis) TCM data

**Fig.5** shows the longitudinal (z-axis) TCM data of CTU-41 phantom represented on Aquilion64 console (represented data) and calculated using simulation. To perform the longitudinal (z-axis) TCM equalizing the image SD of each slice, the value of TCM data is applied to the mAs value at each slice. The form of two data was more or less the same. The simulation data was, however lower than the represented data at slices from first to fifth (neck), slices from eighth to seventeenth (from apex of lung to aortic root) and slices from twenty-fourth to thirty-first (from left ventricle to apex pulmonis). Therefore, it is necessary to make these differences small.

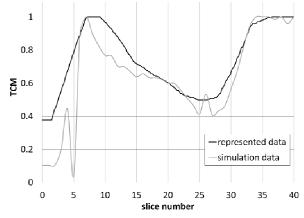


Fig.5 Longitudinal (z-axis) TCM data (represented and simulation)

#### Conclusions

In accuracy validation of dose evaluation for DECT, we calculated the relationship between CTDI and human dose for SE CT and DECT and compared between the two relationships. As a result, the relationship of DECT was slightly different to the one of SECT. This study shows that human dose in DECT was overestimated by 4.5% if human dose was estimated from SECT's relationship between CTDI and human dose. In calculating tube longitudinal (z-axis) TCM data, the form of represented and simulation data was more or less the same. Further studies are needed to make the differences small. Furthermore, we hope to calculate angular (x-y axis) TCM data and to compare with measured data for simulating more accurate CT-AEC.

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#### **Author address**

E-Mail: hayashi.daiki@g.mbox.nagoya-u.ac.jp

## ESTIMATION OF DOSE DISTRIBUTION IN CTDI PHANTOM IN CBCT USING MONTE CARLO SIMULATION

Tomonobu Haba<sup>1)</sup>, Shuji Koyama<sup>1)</sup>

1) Department of Radiological Sciences, Nagoya University Graduate School of Medicine, Nagoya, Japan

#### Introduction

Recently, 320 detector row cone beam CT (CBCT) has been used in clinical examination. In 320 detector row CBCT, dose distribution in phantom is complicated because its wide x-ray beamwidth of 160 mm causes more scattering component of x-ray. The understanding of detailed dose distribution in phantom is useful for dose estimation in CT scanner. However, the measurement of dose distribution in phantom for kilovoltage x-ray beams is difficult because there are problems related to large gradients in the dose distribution and the large energy dependence of most dosimetry systems [1]. In this study, we calculated dose distribution in CT dose index (CTDI) phantom in 320 detector row CBCT using Monte Carlo (MC) simulation.

#### Materials and Methods

#### 1. Conformity of MC simulation with measurement

It is important to checking the conformity of MC simulation with measurement. We calculated and measured CTDI<sub>100</sub> in a non-helical x-ray CT unit TCT-300 (Toshiba Medical Systems, Tochigi, Japan). CTDI<sub>100</sub> is CTDI measured using 100 mm long CT chamber. The x-ray tube voltage was 120 kV, and souce center distance (SCD) was 600 mm. PMMA cylindrical phantom of 300 mm diameter and 150 mm length and CT ionization chamber (CT chamber) of 100 mm length were used. In the phantom, there were five cylindrical cavities in different depth along the cylinder axis to insert the CT chamber; the depths were 11, 59, 81, 115, and 150 mm from the phantom surface. Fig.1 shows measurement geometry. The phantom was supported using wooden blocks and the bed was removed from scan area. This is because it is difficult to incorporate the effect of x-ray scattering and attenuation of CT patient bed in the simulation.

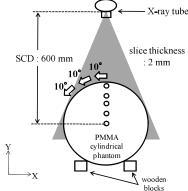


Fig.1 measurement geometry

In addition, it is also difficult to incorporate the effect of x-ray tube rotation overlapping in the simulation because the overlapping angle has not been disclosed. Therefore, a scanogram mode (non-rotating mode) was used. The phantom was rotated by 10 degrees up to full circle in a counterclockwise direction and each dose was integrated by using CT chamber.

In MC simulation, the simulation geometry was the same as the above measurement geometry. Energy spectrums as x-ray source along the fan beam of the CT were generated by Tucker's formula [2] based on AL HVL measured on each angle. The effect of the beam shaping filter was incorporated into the simulation.

#### 2. PDD calculated by MC simulation in CBCT

Percentage depth dose (PDD) along depth direction from surface to surface through the center point in 320 detector row CBCT was calculated using MC simulation. This CBCT geometry was applied to previous TCT-300 geometry, but the beamwidth was changed from 2 mm to 160 mm. Fig.2 shows CBCT geometry in MC simulation. The x-y coordinate plane is parallel to the transverse axis, and the z coordinate axis (z axis) is parallel to the longitudinal axis of cylindrical phantom. The x coordinate axis (x axis) is horizontal to the floor, and the y coordinate axis (y axis) is perpendicular to the floor. Phantom was PMMA cylinder of 320 mm diameter and 600 mm length. In this condition, one rotating scan was performed. PDD was calculated per 1.0 mm depth. The size of calculation region was 10.0 mm (x), 1.0 mm (y), and 100 mm or 300 mm (z). The size of z direction was on the assumption of 100 mm long or 300 mm long CT chamber. Energy deposition by primary x-ray and Compton scatter x-ray was accounted for separately.

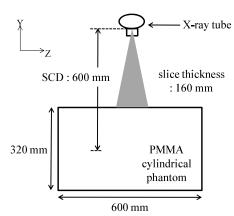


Fig.2 MC simulation geometry in CBCT

#### Results

#### 1. Conformity of MC simulation with measurement

**Table 1** shows the conformity of MC simulation with measurement. The depth showed the distance from the phantom surface to the center of CT chamber. Each depth dose was normalized to 11 mm depth dose in the MC simulation and the measurement. Percent Average Error (PAE) is given as follows:

$$PAE = \frac{Dm - Ds}{Dm} \times 100$$
 [%]

where  $D_m$  was the normalized measured dose,  $D_s$  was the normalized calculated dose. In the **Table 1**, PAE was within  $\pm 2.4$  % in all depth.

Table 1 the conformity of simulation with measurement

depth from the	normal	• PAE [%]	
[mm]	simulation (Ds)	measurement (Dm)	· FAE [70]
11	1.0	1.0	0.0
59	0.94	0.93	-1.5
81	0.84	0.85	2.2
115	0.77	0.77	-0.3
150	0.71	0.73	2.4

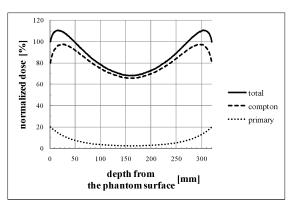
#### 2. PDD calculated by MC simulation in CBCT

**Fig.3 and 4** show PDDs which were calculated on the assumption of 100 mm long and 300 mm long CT chamber, respectively. Continuous line indicated total deposition energy (primary or Compton scatter); broken line indicated deposition energy which only came from Compton scattering component of x-ray; and dotted line indicated deposition energy which came from primary component of x-ray. The depth indicated the distance from the upper surface to the lower surface of the phantom. Each of deposition energies was normalized to the total deposition energy in the surface region. In **Fig.3**, peak dose of total deposit energy was 11.0 % higher than phantom surface dose. The position of maximum dose was 18.0 mm depth from the phantom surface. In **Fig.4**, peak dose of total deposit energy was 22.0 % higher than phantom surface dose. The position of maximum dose was 30.0 mm depth from the phantom surface.

#### Discussion

In **Table 1**, there is a good agreement between MC simulation and measurement because PAE is within  $\pm 2.4$  % in all depth.

In Fig.3 and 4, detail analysis of energy deposition finds that Compton scattering is contributed largely to maximum dose position shifting. This effect is greater with the 300 mm long CT chamber than with the 100 mm long CT chamber. This is because the 300 mm length along the direction of z axis covers wide x-ray beamwidth in 320 detector row CBCT and is more deposited Compton scatter component of x-rays. Our results showed that, in the existing CTDI estimation of CBCT, peripheral measurement position of 10 mm depth was different to maximum dose position. We considered that this effect is very important for CTDI estimation. Dose estimation in CT scanner is now performing using CTDI<sub>100</sub>. In 320 detector row CBCT, however, Geleijns et al. said that CTDI<sub>100</sub> underestimated CTDI<sub>300</sub> [3]. In this research, we also thought that it is better to measure CTDI using 300mm CT chamber because maximum dose position shifting is remarkable.



 ${f Fig. 3}$  PDD which was calculated on the assumption of 100 mm CT chamber

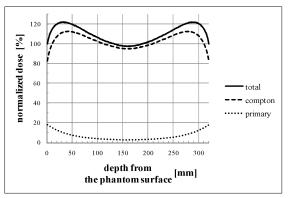


Fig.4 PDD which was calculated on the assumption of 300 mm CT chamber

The measurement using 300 mm long CT chamber is, however, impractical in clinical quality assurance since it is difficult to develop long chamber which has uniform sensitivity and to handle the large and heavy PMMA phantom. Along with the popularization of 320 detector row CBCT, dosimetry of x-ray CT will become even more complex.

#### Conclusion

In this research, we calculated PDD using MC simulation in order to analyze the dose distribution in the CTDI phantom in 320 detector row CBCT. We thought that it is also important to consider about the measurement depth of peripheral positions in CTDI phantom in 320 detector row CBCT.

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#### Author address

E-Mail: <u>haba.tomonobu@f.mbox.nagoya-u.ac.jp</u>

## SIGNAL-TO-NOISE RATIOS CONSIDERED AS HUMAN VISUAL CHARACTERISTICS

Yui Hayashi<sup>1)</sup>, Yukiyoshi Kimura<sup>1)</sup>, Maki Yamada<sup>1)</sup>, Naotoshi Fujita<sup>2)</sup>, Akiko Horii<sup>1)</sup>, Yoshie Kodera<sup>1)</sup>

- 1) Department of Radiological Sciences, Nagoya University Graduate School of Medicine, Nagoya, Japan
  - 2) Department of Radiological Technology, Nagoya University Hospital, Nagoya, Japan

#### Introduction

The effects of various imaging parameters on detectability have not yet been clarified, and image quality indices do not necessarily equate with visual image quality. Therefore, in this study, we investigated the usefulness of signal-to-noise ratios (SNRs) considered as human visual characteristics, such as the visual spatial frequency response and the internal noise that serves as an additional noise component in the eye-brain system of a human observer.

#### **Materials and Methods**

Equipment used in this study: The Mermaid MGU-100B mammogram, REGIUS V stage Model 190 computed radiography (CR) reader, and CP1M200 (with columnar crystal phosphors) CR plate were used in this study. All this equipment was manufactured by Konica Minolta MG. For perceptual evaluation, we used a 5-megapixel liquid crystal display (5-MP LCD; Totoku). To measure Wiener spectrum (WS), a single-lens reflex type digital camera, Nikon D70.

Study.1: Examination by the 16AFC procedure using simulated images.

We calculated three types of SNRs corresponding to the amplitude model (SNRa), matched filter model (SNRm), and internal noise model (SNRi). SNRa is calculated from the amplitude of the signal and the standard deviation of the noise. This is not considered human visual characteristics and the size of the signal.SNRm is defined as

$$SNR_{m}^{2} = 2\pi \int_{0}^{\infty} u \frac{S_{s}^{2}(u)}{S_{w}(u)} du$$
.

Ss(u) and Sw(u) denote the displayed signal spectrum and the overall WS respectively. Ss is the product of the spatial frequency characteristics of the signal, the overall modulation transfer function (MTF). For the WS calculation, we displayed the image on a 5-MP LCD and captured it using a digital camera. We calculated the WS by the two-dimensional fast Fourier transform (2D-FFT) method. SNRm depends only upon the physical characteristics of the image, and thus, it can be used as the physical image quality index of the model. SNRi, which takes into consideration the spatial frequency response of the human visual system and the internal noise of the eye-brain system, is given as

$$SNR_{i} = \frac{S_{p}}{\sqrt{N_{p}^{2} + N_{i}^{2}}} \setminus S_{p} = \left[ 2\pi \int_{0}^{\infty} uS_{s}^{2}(u)VRF^{-2}(u)du \right]^{\frac{1}{2}}$$

$$N_{p} = \left[ \frac{2\pi \int_{0}^{\infty} uS_{s}^{2}(u)S_{w}(u)VRF^{-4}(u)du}{2\pi \int_{0}^{\infty} uS_{s}^{2}(u)VRF^{-2}(u)du} \right]^{\frac{1}{2}}.$$

VRF(u) is the visual spatial frequency response of the human observer. The value of VRF was obtained from previous literature. Ni denotes the internal noise caused by the noise

inherent in the observer, for instance, the noise associated with neurophysiological instability and memory fluctuations of the observer. The internal noise was estimated to be 0.0076 in brightness contrast units.

In this perceptual evaluation, we employed a 16-alternative forced choice (16-AFC) procedure for the observer performance experiments. In such a procedure, the observer is asked to choose one of 16 boxes as the signal location in a test image. The test images were simulated by the superimposition of lowcontrast signals on a uniform noisy background. This involved 15 imaging cases with various signal sizes, signal contrasts, exposure levels, and number of acrylic plates used as breast phantoms. (Table 1) We displayed the test images on a 5-MP LCD and examined the detection performance. The observation distance was 30 cm and observation time was less than 5 s per image. Six observers participated in this experiment. The signal detection rate was defined as the number of detected signals divided by the total number of images. We studied the relationship between SNR and the signal detection rate using Spearman's rank correlation coefficient.

Table 1. Summary of imaging cases.

	exposure ameter [mAs]	Thickness of acrylic plates[cm]	Diameter [number of pixels]	Contrast of brightness
28	50	6	30	1.84
28	50	6	30	3.61
28	50	6	30	4.48
28	50	6	30	5.33
28	50	6	30	6.98
28	50	6	30	8.58
28	50	6	40	4.48
28	50	6	40	8.58
28	16	6	30	8.58
28	32	6	30	8.58
28	50	4	30	5.33
28	50	4	30	8.58
28	50	8	30	8.58
28	50	8	30	10.87
24	50	6	30	8.58

Study.2: Examination of reduced image using mammography phantom.

We obtained the image of the mammography phantom using Phase Contrast Mammography (PCM) system. The mammography phantom is the CIRS Model 011A breast phantom (Fig.1). The exposure condition was 28kV, 50mAs, and target/filter is Mo/Mo. Because the matrix size of the PCM image is very large, we reduced the PCM image by interpolating methods and reduction ratios. Interpolating methods were nearest neighbor (NN), bilinear (BL), and bicubic (BC). The reduction rate was 5 cases from 0.169 to 0.571. In the same way as first examination, we obtained the spatial frequency characteristics of the mass, the overall MTF, and the overall WS. We calculated three types of SNRs corresponding to SNRa, SNRm, and SNRi.In this perceptual evaluation, the observer read masses in the mammography phantom images and scored. For example, 1 point is that the mass looked completely round shape. Zero point is that the observer could not see the mass. We displayed the phantom images on a 5-MP LCD and examined the detection performance. The observation distance was 30 cm and observation time was optional. Ten radiation technologists participated in this experiment. We studied the relationship between SNR and the average score of ten observers

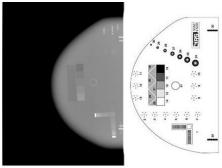


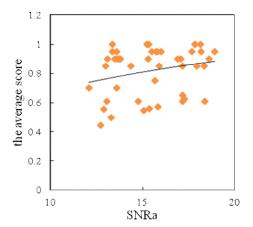
Fig.1. CIRS Model 011A breast phantom

#### Results

Spearman's rank correlation coefficients of Study1 and Study2 are shown in Table 2. The relationships between the average scores and the three SNR types (Study 2) are shown in Fig.2.

Table 2. Spearman's rank correlation coefficients

Perceptual evaluation vs.	Correlation coefficient			
image quality index of:	Study1	Study2		
Amplitude model	0.45	0.26		
Matched filter model	0.90	0.80		
Internal noise model	0.93	0.79		



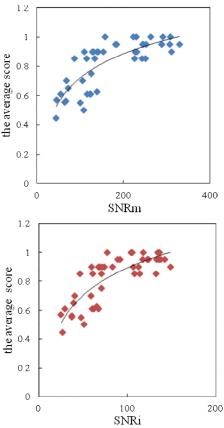


Fig.2. Relationship between the average scores and the three SNR types.

#### Discussion

The correlation coefficient of the SNRa was 0.45 and 0.26. There is poor correlation between the SNRa and the detectability. Because The SNRa depends only upon the signal contrast and the standard deviation of the noise, and the size of the signal is not taken into account. So we think SNRa is inadequate image evaluation. We confirmed that the correlation coefficient of SNRi was the highest among the three SNR types. The SNRm is not considered human visual characteristics, but it was at the same level as the SNRi.

In the previous study, SNR was calculated using film density of screen-film system. However we used brightness of the display in digital mammography systems. We thought that brightness is better to compare SNR with the perceptual evaluation.

#### Conclusions

SNRm and SNRi explained the visual image quality well. Therefore, we conclude that SNRm and SNRi are useful for evaluating low-contrast images.

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#### Author address

E-Mail: hayashi.yui@b.mbox.nagoya-u.ac.jp

## Development of a high resolution gamma camera system with photon counting semiconductor detector: a simulation study

Young-Jin Lee, Hyun-Ju Ryu, Hyo-Min Cho, Seung-Wan Lee, Yu-Na Choi, Hee-Joung Kim.
Department of Radiological Science, College of Health Sciences,
Yonsei University, Gangwon-do, Republic of Korea

**INTRODUCTION:** The photon counting detector based on CdTe or CZT has some benefits compare to the scintillation detector. Especially, the signal from photons was collected individually for each pixel, and thus the intrinsic resolution of the detector is almost the same as the size of a pixel. However a disadvantage of this detector was a loss in sensitivity due to the small pixel on the detector. By using the pixelated parallel-hole collimator, we may be able to improve the sensitivity and the spatial resolution. In this study, we simulated the gamma camera system using the photon counting detector based on CdTe and CZT, and evaluated the performance of these systems.

The purpose of this paper was to evaluate high resolution gamma camera system with semiconductor detector, which had very small pixels, using pixelated parallel-hole collimator. For that purpose, we evaluated the sensitivity, spatial resolution and contrast resolution with Geant4 Application for Tomographic Emission (GATE) simulation.

**METHODS:** To evaluate the image performance of our proposed system we performed simulation with GATE version 6 in this study. The proposed system used the CZT and CdTe detector with small pixel. The size of pixel was  $0.35 \times 0.35 \text{ mm}^2$  and the number of pixels was  $128 \times 128$  such as PID 350 (Ajat Oy Ltd., Finland) CdTe detector. The thickness of the detector was 1 mm. We designed pixelated parallel-hole collimator, which has the same hole size to the pixel size. The shape of the collimator hole was square, and the size of the hole was  $0.3 \times 0.3 \text{ mm}^2$ . The thickness of the septum was  $0.05 \times 0.05 \text{ mm}^2$  and length of a hole was 20 mm. We evaluated the sensitivity, spatial resolution, and contrast resolution to identify the pixelated parallel-hole collimator that provides the best resolution and highest sensitivity of the gamma camera system based on a PID 350 CdTe detector.

**RESULTS:** The average measurement data of the sensitivity was 0.00464 counts/sec/kBq. Also, the proposed system achieved 0.42 mm spatial resolution when the source was located 0 cm from the collimator. The acquired spatial resolution was similar to spatial resolution of the pinhole collimator, which was the best in the field of nuclear medicine. The results showed that the measured average data of CZT detector and CdTe detector was 96.30% and 96.72%, respectively.

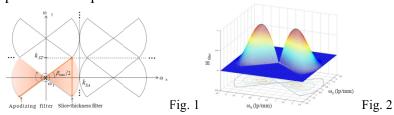
**CONCLUSION:** We simulated a high resolution gamma camera system with a CdTe and CZT detector and pixelated parallel—hole collimator. By using the pixelated parallel—hole collimator, we were able to acquire the excellent spatial resolution since the intrinsic resolution was equal to the pixel size. Also the results of simulations showed that gamma camera images measured with a CdTe and CZT detector had high contrast resolution and superb sensitivity in small pixel condition. In conclusion, our results demonstrated that we established the high resolution gamma camera system with the pixelated parallel—hole collimator.

## Optimal Design of a Deblurring Filter in Digital Tomosynthesis for the Application of Dental X-ray Imaging

J. E. Oh<sup>1),2)</sup>, H. S. Cho<sup>1)</sup>, D. S. Kim<sup>1)</sup>, S. I. Choi<sup>1),2)</sup>, Y. O. Park<sup>1)</sup>, D. K. Hong<sup>1),2)</sup>, U. K. Je<sup>1),2)</sup>, M. S. Lee<sup>1)</sup>, H. J. Kim<sup>1)</sup>, S. H. Lee<sup>1)</sup>, Y. S. Koo<sup>1),2)</sup>, and S. O. Na<sup>2)</sup>
1) Department of Radiological Science, Yonsei University, Wonju 220-710, Korea
2) R&D Center, Vatech Co. Ltd., Hwasung 445-811, Korea

**INTRODUCTION:** The application of digital tomosynthesis (DTS) in dental X-ray imaging such as endodontics or implant placement seems promising since it provides attractive advantages of low patient dose and less motion blur. Since DTS only provides incomplete 3D data of the imaged object(Fig.1), it is critical to design and incorporate an optimal deblurring filter into reconstruction algorithm.

**METHODS**: In this paper, we describe a systematic approach to optimal filter design(fig.2) and investigate the optimization of the scan process such as the scan angle, the number of projections, the object magnification, and so on, for optimal image quality. Tomosynthetic images are reconstructed by filtered backprojection (FBP) method as well as by simple backprojection method. In order to verify the usefulness of the DTS reconstruction algorithm, we developed a simulation code implemented in MALTAB 7.8® for systematic simulation studies, and also performed experimental works.



**RESULTS:** In the simulation, DTS images were reconstructed for several simulation conditions ( $\beta_{\text{max}} = 35^{\circ} \sim 180^{\circ}$ ,  $\Delta\beta = 0.46^{\circ} \sim 3.0^{\circ}$ ) and the performance was evaluated by means of the ASF and the SDNR. As shown in Fig. 3, the ASF, as a measure of deblurring effect, may be sensitive to total scan angle, but not to scan angle step. It also seems to moderately sensitive to voxel size. We applied the same algorithm to our dental cone-beam CTs which have pixel sizes of 48  $\mu$ m and 200  $\mu$ m, and achieved very promising results with test conditions of  $\beta_{max} = 74^{\circ}$ ,  $\Delta\beta = 0.74^{\circ}$ . The blurring was mostly removed by the optimal deblurring filter we designed in Fig. 4.

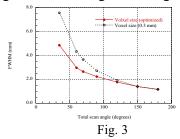




Fig. 4

**CONCLUSION:** According to our results, the blurring due to the incomplete sampling was mostly removed by the optimal deblurring filter we designed, thus recovering high spatial resolution as well as high contrast. We expect that the proposed reconstructed algorithm may be useful for our ongoing application of three-dimensional (3D) dental panoramic tomography.

### **Evaluation of Spectral Distortion Effects on X-ray Imaging with a Photon-Counting Detector**

<u>Hyo-Min Cho</u>, Yu-Na Choi, Seung-Wan Lee, Hyun-Ju Ryu, Young-Jin Lee, and Hee-Joung Kim

Department of Radiological Science, College of Health Sciences, Yonsei University, Gangwon-do, Republic of Korea

**INTRODUCTION:** The photon counting detector has received considerable interest in recent years due to its advantages over charge-integrating detectors. However, there are several factors that can limit to the use of the photon-counting detector. These include the charge sharing effects can't be controlled by operator and the pulse pile-up effects can be reduced by modulating incident number of photons. In this paper, we evaluated the effects of spectral distortion by pulse pile-up effect on X-ray imaging using simulation and experimentation.

**METHODS**: The photon-counting imaging system used in this study consisted of a micro focus X-ray source (L8601-01, Hamamatsu, Japan) and CdTe detector (PID 350, AJAT, Finland). The CdTe detector was positioned 1000 mm from the X-ray source focal spot. Phantom images and relevant energy spectra were acquired at 70 kVp and 10 μA for 20 sec. The photon rejecter can decrease spectral distortion due to pulse pile-up by reducing amount of incident photon. Aluminum plate was used as photon rejecter. The X-ray tube output was filtered with three different aluminum plate thicknesses (1, 5, and 10 mm). The photon counting X-ray imaging system was simulated using the Geant4 Application for Tomographic Emission (GATE) V6. The detected image and spectrum were assumed to be ideal, without spectrum distortion. The contrast-to-noise ratio (CNR) between the material and background was considered as a comparison factor of spectral distortion effect on the image.

**RESULTS:** From the simulation study, the total number of photons was dramatically reduced according to aluminum filter thickness, especially at low energy. By contrast, the spectra showed high number of photons detected in the low energy part in experiment. Pulse pile-up effects that have not been completely corrected with 1 mm aluminum filter contribute to the more counts recorded at energies above 70 keV. Even though 5 and 10 mm aluminum filter minimized pulse pile-up effect the photon rejecter has the limited ability to reduce the pile-up effect. In addition, the photon rejecter separated electrical noise from the spectrum by reducing the number of photons. In the simulation results, the factor that contributed to the low CNR values with the thick aluminum filter was due to quantum noise by a lack of photons. In the experimental results, the effect of noise due to a lack of photons was very slight in comparison to the simulation results because the photon-counting detector was already limited an acceptable number of photons by detector electronics. However, the images were greatly influenced by the electronic noise which is distinguishable by filter thickness.

**CONCLUSION:** In conclusion, the spectral distortion affects the image quality by increasing low energy photons, but optimal photon rejecter is feasible to increase image quality by minimizing the pulse pile-up effect and remove separated electronic noise from the signal.

## Development of a CdTe detector SPECT-CT system for a small animal imaging: a simulation study

Hyun-Ju Ryu, Young-Jin Lee, Seung-Wan Lee, Hyo-Min Cho, Yu-Na Choi, Hee-Joung Kim Department of Radiological Science and Research Institute of Health Science, Yonsei University, Korea

**INTRODUCTION:** Single photon emission computed tomography (SPECT) system with a co-registered x-ray computed tomography (CT) image allows the fusion of functional information and morphologic information. In this study, a pinhole collimator SPECT system sharing a CdTe detector with a CT was designed. Geant4 application for tomographic emission (GATE) version 6 was used for the design simulation. Sensitivity and spatial resolution were measured to evaluate the system characteristics on an ideal condition.

METHODS: The SPECT/CT sharing a single CdTe detector was designed to have one gantry for both x-ray CT and SPECT system. The size of the detector was 44.8×44.8 mm<sup>2</sup> with 128×128 pixels, and the thickness of the detector was 1 mm. The SPECT/CT system was designed with a pinhole collimator and CdTe detector (Oy Ajat Ltd., Finland) using GATE version 6.0. For the SPECT system, a pinhole collimator was designed to have a high spatial resolution. 60 projections were obtained for tomographic image acquisition of the SPECT system. The reconstruction was performed using ordered subset expectation maximization (OS-EM) algorithms. The x-ray generator was designed to rotate around the center of field of view (CFOV), and the gantry was rotated with x-ray tube and detector to have 256 projections of the object over 360 degree. The pinhole collimator was removed while the x-ray imaging was processed. For the CT imaging, 256 projections were acquired on 80 kVp with 50 mm aluminum filter to reduce low energy photon flux. A water phantom with background activity of 25 MBq and hot lesions with 100 MBq was simulated on both CT and SPECT system. Total 256 projections of CT images and 60 projections of SPECT images were reconstructed using OSEM algorithm. The energy window of the CT data acquisition was set from 30 keV to 80 keV.

**RESULTS:** The pinhole collimator was designed to have a sub-mm resolution for a small animal imaging SPECT system. Though the SPECT system was simulated in an ideal condition, the spatial resolution of the system was measured 0.48 mm as expected from the pinhole collimator geometry. The MTF curve was calculated from the PSF of the reconstructed point source image. The sensitivity of the system measured 0.354 cps/kBq from a Tc-99m point source. The phantom images of x-ray CT, SPECT were fused to demonstrate the image registration of different modalities.

**CONCLUSION:** The CdTe detector can be used for x-ray and gamma ray imaging system. The detector can be performed for both CT and SPECT system because of this characteristic. The object stays in a same position, and it gives an advantage on the image registration of different modalities. The designed pinhole collimator for single detector SPECT/CT had a fine spatial resolution for a small animal SPECT imaging. A CdTe detector with 1 mm thickness was evaluated in this study. The system will have better detection efficiency with a thicker CdTe detector. The designed pinhole collimator SPECT/CT with CdTe detector can be applied for the pre-clinical imaging system.

#### Simulation study of in-beam PET system for dose verification in carbon ion therapy

Su jung An, Cheol-Ha Baek and Yong Hyun Chung.

Department of Radiological Science, College of Health Sciences,
Yonsei University, Gangwon-do, Republic of Korea

**INTRODUCTION:** Application of hadron such as carbon ion is being developed for cancer treatment. This is due to eligibility of charged particles in delivering most of their energy near the end of their range, called Bragg peak. However, accurate verification of dose delivery is required since the mis-alignment of the hadron beam can cause serious damage to normal tissues. PET scanner can be utilized to track the carbon beam down to the tumor by imaging the trail of the hadron-induced positron emitters in the irradiated volume. In this study, we designed and evaluated through Monte Carlo simulation the in-beam PET scanner for monitoring patient dose in carbon beam therapy.

#### **METHODS:**

#### 2.1. Designing of in-beam PET scanner

PET scanner with 30.2 cm inner diameter was designed for brain imaging. Each detector module consists of an LYSO array of  $13 \times 13$  elements with pixel size of  $4 \times 4 \times 30$  mm<sup>3</sup> and four round PMTs with 25.4 mm diameter.

A C-shaped PET and a partial-ring PET were designed to avoid interference between PET detectors and the therapeutic carbon beam delivery and their performance were compared with a full-ring PET scanner. The C-shaped, partial-ring and full-ring scanners consist of 14, 12 and 16 detector modules, respectively,

To evaluate three types of PET, we simulated five point sources at different positions and measured spatial resolution and sensitivity.

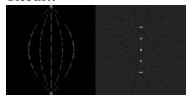
#### 2.2. Generation of positron-emitting nuclei by carbon ions

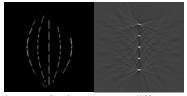
GATE (Version 6.1) was used to simulate the generation of positron emitting radio-nuclides by carbon irradiation in PMMA phantom. The beam profiles in the transverse directions were assumed to be a Gaussian with a FWHM of 10 mm. The beam energy spread was taken with a FWHM of 0.2%. To validate the simulator, yields of positron-emitting nuclei( $^{11}$ C,  $^{10}$ C, and  $^{15}$ O) produced by 212.12, 259.5, 343.46 AMeV carbon in the PMMA phantom with  $9 \times 9 \times 30 \text{ cm}^3$  were compared to simulated and measured data from other groups. The yields of  $^{11}$ C,  $^{10}$ C,  $^{15}$ O produced by 170, 290, and 350 AMeV carbon beams (those energies were selected to be used in KHIMA) in the PMMA cylinder phantom with 20 cm diameter and 20 cm height were simulated. This output was used as an input file in subsequent PET image acquisition simulations.

#### 2.3. In-beam PET imaging with three types of PET scanners

To calculate the number of positron annihilations used as source activity in PET imaging, ion beam was assumed that has a tunable time structure given by repetition of particle extractions (spills) and pause. PET images are acquired during half life of  $^{11}$ C nuclei on the assumption that carbon beam intensity was  $1 \times 10^8$  #/sec and total therapeutic time of 2 minutes (48 seconds of irradiation). Phantom images were acquired for three types of scanners. Dose distribution was compared  $\beta^+$  activity distribution and PET image profile, respectively.

#### **Result:**





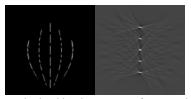


Fig. 1. The sinograms and reconstruction images of point sources at different positions obtained by three types of scanner by GATE simulation.

Fig 1 demonstrates simulated sinograms and reconstructed images of point sources at different positions acquired by three types of scanners. Spatial resolution in x- and y-directions and sensitivity are summarized in Table 1, 2 and 3. Results demonstrate that the spatial resolution in x-direction is reduced for sources located at periphery of FOV where detector modules are removed for carbon beam line. Sensitivity depends on the number of detector modules.

Detector	X-axis Resolution [mm]					
type	1	2	3	4	5	
Full ring	7.93	6.23	5.88	6.36	7.70	
C-type	9.29	7.15	7.33	8.63	14.59	
Partial- ring	15.51	8.47	7.41	8.65	14.64	

Detector	Y-axis Resolution [mm]					
type	1	2	3	4	5	
Full ring	4.89	5.15	5.28	4.97	4.98	
C-type	4.90	5.17	5.30	4.93	4.97	
Partial- ring	4.88	5.13	5.32	4.94	4.98	

Detector type	Sensitivity (%)
Full ring	1.69
C-type	1.26
Partial-ring	1.12

Table 1. X-axis Resolution of 5 points.

Table 2. Y-axis Resolution of 5 points.

Table 3. Sensitivity in 3 types of scanners.

Table 4 shows calculated yields of positron-emitting nuclei produced by 212.12, 259.5, and 343.46 AMeV of <sup>12</sup>C ions to verify GATE simulator and results agree well with reference data. (per beam particle, in %) MCHIT is Simulated data and Experiment is measured data from [Phys. Med. Bio. 51 (2006) 6099-6112]. Table 5 summarized the calculated yields of positron-emitting nuclei produced by 170, 290, and 350 AMeV of <sup>12</sup> C ions in the PMMA phantom. (per beam particle, in %)

	2	12.12 AMe	V		259.5 AMeV	/	343.46 AMeV		343.46 AMeV		170 AMeV	290 AMeV	350 AMeV
	MCHIT	Experime nt	GATE6	MCHIT	Experime nt	GATE6	мсніт	Experime nt	GATE6	пС	6.86	15.06	18.80
11 <b>C</b>	11.9	10.5±1.3	9.73	16.83	14.7±1.6	13.11	25.25	19.9 <u>±</u> 2.4	18.43	10C	0.99	2.08	2.62
<sup>10</sup> C	1.97	0.8±0.3	1.38	2.79	1.2±0.3	1.85	4.27	1.5±0.3	2.57		0.99	2.00	2.02
15 <b>O</b>	2.38	2.1±0.3	1.71	3.69	3.1±0.4	2.36	6.09	5.0±0.4	3.48	<sup>15</sup> O	1.17	2.79	3.57

Table 4. Calculated yields of positron-emitting nuclei(per beam particle, in %) produced by 212.12, 259.5 and 343.46 AMeV <sup>12</sup> C ions in the PMMA phantom.

Table 5. Calculated yields of positron-emitting nuclei(per beam particle, in %) produced by 170, 290, and 350 AMeV <sup>12</sup> C ions in the PMMA phantom.

Reconstructed PET images and their longitudinal profiles are shown in Fig 3. For comparison, simulated dose distribution and  $\beta^+$  activity distribution are also shown.

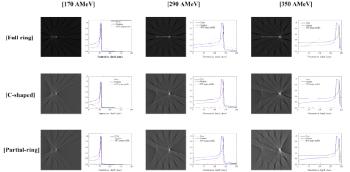


Fig. 3. Reconstructed PET images and their longitudinal profiles by three types of scanner by GATE simulation.

**CONCLUSION:** We proposed C-shaped and partial-ring scanners for dose verification in carbon ion therapy. We validated that GATE is feasible to predict the total yields of positron emitting nuclei with reasonable accuracy. The C-shaped scanner shows better spatial resolution and sensitivity than the partial-ring scanner. The accuracy of range estimation, especially for higher energy of carbon beam, is higher in the C-shaped scanner in comparison to partial-ring scanner due to their geometric difference. Though  $\beta^+$  activity distributions induced by carbon beams differ in shape from the corresponding dose distribution, there exists a decisive correlation between them, which can be used for the dose and range monitoring. Because the PET image profile is well matched with  $\beta^+$  activity distributions, we can conclude that PET has the potential feasibility for dose verification. Our investigation indicated that C-shaped scanner is more suitable as the in-beam PET.

# Abstracts Physical Therapy

## ACUTE BUT NOT DELAYED ONSET OF FORCED IMPAIRED FOREPAW USE PROMOTES PLASTICITY AND FUNCTIONAL RECOVERY IN RATS AFTER CAPSULAR HEMORRHAGE

Akimasa Ishida<sup>1), 2)</sup>, Keigo Tamakoshi<sup>1)</sup>, Hiroki Nakashima<sup>1)</sup>, Haruka Shimada<sup>1)</sup>, Hideki Hida<sup>2)</sup>, Kazuto Ishida<sup>3)</sup>

Program in Physical and Occupational Therapy, Nagoya University Graduate School of Medicine, Nagoya, Japan
 Neurophysiology and Brain Science, Nagoya City University Graduate School of Medicine, Nagoya, Japan
 Department of Physical Therapy, School of Health Science, Nagoya University Nagoya, Japan

#### Introduction

Upper limb hemiparesis often occurs after stroke, and it disturbs patients' ability to complete activities of daily living [1]. Forced impaired limb use (FLU), which is known as constraint-induced movement therapy, is promising method to promote functional recovery after stroke. However, little is known about the detailed changes in the brain caused by FLU. The present investigation is aimed at (1) examining behavioral and histological changes caused by FLU after internal capsule hemorrhage (ICH) and (2) comparing the effect of early- (1-8 days after ICH) and late- (17-24 days) FLU in ICH model rats.

#### **Materials and Methods**

Experimental setup: Adult male Wistar rats (250-300g) were housed at a 12 h light/dark cycle with food and water ad libitum. Rats were divided into the following experimental groups: animals receiving a sham operation (sham; n=6), sham operation with forced-use of dominant forelimb (Sham-FLU; n=6), ICH with no treatment (ICH; n=9), and animals with early and late onset of FLU after ICH (ICH-E-FLU; n=6, ICH-L-FLU; n=6). All experimental procedures were performed in accordance with the animal care guidelines of the Nagoya University. Figure 1 shows a timeline of the performed experiments.

Intracerebral hemorrhage: In the present study, we used internal capsule hemorrhage model [2]. Under deep anesthesia by sodium pentobarbital (45 mg/Kg, intraperitoneally), rats were injected collagenase (15 Units/ml, 1.4 µl, Type IV; Sigma-Aldrich, St. Louis, MO, USA) or sterile saline into the internal capsule contralateral to the dominant forepaw. Figure 2 shows a typical histological appearance of hemorrhage.

Forced-impaired limb use: FLU-treated rats were fitted with a 1-sleeve plaster cast at 24 hrs after ICH surgery. The upper torso and the unimpaired/unpreferred forelimb were wrapped in soft felt and Plaster of Paris strips. Rats were forced to completely rely on either their impaired/preferred forelimb for one week beginning 1 or 17 days after surgery.

Behavioral assessments: Behavioral recovery was tested in single pellet reaching test (for skilled reaching function) and horizontal ladder test (for forelimb stepping function) on 10-12 and 26-28 days post ICH. Figure 3 shows the appearances of these tests.

 $\Delta FosB$  Immunohistochemistry: Immediately after the FLU period of each group, the rats were deeply anesthetized and perfused transcardially with 0.9% saline followed by 4% phosphate-buffered paraformaldehyde (pH 7.4). The brains were removed and postfixed, and then 40  $\mu m$  thick coronal sections were obtained using a cryostat. Sections collected form sensorimotor cortex (SMC) forelimb area were processed with  $\Delta FosB$  immunostaining. The primary antibody was rabbit polyclonal anti-FosB/ $\Delta FosB$  sc-48 (1:400, Santa Cruz Biotechnology, Santa Cruz, CA, USA),

and the secondary antibody was goat anti-rabbit IgG (1:200, Sigma). The number of  $\Delta FosB$ -positive cells located in the SMC of the injured and intact hemisphere was counted from six sections per animal.

Real-time PCR assay: Separate cohorts of animals exposed to the same FLU treatment were used for quantitative transcription polymerase reaction (PCR) analysis. SMC forelimb region harvested at the end of the FLU period was analyzed by real-time PCR of brain-derived neurotrophic factor (BDNF) and growth-associated protein 43 (GAP43).

Golgi-COX staining: To investigate anatomical changes of SMC neurons, Golgi-COX staining was conducted. Rats were perfused with 0.9% saline and extracted their brains on 14 and 30 days after ICH. Collected brains were stored in Golgi-Cox solution for 14 days in the dark and then immersed in 30% sucrose solution for another 2 days before sectioning. Coronal brain sections were cut using a vibratome at 200  $\mu m$  and developed as previously described [3]. Six pyramidal neurons located to layer V in the contralateral and ipsilateral SMC were selected per animal. Dendritic branching was analyzed by Sholl analysis, which examines the number of intersections of dendritic branches and rings, at 20  $\mu m$  intervals from the cell body [4].

Statistical analyses: All data were analyzed using parametric ANOVA of the appropriate design, followed by Tukey-Kramer post hoc comparisons whenever a main effect or interaction attained statistical significance. All statistical analyses were conducted using the statistical software SPSS (release 12.0). Data are presented as means ±SEM.

#### Results

Behavioral assessment: After FLU treatment, improvement of the skilled reaching task in single pellet reaching test was found in the ICH-E-FLU group in comparison with ICH untreated. Better performance of skilled forelimb stepping in ladder test was also shown in the ICH-E-FLU group than ICH group. Although ICH-L-FLU rats also showed a slight recovery in ladder stepping task, they could not show functional recovery in the pellet reaching task.

 $\Delta FosB$  Immunohistochemistry:  $\Delta FosB$ , which is cumulatively and persistently expressed in response to repeated neuronal activation [5], is suitable molecular marker for investigations of practice-dependent plasticity. Abundant  $\Delta FosB$ -positive cells were found in SMC forelimb region of lesioned hemisphere after early-FLU. In contrast, no significant changes of the number of  $\Delta FosB^+$  cells among groups were found after late-FLU. In the intact SMC, all groups showed similar  $\Delta FosB^+$  cells number.

Real-time PCR assay: BDNF and GAP43 are known as growth-related factors and involved in synaptic plasticity and axonal expansion. As the results of  $\Delta FosB$  assay, BDNF and GAP43 mRNA expressions were significantly increased in the

affected side of SMC in ICH-E-FLU group compared with sham and control group, but were not in ICH-L-FLU group.

Golgi-COX staining: Golgi-Cox staining revealed that the increase of dendritic arborization was occurred in affected SMC of ICH-E-FLU group compared to ICH only group, whereas significant changes were not seen between ICH-L-FLU group and ICH group.

#### Discussion

These data demonstrated that forced-use of impaired forelimb after internal capsule hemorrhage induces repetitive neuronal activation and upregulation of trophic factor expression in the forelimb sensorimotor cortex of affected side of brain. Additionally, plastic change of dendrites was enhanced by FLU in the same area in parallel with behavioral recovery. These data suggest that FLU after brain injury could cause functional and anatomical plastic changes in the SMC. Additionally, in the case of small ICH, SMC in the affected hemisphere may be a key region for functional recovery. The plastic changes caused by FLU were not seen in the rats treated delayed onset of FLU after ICH. These results raise the possibility that FLU may involve the acute event of brain injury (e.g. temporal increase of neuronal excitability).

#### Conclusions

Forced-use of impaired forelimb after capsular hemorrhage induced better recovery of skilled reaching and stepping of the impaired limb. This functional recovery might be related plastic changes of neuronal activity, growth-related factors expression, and dendritic branching in the affected sensorimotor cortex. These plastic changes caused by FLU were more apparent in the rats treated early onset of FLU than in the rats of delayed after subcortical small hemorrhage.

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#### **Author address**

E-Mail: ishida.akimasa@c.mbox.nagoya-u.ac.jp

Figure 1. Timeline of the experiments

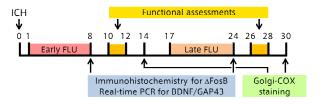


Figure 2. Typical photograph of internal capsule hemorrhage

Hematoxylin and eosin staining 30 days after ICH shows small hemorrhage localized the internal capsule.



#### Figure 3. Behavioral tests

(A) Single pellet reaching test: Reaching to retrieve pellets through a narrow slit by their impaired forelimb was analyzed.(B) Ladder test: Crossing the 1-m long ladder was videotaped and assessed the rate of fall step.





#### THE EFFECT OF PASSIVE MOVEMENT ON HETEROTOPIC OSSIFICATION

#### IN EXPERIMENTAL MODEL MICE OF SPINAL CORD INJURY

K. Murase<sup>1)</sup> , M.Kawamura<sup>2)</sup>

- 1) Nagoya University Graduate School of Medicine, Nagoya, Japan
- 2) Department of Physical Therapy, School of Health Sciences, Nagoya University, Nagoya, Japan

#### Introduction

Heterotopic ossification (HO) is a pathological bone formation which is induced in normal soft tissue around a bone and/or a joint. It is known as a sequela of spinal cord injury, a cerebrovascular accident, a trauma in four extremities and a postarthroplastic surgery. It often occurs around large joints and causes meticulous pain and a limitation of range of motion in pathological joints. Consequently, it could be a great obstacle in rehabilitation process.

However, the reason for the development of HO is still unclear. Clinically, some written articles report that high incidence of HO can be seen in paralytic patients due to damage of central nervous system, for example in spinal cord injury [1]. It is still disputable whether passive movement for paralytic extremities enhances or inhibits the development of HO [2][3].

In this study, we made experimental model mice of HO under spinal cord injury, and investigated the effects of enforced passive movement on the new bone formation in the paralytic limbs of these animals.

#### **Materials and Methods**

Eleven ddY-line male mice, 6-weeks-old, underwent laminectomy at the level of 8th thoracic vertebra while under anesthesia of pentobarbital. A weight of 3 grams was dropped directly onto the exposed spinal cord of each mouse from a height of 3 centimeters to make the experimental model mouse of spinal cord injury [4][5]. After a week of evaluation of the grade of paralysis, all the animals were recognized to be completely paralytic.

Three milligrams of powdered bone morphogenetic protein (BMP) was stuffed into the gelatin capsule and implanted in the muscle pouch of their hamstrings. BMP is a non-collagenous protein which is usually extracted from the matrix of the cortical bone, enamel bone or osteosarcoma, and has biological ability to differentiate the mesenchymal cells into bone and/or cartilage tissue. Therefore, it is an expected material to use when making an experimental animal model of HO [6][7]. This time, we prepared the BMP, which had been crudely extracted from a porcine long bone cortex and had been verified to have the appropriate activity to make HO.

From the day after implantation, passive flexion-extension movement was applied to the left side of the knee joints of 11 mice (CPM group) with a continuous passive movement (CPM) machine. This involved passive movement 60 times per minute, 20 minutes per day, 6 days a week, with 60 degrees of knee flexion-extension, for 3 weeks. The contralateral side of the knee joint of each mouse were assigned to the non-CPM group.

After 3 weeks of passive movement, the new bone formation was identified through soft X-ray film. According to the film image, the new bone tissue was excised out from the sample, and sintered at 1,000  $^{\circ}$ C for 60 minutes to obtain the ash weight of the sample. The ash weight was calculated per gram body weight of each animal. A statistical difference between two groups was studied by unpaired t analysis. The significance was set at P < 0.05.

#### Results

Figure 1 shows new bone formation images through a soft X-ray film. The CPM group (fig.1, left) shows more extensive new bone formation compared with the non-CPM group (fig.1, right).

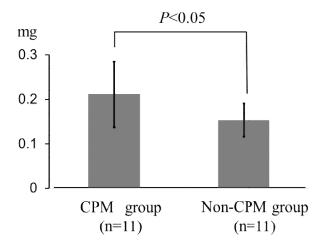
The volume of newly formed bone (ash weight per gram body weight of each mouse, mean  $\pm$  SD) was  $0.21 \pm 0.07$  mg / gram body weight (n=11) in the CPM group and  $0.15 \pm 0.04$  mg / gram body weight (n=11) in the non-CPM group (Figure 2). A Statistical difference was recognized between the two groups (P<0.05).

Figure 1: Soft X-ray image of the new bone formation



An extensive new bone formation was recognized in CPM group (left), but was not in the non-CPM group (right).

Figure 2: Ash weight (mg) per gram body weight



The ash weight in the CPM group showed more new bone formation than that of the non-CPM group. It was statistically significant (P < 0.05)

#### Discussion

In this study, the more extensive new bone formation was recognized in the experimental spinal cord model mouse. Furthermore, the enforcement of passive movement on the murine knee joints with a CPM machine enhanced a new bone formation compared with the non-CPM group. It means that HO in mice under the condition of spinal cord injury will be enhanced by enforced passive joint movement.

It is considered that not only paralytic state or enforced passive movement, but also local edema, poor circulation, local infection and metabolic dysfunction, might be pathogenetic factors of HO. It is also considered that the combination of these factors might enhance the incidence of the growth of HO<sup>[8]</sup>. Especially, in the state of spinal cord injury, we often observe some of these factors in which HO occurs much more easily. In this study, we further added the enforced passive joint movement to the state of spinal cord injury, and consequently the growth of HO might be enhanced.

The results of this study show that enforced passive movement enhances HO. On the other hand, a report has been written that passive movement inhibits HO. The extent of passive joint movement might have an effect on the growth of HO. Therefore, further investigation under the various condition of enforced passive movement, especially under the lower extent of enforcement, will be needed.

#### Conclusion

The extensive volume of new bone formation was recognized in the experimental model mouse of spinal cord injury. Enforced passive joint movement also enhanced the new bone formation in the same model. The process of the growth of HO which was seen in this study, resembled the clinical case of HO in the human body. Consequently, this kind of study could be a clue to clarify the pathogenesis of HO and developing the preventive modality for HO.

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#### **Author address**

E-mail: <u>murase.kazuma@c.mbox.nagoya-u.ac.jp</u> <u>kawamura@met.nagoya-u.ac.jp</u>

## Association between intensity of physical activity and arterial stiffness in older adults.

Y. Hagiwara<sup>1)</sup>, H.Okumura<sup>1)</sup>, T.Kitano<sup>1)</sup>, S.Ishida<sup>1)</sup>, Y.Kono<sup>1)</sup>, H.Sampei<sup>1)</sup>, M.Yoshida<sup>1)</sup>, K. Iwatsu, S.Yamada<sup>2)</sup>

Program in Physical and Occupational Therapy, Nagoya University Graduate School of Medicine, Nagoya, Japan
 Department of Physical Therapy, School of Health Sciences, Nagoya University, Nagoya, Japan

#### Introduction

Arterial stiffness, one of the indices of arteriosclerosis, has been established as a predictor of coronary heart disease and stroke [1]. Aging is associated with structural and functional changes of the vessel wall, and resulted in worsening of arterial stiffness. Previous studies reported that amount of physical activity associated with improved arterial stiffness [2,3]. However, the relationship between intensity of physical activity and arterial stiffness were unclear. This, this study aimed to examine the relationship between intensity of physical activity and arterial stiffness.

#### **Materials and Methods**

Subjects: Study subjects were comprised of 147 community-dwelling elderly people over 60 years old (73.5  $\pm$  5.7 yo, 39 males and 108 females). People who had smoking habit, abnormal ankle-brachial pressure index (ABI) and any orthopedic disorders were excluded.

Study Protocol: We assessed cardio ankle vascular index (CAVI), physical activity, body mass index (BMI), home blood pressure, lipid profile(HDL, LDL-cholesterol), HbA1c. Written informed consents were obtained from all participants, and this study protocol was approved by the Ethics Committee of the school of Health Sciences, Nagoya University.

Assessment of arterial stiffness: We assessed CAVI as a parameter of arterial stiffness. Measurements were carried out after a 5-min rest in the supine position with the upper body as flat as possible. CAVI was mesured from pulse wave velocity and blood pressure by using a Vasera VS-1000 vascular screening system (Fukuda Denshi). CAVI has characteristics of less influenced by blood pressure.

Assessment of physical activity: We assessed physical activity by using an electrical accelerometer (Kenz Lifecorder, Suzuken). The device mesures the number of steps and intensity of physical activity. The intensity was classified ranged 0-9 based on Lifecorder intensity. All participants were instructed to put on the accelerometer themselves and were instructed to use the pedometer 24 h/day for 1 week, except while bathing and sleeping.

Data analysis: Continuous variables are expressed as mean  $\pm$  standard deviation (SD). The association between PMADL-8 and clinical variables were analyzed by Pearson $\Box$ s or Spearman correlation coefficients. For investigating differences affected by aging, subjects divided into two groups (60-74 years old or over 75 years old). All statistical analyses were performed by SPSS 16.0 software package (SPSS Japan, Tokyo, Japan), and a P<0.05 was considered statistically significance.

#### Results

Subject characteristics are showed in Table 1. The correlations between CAVI and other parameters are presented in Table 2. Intensity of physical activity indicated weak but significant negative correlation with arterial stiffness.

(Figure 1). On the other hand, daily step count did not indicated significant correlations.

Age was most related to CAVI. To examine the influence of age-related increases in arterial stiffness on association between CAVI and physical activity, we divided subjects into two groups(60-74years old or over 75years old). In 60 - 74 years old group, duration of physical activity over Lifecorder intensity 6 and intensity 7 were significant negative correlations. Meanwhile, in over 75 years old group, intensity of physical activity tended to relate to CAVI, but there was no significance.

In other factors, home systolic blood pressure and HbA1c showed significant but weakly correlation. BMI, home DBP, LDL cholesterol, HDL choresterol did not indicate any correlation

Table 1 Subject characteristics

	$Mean \pm SD$				
Age	73.5	±	5.7		
BMI (kg/m²)	21.8	$\pm$	2.8		
CAVI	9.1	$\pm$	0.9		
Home SBP (mmHg)	135.5	$\pm$	19.6		
Home DBP (mmHg)	78.7	$\pm$	11.1		
LDL cholesterol(mg/dL)	115.8	$\pm$	25.4		
HDL cholesterol(mg/dL)	61.3	$\pm$	13		
HbA1c(%)	5.5	$\pm$	0.58		
Daily step count	7908.2	$\pm$	3521.6		
Duration of physical activity					
in mild intensity ( Lifecordere intensity 1-3 )	55.2	±	19.7		
in moderate intensity ( Lifecordere intensity 4-6 )	24.2	±	19.4		
> Lifecorder intensity 4	25.2	$\pm$	20.4		
> Lifecorder intensity 5	11.7	$\pm$	13.2		
> Lifecorder intensity 6	7.0	$\pm$	9.4		
> Lifecorder intensity 7	1.3	$\pm$	2.6		

Table 2 Relationships between CAVI and other parameters

	r	P
Age	0.504	< 0.001
BMI	-0.076	0.359
Home SBP	0.194	0.018
Home DBP	-0.126	0.127
LDL cholesterol	0.003	0.697
HDL cholesterol	-0.129	0.122
HbA1c	0.187	0.024
Daily step count	-0.105	0.204
Duration of physical activity		
in mild intensity ( Lifecordere intensity 1-3 )	-0.087	0.293
in moderate intensity ( Lifecordere intensity 4-6 )	-0.083	0.310
> Lifecorder intensity 4	-0.097	0.241
> Lifecorder intensity 5	-0.192	0.012
> Lifecorder intensity 6	-0.221	0.007
> Lifecorder intensity 7	-0.310	< 0.001

BMI: Body mass index, SBP: Systolic blood pressure DBP Diastolic blood pressure LDL: Low-density lipoprotein HDL: High-density lipoprotein

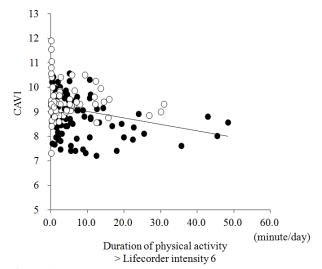


Figure 1
Relationship between CAVI and duration of physical activity more than Lifecorder intensity 6

#### Discussion

The results of present study suggest that duration of high intensity physical activity, rather than total amount of daily steps, associates arterial stiffness in community-dwelling elderly people.

Previous studies reported that habitual exercise associated with improved arterial stiffness. Tanaka et al [4] reported that the relationship between daily exercise and the arterial stiffness by comparing among three different intensity exercise. There was no significant difference between sedentary group and recreationally active group (mild intensity). However, Arterial stiffness in endurance trained group was lower than the other two groups. This result suggested that not only amount of physical activity but also

intensity of physical activity related to arterial stiffness. Our findings support the previous study and suggest that intensity of physical activity is important for preventing age-related increases in arterial stiffness.

It is considered that exercise affects arterial function and structures. In the present study, a certain intensity level of physical activity may have these effects. Matsuda et al evaluated effects of exercise training on aortic wall elasticity and elastic components in rat [5]. Exercise rats had more distensible and higher elastin content in aorta than sedentary rats. But this study was conducted on younger rats. It was unclear that whether exercise affect on arterial structure in elderly adults or human. However, it is possible that pulse pressures and mechanical distensions during the exercise stretch collagen fibers and modify cross-linkings. Therefore increasing arterial extensibility could be expected in human. There is endothelium-depended vasodilation which is arterial function related to arterial stiffness. Desouza et al examined the influence of habitual aerobic exercise on the age-depended reduction in endothelium-depended vasodilatation [6]. The result showed that they did not find any relationship between age and endothelium-dependent vasodilatation in endurancetrained men. Therefore these results indicate that regular aerobic exercise can prevent the age-depended worsening in endothelium-dependent vasodilatation.

We must describe that our recruitment policy tended to favour healthy members of the community. Thus, the sample could have been more active than population of Japan in the same age group, we couldn't find out the threshold of physical activity which has effect of preventing age-depended increases in arterial stiffness.

#### **Conclusions**

The findings of the present study suggest that intensity of physical activity associates with arterial stiffness in community-dwelling elderly population. This result suggests that intensity of physical activity is required to countermeasure age-depended increases in arterial stiffness.

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Author: Yuta Hagiwara

E-Mail: hagiwara.yuta@h.mbox.nagoya-u.ac.jp Corresponding Author: Sumio Yamada E-Mail: yamadas@met.nagoya-u.ac.jp

## EFFECTS OF BIOFEEDBACK USING A HOME TRAINING DEVICE FOR STRESS URINARY INCONTINENCE : A RANDOMIZED CONTROLLED TRIAL

T. Hirakawa<sup>1)</sup>, S. Suzuki<sup>1)</sup>, K. Kato<sup>2)</sup>

1) Program in Physical and Occupational Therapy, Nagoya University Graduate School of Medicine, Nagoya, Japan 2) Department of Female Urology, Japanese Red Cross Nagoya First Hospital, Nagoya, Japan

#### Introduction

Stress urinary incontinence (SUI) is defined as the complaint of any involuntary leakage on effort or exertion, or on sneezing or coughing<sup>1)</sup>. SUI is a common and distressing condition among parous women that can considerably impact quality of life. Although surgery is widely accepted as the treatment of choice for SUI, conservative management of this condition has received little focus in Japan. In the previous study, pelvic floor muscle training (PFMT) has been recommended as the first option for the treatment of SUI<sup>2)</sup>. On the other hand, the additive effect of biofeedback training is still controversial<sup>3, 4)</sup>.

The present study compares the effects of PFMT with or without biofeedback to treat SUI at home.

#### **Materials and Methods**

Subjects: The subjects were recruited consecutively from the female urologic outpatients during October 2008 to April 2011. Inclusion criteria were history of stress urinary incontinence diagnosed by an urologist and leakage more than once a week. Exclusion criteria were genital protrusion beyond the vagina hymen, pregnancy, previous surgery for urology or gynecology at least within one year, use of medicine to counteract functional disabilities of the lower urinary tract, use of concomitant treatment during trial period, neurologic or psychiatric disease, urinary tract infection, any severe disease such as malignancy, and inability to understand instructions. 37 women were randomized to PFMT groups with (BF) or without (PFMT) biofeedback. The Research Ethics Committee of Nagoya University School of Medicine approved the study, and all of the study participants provided written informed consent.

Intervention: All the women visited the same physical therapist five times (0, 2, 4, 8, 12weeks). At the first visit, all the women individually received verbal information about pelvic floor anatomy, muscle localization, and function with the use of anatomical models and illustration. After that they learned a correct pelvic floor muscles (PFM) contraction without contracting adjacent muscles, such as the abdominal, gluteal, and hip adductor muscles with verbal instruction and palpation of perineal body. The women in the BF group learned correct contraction using biofeedback device (FemiScan clinic system, MegaElectronics, Kuopio, Finland, figure 1).

Home Program: All women were given verbal and written instructions for home practice and advised to practice for 10 minutes, twice per day, everyday in principle. The exercise session was designed to include short and long duration exercises, as both type I and type II muscle fibers need to be exercised. Additionally, all women were advised to pre-contract and hold a contraction before and during coughing, sneezing, and lifting.

EMG-assisted home training device: Each woman in the BF group received an individual EMG-assisted home training

device (FemiScan home trainer, MegaElectronics, Kuopio, Finland, Figure 2) at the first visit and returned the device at the last visit. The device was consists of a vaginal probe and connected headphones, and is based on surface EMG for home use. While practicing the home program, the device emits a voice signals if the contraction is too weak or enough. The device can modify the exercise program according to change of PFM strength, and record PFM activities.

Outcome measure: The PFM strength was measured by perineometry. Perineometry was performed by use of air-filled silicone sensor connected portable perineometer with a pressure transducer (Peritron 9300V, Cardio-Design Pty Ltd, Australia, Figure 3). All women were encouraged to contract the PFM, and maximum contraction pressure was recorded. A three-day voiding dairy was completed to assess the numbers of incontinence episodes and of pads used, and voiding frequency. 1-hour pad test was performed to quantitatively evaluate the results. The King's health questionnaire (KHO) was applied to assess a women's quality of life<sup>5)</sup>. The instrument yields score for nine domains: general health perceptions, incontinence impact, role limitations, physical limitations, social limitations, personal relationships, emotions, sleep/energy, incontinence severity measures. Each KHQ domain obtains a score and therefore there is no general score. The scores range from 0 to 100 and the higher the score, the poorer the quality of life. The International Consultation on Incontinence questionnaire-short form (ICIQ-SF) is a disease-specific questionnaire that assesses the symptoms and the quality of life of patients with urinary incontinence<sup>6)</sup>. The questionnaire consists of four questions pertaining to the frequency of leakage, amount of leakage, interference with everyday life, and the perceived cause of leakage. The scores for the first three questions were added to obtain the total score. The total score ranges from 0 to 21, and higher score indicates a more severe condition.

Analysis: As several variables were not normally distributed, pair-wise comparisons were made with the Mann-Whitney U test for between-group comparisons, and the Wilcoxon signed rank test compared changes within groups. All data were statistically analyzed using the SPSS 12.0J program, and p-values < .05 were considered significant, and were adjusted for multiple testing using Bonferroni correction.

#### Results

Maximum vaginal squeeze pressure significantly increased after exercise in both groups (both p < 0.01). At the point of 2, 8w, maximum vaginal squeeze pressure was higher in the BF group than the PFMT group (p < 0.005).

The number of incontinence episodes significantly decreased after exercise in both groups (both p < 0.05). The number of pads used per day and voiding frequency decreased in both groups, but the differences between before and after exercise in each did not reach significance.

The leakage of 1-h pad test decreased in both groups, and the difference between before and after exercise reached significance in the PFMT group (p < 0.05).

The total score for ICIQ-SF significantly decreased in both groups after exercise (both p < 0.05).

Scores for most domains of KHQ significantly decreased in both groups after exercise (both p < 0.05).

However, no differences in any assessed parameters between the groups were significant after exercise.

#### Discussion

The results of the present study showed that PFMT with or without biofeedback increased the strength of the PFM, decreased the number of incontinence episodes, and improved the quality of life of women with SUI. However, no statistically significance between the two groups was shown in any of the outcome variables after exercise. The results of the present study correspond with the largest randomized controlled trial of Mørkved et al<sup>4</sup>).

In our study, PFMT with biofeedback promoted early progress in the PFM strength. On the other hand, no difference between the groups reach significant in the total score for ICIQ-SF. In previous study, Berghmans et al. demonstrated quicker reduction of leakage in the BF group<sup>7)</sup>. The results of the present study contradicted the data from previous study.

The benefit of using biofeedback is that a small amplitude contraction with low force can be visualized. Using a device during training may motivate many women, thus this should be one of the options in the clinical practice.

#### **Conclusions**

The present study showed that PFMT with or without biofeedback increased the strength of the PFM, decreased the number of incontinence episodes, and improved the quality of life of women with SUI. However, the additive effects of biofeedback training were not discernable.

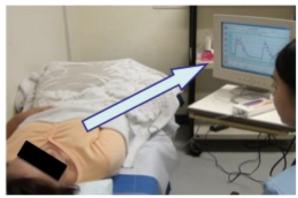
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#### **Author address**

E-Mail: <u>hirakawa.tomoe@a.mbox.nagoya-u.ac.jp</u>



**Figure 1. PFMT using biofeedback device**Muscle activity signals were visible on the computer screen.



**Figure 2. Home training device (FemiScan)** The device was consists of a vaginal probe and connected headphones, and is based on surface EMG for home use.



Figure 3. Perineometer (Peritron 9300V)
Perineometry was performed by use of air-filled silicone sensor connected portable perineometer with a pressure transducer.

## Relationship between Coronary Risk Factor and Endothelial Function in Community - Dwelling Elderly Female.

T. Kitano<sup>1)</sup>, H.Okumura<sup>1)</sup>, Y. Kono<sup>1)</sup>, Y. Hagiwara<sup>1)</sup>, S. Ishida<sup>1)</sup>, H. Sampei<sup>1)</sup>, M. Yoshida<sup>1)</sup>, H. Nagata<sup>1)</sup>, J. Yamaguchi<sup>1)</sup>, C. Asai<sup>1)</sup>, H. Sakakibara<sup>2)</sup>, S. Yamada<sup>1)</sup>

- 1) Program in Physical and Occupational Therapy, Nagoya University Graduate School of Medicine, Nagoya, Japan
- 2) Program in Nursing, School of Health Sciences, Nagoya University, Nagoya, Japan

#### Introduction

Endothelial dysfunction is independent risk factor of cardiovascular events and affected by coronary risk factors such as hypertension (1). Previous study demonstrated that lower physical activity level was associated with endothelial dysfunction suggesting that lower physical activity might affect on vascular endothelial dysfunction (2).

Endothelial function is maintained until 40 years old in male and 50 years old in female, after that it decreases with aging (3). However, there are few reports of the factors which affect vascular endothelial function in community-dwelling elderly population, especially Japanese over 60 years old (4).

Therefore, this study aimed to investigate the association between vascular endothelial function and coronary risk factors including physical inactivity in community-dwelling elderly population.

#### **Materials and Methods**

*Subjects*: We enrolled 71 subjects in this research. Inclusion criteria were 60-74 years old in community-dwelling elderly female.

Measurements: We evaluated age, body mass index (BMI) and home blood pressure as baseline data. The number of steps, low intensity, moderate intensity, and high intensity activity time were measured by using an electrical accelerometer (Life Corder, Suzuken.Co). All participants were instructed to put on the accelerometer themselves and were instructed to use the accelerometer 24 h/day for 1 week, except while bathing and sleeping. High-density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and HbA1c were measured by blood sample. Blood pressure was measured for consecutive three days in each subject by same type digitral sphygmomanometer and average value for three days was calculated as home blood pressure.

n this research, we defined hypertension (>135/80 mmHg and/or current use of antihypertensive agents), dyslipidemia (HDL-C<40mg/dl, LDL-C $\ge$ 140mg/dl and/or current use of lipid-lowering agents), diabetes mellitus (HbA1c  $\ge$  5.8% and/or current use of insulin or oral medication for diabetes), Obesity (BMI  $\ge$  25), and physical inactivity (< median number of steps per day) as coronary risk factors.

The vascular endothelial function was assessed by measuring flow-mediated dilatation (FMD) of the brachial artery by ultrasonic diagnostic equipment (UNEXEF, UNEX.Co). The participants were instructed to fast and to abstain from smoking and from ingesting alcohol, caffeine prior to testing in the morning. They took medicines as usual. The participants had a supine position after 15 minute rest in a quiet temperature-controlled (22–24°C) laboratory setting. Using a 10-MHz linear array transducer probe, the longitudinal image of the right brachial artery was continuously recorded from baseline to at 2 minute after the

cuff deflation that followed super systolic compression (50mmHg above systolic blood pressure) of the right forearm for 5 minute. We use flow-mediated total dilation %FMTD as index of vascular endothelial function because of good reproducibility (5). %FMTD was calculated as the maximum percent increase in arterial diameter from the diameter immediately after cuff deflation.

Data analysis: In order to investigate the relationship between coronary risk factors and endothelial function, we divided the subjects into two groups by coronary risk factors: no or 1 risk factor group and 2 or more factors group. Then we performed Mann-Whitney U test to compare %FMTD between each group. Secondly, we divided the subjects into two groups by median value of %FMTD and Mann-Whitney U test or unpaired t-test were used to compare age, SBP, DBP, HDL-C, LDL-C, HbA1c, BMI, number of average steps per day, duration in low intensity, middle intensity, and high intensity activity time. Variables with a p < 0.1 from this analysis were entered into the multiple logistic regression analysis for selecting independent associate factors. All analyses were performed by the SPSS 12.0J software package (SPSS Inc, Tokyo, Japan). A p value of < 0.05 was considered statistically significance.

#### Results

Table 1 shows the characteristics of all participants. %FMTD was significantly higher in lower coronary risk factor group (Fig1). Table 2 shows the clinical characteristics of higher and lower %FMTD groups. HDL-C, number of steps and low intensity activity time were significantly better in higher %FMTD group. Table 3 shows the result of the multiple logistic regression analysis. HDL-C and number of step were selected as independent factors for higher %FMTD group.

Table 1 Characteristics of participants

	Female n=71
Age	69.6±3.2
Hypertension	43 (60.6%)
Dyslipidemia	37(52.1%)
Diabetes mellitus	10(14.1%)
Obesity	10(14.1%)
Physical inactivity	36(50.7%)
Coronary risk factor	$1.96 \pm 1.0$
Average number of step (step/day)	8295±3296
Low intensity activity time (min/day)	$57.7 \pm 18.2$
Moderate intensity activity time (min/day)	$25.0 \pm 19.2$
High intensity activity time (min/day)	$1.8 \pm 3.3$
FMTD (%)	$4.84 \pm 2.3$
•	

Data are presented as means  $\pm SD$ .

FMTD; flow-mediated total dilation

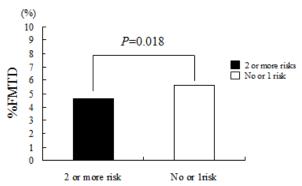


Fig1 Comparison of %FMTD in low and high coronary risk factor group

Table 2 Difference in each factors between high and low FMTD

	Low %FMTD n=35	High %FMTD n=36	Р
Age	69.3±3.6	70.0±2.9	0.586
SBP	$134.1 \pm 13.9$	$134.7 \pm 19.2$	0.565
DBP	79.7±8.1	$80.4 \pm 10.8$	0.818
HDL-C	$60.3 \pm 9.9$	$68.6 \pm 11.4$	0.002
LDL-C	$111.9 \pm 24.2$	120.4±29.4	0.199
HbA1c	$5.5 \pm 0.5$	$5.4 \pm 0.6$	0.332
BMI	$21.3 \pm 2.9$	$22.7 \pm 3.4$	0.089
Average number of step	$7076 \pm 2253$	9448±3718	0.003
Low intensity activity time	$53.1 \pm 13.1$	$62.0\pm21.2$	0.037
Moderate intensity activity time	$19.5 \pm 11.7$	$30.3 \pm 23.2$	0.059
High intensity activity time	$1.1 \pm 1.1$	$2.5 \pm 4.4$	0.141

Data are presented as means  $\pm$ SD.

%FMTD; %flow-mediated total dilation, SBP; systolic blood pressure DBP; diastolic blood pressure, HDL-C; high-density lipoprotein cholesterol LDL; low density lipoprotein cholesterol, HbA1c; hemoglobin A1c BMI; body-mass index

Table 3 Result of Multivariate regression analysis

	Odds ratio (95%CI)	P
HDL-C	1.05 (1.00 -1.11)	0.045
Average number of step	1.00 (1.00 -1.0004)	0.037

HDL-C; high-density lipoprotein cholesterol Dependent variables: High %FMTD group

Independent variables: HDL-C, BMI, Average number of step, Low intensity, Moderate intensity, High intensity activity time

#### Discussion

The main finding of this study was that vascular endothelial function was associated with physical activity in community-dwelling elderly female population as well as HDL-C. To our knowledge, this is the first report to demonstrate the relationship between vascular endothelial function and coronary risk factors including physical inactivity in the community-dwelling female elderly.

Tomiyama et al. reported that coronary risk factors such as age, gender, BMI, systolic blood pressure, diastolic blood pressure, HDL-C, triglycerides, fasting glucose and smoking habit were independently associated with endothelial function in Japanese normal subjects. (4). Their study reported that subjects in low Framingham risk score group showed higher %FMD than those with high score group. The results in this study are in line with their results, adding new aspect of the effects of physical inactivity. However, they did not analyze the effects of physical activity. Our findings add the physical inactivity as well as HDL-C is also a keen factor for endothelial dysfunction even in the elderly female population. The effect of physical inactivity on endothelial

function is also reported in peripheral artery disease (2). Thus, several reports including our findings suggest the physical activity level should take into account to assess endothelial function.

There are several potential limitations to the findings in the present study. A relatively small sample size might affect the results. Therefore, this study could function as a preliminary study for vascular endothelial dysfunction in community-dwelling female population. Other coronary risk factors, such as smoking, alcohol, metabolic syndrome and chronic kidney disease, potential factors to associate with endothelial dysfunction, may need to be studied to provide more details. Nevertheless, the present study is the first report of clinical associates of vascular endothelial function in the female elderly.

#### Conclusion

The findings of the present study suggest that endothelial function in the community-dwelling female elderly is associated with the number of coronary risk factors including physical inactivity.

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#### **Author address**

E-Mail: <u>kitano.takayuki@a.mbox.nagoya-u.ac.jp</u> <u>corresponding: yamadas@met,nagoya-u.ac.jp</u>

#### A Comparison of Pelvic and Spine Angle in Various Cross-legged Sitting Postures

Sun-Young Kang. B.H.Sc., PT Hye-Seon Jeon PhD. PT Department of Rehabilitation Therapy, College of Health Sciences, Yonsei University, Kangwondo, Republic of Korea

#### **INTRODUCTION:**

Orientation of pelvis during sitting influences on spine curve because the pelvis is considered as the base for the spine in the spine-pelvic complex. According to the Tully's buttom-up mechanism, in sagittal plane, increased anterior pelvic tilt leads to a larger lumbar lordosis and compensatory increases in the thoracic and cervical kyphosis. In addition, in frontal plane, postural and structural pelvic asymmetry is related to compensatory scoliosis.

Cross-legged sitting is one of the most preferred sitting postures. Because cross-legged sitting requires less effort of the internal and external oblique abdominal muscles, people feel less fatigue in this posture compared to uncrossed sitting. Also, adducted and flexed hip joints in leg crossing contribute to the stability of the sacroiliac joints. However, prolonged asymmetric use of abdominal muscles and uneven pressure distribution to the buttocks increase pelvic and lumbar rotation, and may cause lower back pain in the long run. Previous studies have primarily focused on the influence of the cross-legged sitting on the muscle activation not on the biomechanical aspects of pelvic and spine structures. Therefore, the objective of current study was to investigate possible kinetic and kinematic changes that may occur in the pelvic and spine regions during cross-legged sitting postures.

METHODS: Experiments were performed on sixteen healthy subjects. Kinetic and kinematic data were collected while the subject sat in 4 different sitting postures for 5 seconds: sitting while placing his right knee on the left knee (KK), sitting by placing right ankle on left knee (AK), sitting by placing right ankle over the left ankle (AA), and uncrossed sitting with both feet on the floor (US). The order of the sitting posture was random. The sagittal plane angles (pelvic tilt, lumbar A-P curve, thoracic A-P curve) and the frontal plane angles (pelvic height, lumber lateral curves, thoracic lateral curves) were obtained using Vicon system with 6 cameras and analyzed with Nexus software. The pressure on each buttock was measured using Tekscan. Repeated one-way analysis of variance (ANOVA) was used to compare the angle and pressure across the four postures. The Bonferroni's post hoc test was used to determine the differences between upright trunk sitting and cross-legged postures.

RESULTS: In sagittal plane, cross-legged sitting postures showed significantly greater kyphotic curves in lumbar and thoracic spine when compared uncrossed sitting posture. Also, pelvic posterior tilting was greater in cross-legged postures. In frontal plane, only pelvic height of the right leg was significantly higher in KK sitting than in US. Finally, in KK sitting, the pressure on the right buttock area was greater than US and ,in AK sitting, the pressure on the left buttock area was greater than US. However, all dependent variables in both planes did not demonstrate any significant difference among the three cross-legged postures (p>.05).

CONCLUSION: The findings suggest that asymmetric changes in the pelvic and spine region secondary to the prolonged cross-legged sitting postures may cause lower back pain and deformities in the spine structures.

#### Comparison of Abdominal Muscle Activity During a Single-Leg Hold in the Hook-Lying Position on the Floor and on a Round Foam Roll

Su-Jung Kim, MSc, PT\*; Oh-Yun Kwon, PhD, PT\*; Chung-Hwi Yi, PhD, PT\*; Hye-Seon Jeon, PhD, PT\*; Jae-Seop Oh, PhD, PT†; Heon-Seock Cynn, PhD, PT\*; Jong-Hyuck Weon, PhD, PT\*

\*Department of Rehabilitation Therapy, Graduate School, Yonsei University, Kangwon-do, South Korea;

†Department of Physical Therapy, Inje University, Gyeongsangnam-do, South Korea; ‡Department of

Rehabilitation Therapy, Wonju Christian Hospital, Kangwon-do, South Korea

**INTRODUCTION:** To improve trunk stability or trunk muscle strength, many athletic trainers and physiotherapists use various types of unstable equipment for training. The round foam roll is one of those unstable pieces of equipment and may be useful for improving trunk stability. To assess the effect of the supporting surface (floor versus round foam roll) on the activity of abdominal muscles during a single-leg hold exercise performed in the hooklying position on the floor and on a round foam roll. We hypothesized that performing the exercise on a round foam roll would induce greater muscle activity than the same maneuver on the floor.

**METHODS**: Nineteen healthy volunteers (11 men, 8 women) from a university population. The participants were instructed to perform a single-leg hold exercise while in the hook-lying position on the floor (stable surface) and on a round foam roll (unstable surface). Surface electromyography (EMG) signals were recorded from the bilateral rectus abdominis, internal oblique, and external oblique muscles. Dependent variables were examined with a paired *t* test.

**RESULTS:** The EMG activities in all abdominal muscles were greater during the single-leg hold exercise performed on the round foam roll than on the stable surface. The percentage increment of muscle activity was 88.08% in the contralateral RA (Padj = .003), 107.81% in the ipsilateral RA (Padj < .001), 51.67% in the contralateral EO (Padj = .003), 96.59% in the ipsilateral EO (Padj < .001), 172.24% in the contralateral TrA/IO (Padj < .001), and 118.88% in the ipsilateral TrA/IO (Padj = .001).

**CONCLUSION:** The single-leg hold exercise in the hook-lying position on an unstable supporting surface induced greater abdominal muscle EMG amplitude than the same exercise performed on a stable supporting surface. These results suggest that performing the single-leg hold exercise while in the hooklying position on a round foam roll is useful for activating the abdominal muscles.

## Relationship between electromyographic activity of the abductor hallucis and the pressure of a pinch gauge during short foot exercise

Kyung-Mi Park, and Heon-Seock Cynn

Department of Rehabilitation Therapy, The Graduate School, Yonsei University, Gangwon-do, Republic of Korea

#### **INTRODUCTION:**

The abductor hallucis (AbdH) muscle has important roles in maintaining stance, gait, and balance. Several different strengthening methods for the AbdH have been described in order to prevent overuse injuries in people with problems from excessive pronation. One of the recommended exercises is the "short foot" (SF), which is accomplished by bring the head of the first metatarsal toward the heel without toe flexion. Previous study reported that SF exercise showed great electromyographic (EMG) activity in the AbdH. However, it is difficult to keep the first metatarsal head and heel simultaneously on the ground during the SF exercise. Therefore, the aim of this study is to investigate the correlation between the EMG activity of AbdH and the amount of pressure measured by a pinch gauge (PG), and to compare the AbdH activity and the pressure measured by the PG during SF exercise between subjects with pes planus and in subjects with a neutral foot alignment.

**METHODS**: Fourteen subjects were recruited for this study (pes planus group=7; neutral foot alignment group=7). We screened the foot type of the subjects by measuring the resting calcaneal stance position (neutral alignment: between 2° of inversion and 2° of eversion) and their scores on the navicular drop test (neutral alignment: between 5 and 9 mm). A surface EMG was used to collect AbdH activity, and a PG was positioned under the first metatarsophalangeal joint to measure the pressure produced by the first metatarsal head during the SF exercise. The means of three trials for each exercise were used for data analysis.

**RESULTS:** The muscle activity of the AbdH and the pressure measured by the PG showed a high correlation (r=.80, p=.001). The EMG activity of the AbdH and the pressure measured by the PG, is significantly lower for subjects with pes planus than for those with a neutral foot alignment (p<.05).

**CONCLUSION:** Based on these findings, the PG can be recommended as an effective instrument for evaluating the performance of the AbdH. It may also be beneficial for monitoring how well the SF exercise is performed, and for providing visual feedback to patients during SF exercise in a clinical setting.

#### A Novel EEG-based Brain Mapping to Determine Cortical Activation Patterns in Normal and Cerebral Palsy during Motor Imagery Tasks

<u>Yoon-Kyum Shin,</u> Dong Ryul Lee, Han Jeong Hwang, Sung (Joshua) Hyun You, Chang Hwan Im

Movement Healing Lab., Department of Physical Therapy, Yonsei University, Wonju, Republic of Korea

INTRODUCTION: Motor imagery is a promising neurorehabilitation technique, which plays a crucial role in motor relearning and associated skill reacquisition in children with cerebral palsy (CP). Recent empirical evidence suggests that the motor impairments in children with CP are associated not only with movement execution dysfunction, but also with impaired motor planning and motor imagery, which involve an important cognitive-motor process and motor control. Nevertheless, there is a dearth of evidence highlighting neural substrates underpinning motor imagery. Hence, our study was to determine and compare cortical activation patterns using the obtained EEG topographical maps in normal and children with cerebral palsy during motor execution and motor imagery tasks.

METHODS: Four normal and four children with CP (mean 11.7 y) were recruited from a community medical center. A EEG-based brain mapping system with 30 scalp sites (extended 10-20 system) was used to determine cortical reorganization in the region of interests (ROIs) during four motor tasks; movement execution (ME), kinesthetic-motor imagery (KMI), observation of movement (OOM), and visual motor imagery (VMI). ROIs included the primary sensorimotor cortex (SMC), the premotor cortex (PMC), and the supplementary motor area (SMA).

RESULT: EEG brain mapping data showed increased activation in SMC during the ME-KMI block and in SMC and visual cortex (VC) during KMI in normal children, respectively. Children with CP showed relatively similar SMC activation along with other motor network areas (PMC, SMA and VC) activation. During the OOM-VMI block, normal children primarily activated VC or occipital area whereas children with CP activated VC and SMC and bilateral auditory areas.

CONCLUSION: This is the first study highlighting different neural substrates used for motor imagery tasks in normal and children with CP. In conclusion, given the status of the real-time EEG-based brain mapping system as a new technology, examination of its potential efficiency in rehabilitation has only just begun. However, our brain mapping system can be used as an alternative neuroimaging vehicle to probe underlying neural recovery mechanisms and as a powerful real-time neurofeedback system for individuals with stroke or CP. Further studies with a larger sample size are warranted for generalization of our EEG measurement.

Keywords: Motor imagery, EEG, Cortical activation, Topographical map

## Inter-rater Reliability of Thickness Measurement of the Abdominal Muscles Using Ultrasonography According to Different Probe Location and Measurement Technique

One-bin Lim, B.H.Sc., P.T.

Dept. of Rehabilitation Therapy, The Graduate School, Yonsei University

**INTRODUCTION:** The ultrasonography (US) is useful for assessing muscle thickness and guiding rehabilitation decision-making for clinicians and researchers recently. The previous studies have not reported about the inter-rater reliability of ultrasound measurements from different probe location and measurement technique. Thus, the purpose of this study was to determine the inter-rater reliability of the ultrasound measurement according to different probe location and measurement technique for thickness measurement of the abdominal muscles.

**METHODS:** Twenty healthy volunteers were recruited in this study. Muscle thickness of the transversus abdominis (TrA), internal oblique (IO) and external oblique (EO) were measured over the 3 times in the supine position. Prior to muscle thickness measurement, two examiners underwent 20 hours of hands-on training for the specific US protocol. The 3 different probe locations were as follows; 1) Probe location 1 (PL1) was located immediately below the rib cage in direct vertical alignment with the anterior superior iliac spine (ASIS). 2) Probe location 2 (PL2) was located halfway between the ASIS and the ribcage along the midaxillary line. 3) Probe location 3 (PL3) was located halfway between the iliac crest and the inferior angle of the rib cage and then adjusted to ensure the medial edge of the TrA. The 2 different measurement techniques were as follows; 1) Measurement technique A (TA) was in the middle of the captured image. 2) Measurement technique B (TB) was along a horizontal reference line located 2 cm apart from the medial edge of the TrA in the captured image. All US were captured at the end of inspiration at rest (RI), the end of expiration at rest (RE) and with abdominal drawing-in maneuver at the end of inspiration (AI). Intraclass correlation coefficient (ICC) (3,1) was used to calculate the inter-rater reliability of the thickness measurement of TrA, IO and EO using the values from both the first and second examiner.

**RESULTS:** The ICC(3,1) value of inter-rater reliability of IO in RI, RE and AI for all different probe location and measurement technique demonstrated excellent reliability value ICC(3,1)= $.92\sim.97$ . The ICC(3,1) value of inter-rater reliability of TrA and EO in RI, RE and AI for all different probe location and measurement technique demonstrated moderate to excellent reliability value ICC(3,1)= $.68\sim.94$ ; except ICC(3,1) of TrA in RE for PL2-TA=.19.

**CONCLUSION:** All the ICC(3,1) value of inter-rater reliability for three probe location and two measurement technique were moderate to excellent. Especially, The ICC(3,1) value of inter-rater reliability of IO in RI, RE and AI for three probe location and two measurement technique were excellent. In conclusion, the use of US in different probe location and measurement technique would be recommended for thickness measurement of the abdominal muscles.

**Key Words:** Abdominal muscles; Inter-rater reliability; Muscle thickness; Ultrasonography.

# Abstracts Occupational Therapy

#### MIRROR NEURON SYSTEM: BRAIN ACTIVITY AND CLINICAL APPLICATION

#### Mari Kuroda (Ms., Master course student)

Division of Occupational Therapy, Department of Rehabilitation Sciences Postgraduate School of Health Sciences, Nagoya University

#### Introduction

Mirror neuron system (MNS) is an important brain network for motor recognition and execution during sequential movement in human. The network connects frontal and parietal neural activities, and it works not only during performance but also during observation of movements of other persons.

The MNS system is not a theoretical system. The latest brain imaging techniques, such as magnetoencephalography (MEG) and magnetic resonance imaging (MRI), has shown responsible brain areas for MNS.

In the present study, I conducted an experiment to show the brain activity related to MNS during a daily performance. I also present a clinical case, whom a theoretical intervention relating to MNS was effective.

#### 1. Experimental study of MNS using a MEG system

In the present experimental study, brain activity in the parietal cortex, which may relate MNS during sequential movement, was detected by MEG system. Nine healthy adults participated in the study (3 men and 6 women, mean age:  $26.4 \pm 8.10$  years). Participants were asked to watch pieces of movie showing four sequential movements without any voluntary movements (Table 1). Three of four movements included am identical target movement, putting spoon into a cup. Brain activity before and after the onset of the target movement were recorded, and an activated area was estimated.

Figure 1 shows a representative brain activity recorded from a subject by MEG. Parietal brain activity was identified in both hemispheres during the target movement. Estimated brain activity in the parietal cortex was obtained in the period between 175 ms before and 600 ms after the onset of the target movement although the timing and duration of the activity was varied among subjects (Fig. 2). On a different movement from putting a spoon into a cup, T4, parietal activity was obtained in a similar area of parietal cortex (Fig. 1).

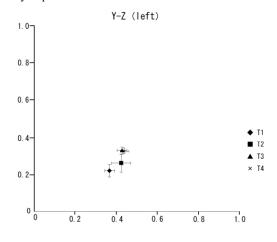
The experimental results were summarized as: 1) brain activity during watching a video of other's movement included the parietal activity, 2) The parietal activity might cause at each part of movement during sequential movement.

Table. 1: Hand activities in short film (T1-4). These have same movement but different meaning except for T4.

	T1	T2	T3	T4
Preceded movement	Putting sugar into a cup	None	Cleaning the table	None
Target movement	Putting a spoon into a cup	Putting a spoon into a cup	Putting a spoon into a cup	Holding-up a cup
Following movement	Stirring sugar	None	Clearing the table	Drinking coffee

#### 2. Application of MNS theory to intervention

With understanding MNS, some types of intervention for stroke patients have been developed. Previous studies reported that motor exercise by showing video of instructive movements facilitates recovery of patients' motor performance (Franceschini M et al., 2010). Imagination trainings of sequential movements have been used not only in the sports training, but also applied in the rehabilitation (Mulder T, 2007). The theoretical background of such intervention is that the visual information of other's movements activates MNS and motor-related cortices, including cortices relating the spatial and movement recognition in the parietal cortex. By measuring brain activity using functional MRI, improvement in activity of motor related cortices has been demonstrated (Ertelt D et al., 2007). Such interventions by watching video have been mainly applied to patients with motor paresis in the field of rehabilitation. However, there are very a few studies that applied interventions based on the MNS to improve daily activity in patients with dementia.



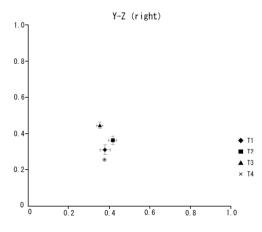


Fig. 1: Dipole localization on the Y-Z axes in the left (top) and right (bottom) hemispheres. Y and Z axis was of antero-posterior and vertical direction, respectively. Values indicate standardized size of brain from the center of the brain (0) to the scalp surface (1.0).

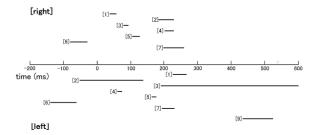


Fig. 2: Temporal course of parietal activity in the left (top) and right (bottom) hemisphere observed during the presentation of the video. At zero point of the time course, a person on the video started putting spoon into a cup.

#### 3. Case study

Since the experimental research showed that watching video evoked the parietal activity, we considered such visual intervention might activate cognitive function relating with motor performance in daily life via activation in the visuo-spatial and mirror neuron systems. This case study was a challenging one based on an experimental theory regarding MNS.

The case was a 74-year-old female with Alzheimer disease (4 years after onset). It was difficult to communicate verbally with her due to severe symptom of dementia. Her eating in oral movement was preserved, but she did not use chopsticks or spoon, but she ate meal with her hands and fingers. She occasionally did not eat meal at table but played with food.

I planed an intervention, in which a video showed a person eating meal using chopsticks or spoon. I expected that the movie evoked MNS related cortical activities, and her to eat with chopsticks as the movie showed. The short movie was presented on a monitor screen (14 inch, diagonal) in front of the subject on the table at lunch. The intervention was conducted initially for 9 days and after 8-days interval it applied again for 3 days again. Percentage of time period, when she used chopsticks or spoon, during her eating time was measured.

During the intervention, amount of food eaten at lunch was 80-100~% of full-served, and the amount was not changed, compared to that before the intervention. Duration of time taken for lunch was  $35~\text{min}~\pm 4~\text{min}~28~\text{sec}$  and  $50~\text{min}~25~\text{sec}~\pm 6~\text{min}~54~\text{sec}$ , before and during the intervention, respectively. Before the intervention, she used chopsticks or spoon  $23.5~\pm 25.4\%$  of eating period, but the value increased to  $69.3~\pm 29.0~\%$  during the intervention. When a caregiver helped to use chopsticks or spoon she used it only  $18.3~\pm 13.3~\%$  of eating time before the intervention, but it became  $75.8~\pm 37.3~\%$  during the intervention (Fig. 3).

The present intervention was conducted only for lunch; and there was no change of her manner in other meals, e.g., she used her hands and fingers to eat food during breakfast and supper. The effect of the intervention did not continued after the intervention. She again used her hands and fingers without chopsticks and spoon at lunch during the 8-days interval. However, in the second term of the intervention, she again began to use chopsticks and spoon to eat lunch.

#### 4. Discussion

The case report suggested that the visual intervention, which gave the subject other's movement of eating with chopsticks and spoon, was obviously effective to improve her manner at eating. She might just copy the movement presented in front of her, but even in such case of copying,

brain activities relating MNS should worked to lead her movements to similar ones presented on the movie as shown in the experimental study. She did not suffer from motor paresis but dementia. Therefore, this present intervention was effective to improve cognitive function relating motor performance.

Reproducibility of the effect of the intervention was observed, but due to her physical problem, the intervention could not apply after the second period. Since I could applied the intervention only two periods, generalization of the effect on other meals was not recognized, and learning effect was not obtained at lunch during the interval period. However, the effect of video presentation was so dramatic on her eating manner, application of modified intervention by showing video of motor performance could be considered for patients with cognitive disturbance and dementia.

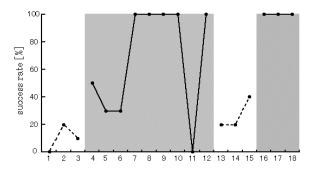


Fig. 3: Percentage of successful behavior with chopsticks or spoon during eating in the subject. During presentation of video (gray periods), the patient used tools to eat than during periods without video (white).

#### Conclusions

In conclusion, I investigated the brain activity during watching motor performance. Activation of the parietal cortex was consistently observed, which might relate with MNS. In a case study, showing motor performance my video movie was effective to improve eating manners in a patient dementia. The present study suggested that the visual stimulation of other's motor performance could stimulate subject's cognition or motivation, possibly via MNS.

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#### **Author address**

E-Mail: kuroda.mari@f.mbox.nagoya-u.ac.jp

# Effects of mental sweating and skin blood flow during Trail Making Test

#### Masahiro Tanaka

(Mr.. Master course student)

Division of Occupational Therapy, Department of Rehabilitation Sciences Postgraduate School of Health Sciences, Nagoya University

#### 1. Introduction

Patients with dementia or psychological disorders often suffer from symptoms caused by attention deficit [1], and the symptoms cause various problems in their daily life. For such patients, one of the objectives in the intervention provided by occupational therapists is to minimize the problems and to support their daily activities.

Situation requiring attention or concentration may lead mental stress and stress-related biological responses [2]. We may experience spontaneous sweating on palm and flushing of face in such situation. Therapists need to observe clients' physical condition as well as emotional expression during intervention to know their mental stress. The present study is a basic research to elucidate relationship between tasks with attention effort and biological autonomic responses.

Trail Making Test (TMT, [3]) is a widely used conventional task to evaluate attention function. TMT comprises two parts, Part-A and -B, which is simple and complex character-searching task, respectively. We measured skin perspiration and vascular responses on hand during TMT to evaluate sympathetic nerve activity during the tests.

#### 2. Methods

Fourteen young healthy subjects participated in the study (7 females and 7 males, mean age:  $20.7 \pm 0.5$  (SD) years). Perspiration on the left palm and blood flow at the left index finger were continuously recorded during TMT every 60 sec, using a diaphoremeter (SKD-2000, Skinos, Nagoya) and a laser doppler blood flow imaging system (ALF-21, Advance, Tokyo). Subjective feeling regarding effort and stress during TMT was asked by questionnaires after the test.

Subjects were seated on a chair in front of a desk in a quiet room with sensors of diaphoremeter and blood flow meter attached on

the tip of index and on the central area on the left palm, respectively.

After a five-minutes rest, subjects were asked to perform Part-A of TMT as quick as possible. Then, they were asked to answer questionnaires for Part-A, and took a short rest for 5 minutes. Part-B of TMT was similarly performed after the session for Part-A. The questionnaires included questions for attention, fatigue and stress during each test.

Time periods needed for each Part of TMT were measured in each subject, and they were compared by a paired-t test. Amount of mean and maximum change ratio (per 60 sec) in perspiration and blood flow during the record were assessed to statistical analysis. Those values at rest and during two TMT, Part-A and -B, were compared using one-way (rest or tasks) analysis of variance repeated measures (ANOVA), followed by Turkey Kramer's test for multiple comparisons. Scores in questionnaire were compared between Part-A and -B of TMT using a Wilcoxon signed-ranks test. A p value less than 0.05 was considered to be significant.

#### 3. Results

Subjects needed longer time to complete Part-B than Part-A of TMT (p<0.01, t-test). There was a main effect of TMT on the perspiration (F [2, 41] = 10.7, p<0.01, Fig. 1) and blood flow (F [2, 41] = 23.9, p<0.01, Fig. 2). Multiple comparisons revealed the mean palmar perspiration significantly increased (p<0.01), and the blood flow decreased (p<0.01), during both Parts of TMT, than those at rest. However, there was no difference of the values between Part-A and -B of TMT. The maximum change ratio of palmar perspiration significantly larger during Part-B than -A (p<0.05, Fig. 3). Scores in questionnaires showed that the subjects answered Part B more difficult than -A (p<0.01, 0000).

#### 4. Discussion

The present study showed that sympathetic activities on skin were facilitated during TMT. Sympathetic response of palmar perspiration and blood flow reciprocally changed as shown in the previous reports [4][5].

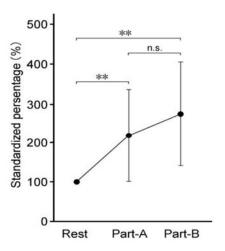


Fig.1: Effect of TMT Tasks on palmar perspiration. The values were standardized and each vertical bar indicates standard deviation (\*\* p<0.01).

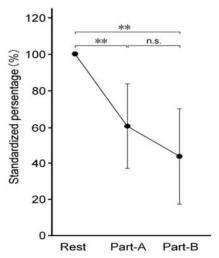


Fig.2: Effect of TMT Tasks on blood flow in the finger. The values were standardized and each vertical bar indicates standard deviation (\*\* p<0.01).

Difference of the maximum change ratio of palmar perspiration may indicate the difference effect on the sympathetic response between the Parts of TMT. Part-B requires more in attention and concentration, as seen in the results of questionnaires in the present subjects. Since the qualitative difference between the Parts was of frontal function required, i.e., attention maintenance, attention shift or working memory,

such frontal activities induced more stress and sympathetic responses in the peripheral area.

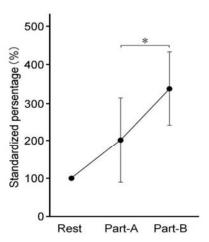


Fig.3: Maximum palmar perspiration during tasks. The values were standardized and each vertical bar indicates standard deviation (\* p<0.05, \*\* p<0.01).

Another factor should be considered. The subjects needed longer time to complete Part-B of TMT and they felt the Part difficult than Part-A. Apart from higher brain functions to solve TMT, a preconception that Part-B seemed to be difficult might cause mental stress and more sympathetic response than for Part-A.

From the present results, we occupational therapists may know that tasks to evaluate clients' higher brain function, including frontal functions, induced considerable sympathetic responses in the subjects.

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#### Author address

E-Mail:tanaka.masahiro@a.mbox.nagoya-u.ac.jp

#### Mismatch response modified by synchronous visual stimuli.

#### Yoshiro Nakagawa

Division of Occupational Therapy, Department of Rehabilitation Sciences

Postgraduate School of Health Sciences, Nagoya University

#### Introduction

We detect changing stimuli in our surrounding events without paying attention. Clinical studies revealed that this process of automatic detection system was abnormal in patients with schizophrenia, dementia, or developmental disorders. The automatic discrimination processes have been measured as an event-related component called mismatch negativity (MMN) using electroencephalography (EEG) [1], or mismatch magnetic field (MMNm) recorded by magneto-encephalography (MEG) [2]. Conventional MMN has been investigated using single modality of auditory stimulation, but in our daily life, surrounding stimulation is usually multi-modal, i.e., audio-visual and visuo-tactile, etc. Therefore, I investigated mismatch response evoked by multi-modal stimulation, which could be applicable to our stimulus situation in daily life.

#### Method

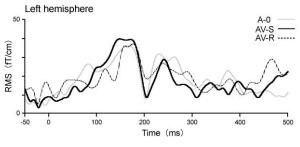
Ten healthy righted-handed volunteers (6 males and 4 females: mean age,  $29.5\pm7.2$  years) participated. Auditory MMNm was recorded during synchronous visual stimulation with auditory stimulation by MEG (PQ1160C, YOKOGAWA, Japan). Three experimental conditions were conducted; 1) Auditory stimulation consisted with standard and deviant stimuli (A-0) condition, 2) Consistent visual stimulation synchronized with auditory and standard stimulation (AV-S) condition, 3) Consistent visual stimulation at

random timing to auditory and deviant stimulation (AV-R)

Auditory stimuli included two tones (standard and deviant tones), and were presented by ear tips. Deviant stimuli were 2000 kHz pure tone (20%), and standard was 1000 kHz (80%). The duration of each tone was 500 ms and an inter-stimulus interval (ISI) was 500 ms, and intensity was 80 dB for both stimuli at the ear tips. Visual stimulus was pattern-reversal black and white checkerboard stimulation in the peripheral eye field, and was projected using a crystal digital light projector. Auditory evoked MMNm were analyzed. Thirty channels gradiometers were selected from the temporal lobe in each hemisphere to calculate MMNm responses. The amplitude of MMNm was calculated in 30 channels. For the MMNm, the amplitude ware compared among conditions using a one-way (stimulus conditions) repeated measures analysis of variance (ANOVA) followed with a Fisher's protected least significant difference (Fisher's PLSD) test for multiple comparisons. The significance of statistical threshold was set as p < 0.05.

#### Result

Figuer.1 shows the grand average of MMNm waveform in each condition. The MMNm amplitude in root mean square (RMS) value during AV-S condition was enhanced compared to other conditions in the right hemisphere (p=0.0087, ANOVA)(fig.2).



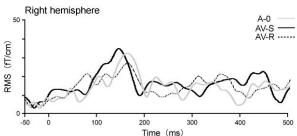


Fig. 1: Grand-average RMS waveforms of MMNm in each condition.

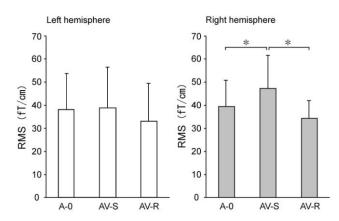


Fig. 2: Root mean square values of the MMNm response in each condition. (\*p < 0.05, ANOVA).</p>

#### Discussion

The results indicated that simultaneous visual stimulus enhanced auditory MMNm, although the additional visual stimulus was similarly given with both standard and deviant stimuli. The result could be interpreted in two ways. Firstly, MMN depended on the amount of physical changing and on the feature changing [3]. In this present study, MMN was produced not only by difference in physical amount of stimuli but also in stimulus feature, which was in line. Secondly,

there were two types of MMN elicited in this study. One is conventional MMN elicited by the mismatch between standard and deviant tones. Another is elicited by the difference between audio-visual sets (Fig.3).

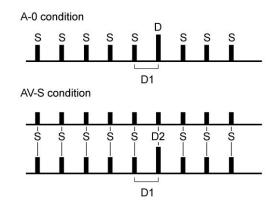


Fig. 3: Conventional auditory MMN production by standard (S) and deviant (D) stimuli with no visual stimulation (A-0) in a temporal sequence. In the A-0 condition conventional MMNm (D1). In the AV-S condition, deviation of combined feature of stimuli (D2) was added to D1 to produce MMNm.

The mismatch response could be evoked not only by temporal dimension of stimulus deviation but also by a deviated feature produced by two modalities of stimulation at a time. This study indicated that bimodal stimulation might effect on pre-attentive automatic detection.

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Author's address

E-Mail: nakagawa.yoshiro@mbox.d.nagoya-u.ac.jp

# Internet communication of outpatients with schizophrenia or pervasive developmental disorders

#### Takashi Watabe

Division of Occupational Therapy, Department of Rehabilitation Sciences Postgraduate School of Health Sciences, Nagoya University

#### Introduction

In Japan, the number of Internet users reached 94.08 million people as of the end of 2009 with an Internet penetration rate of 78.0% [1], and the population diffusion rate of the Internet is 95% or more among people aged 20 to 39. Most psychiatry hospitals have not allowed the inpatients of this age group use of the Internet. As a result, these young patients have to choose shortly after discharge whether to avoid use of the Internet or to attempt to use it without preparation.

Although many studies have been carried out concerning Internet usage, participants of most studies have been normal teenagers. To our knowledge, there are few studies concerned with how patients with schizophrenia or pervasive developmental disorders (PDD) use the Internet to communicate with other people. The objective of the present study was to investigate Internet communication used by young patients with schizophrenia or PDD, which impair social cognition and communication.

#### **Materials and Methods**

We conducted a cross-sectional study over seven months from January 1, 2011 to July 31. The present study, approved by the ethics review committee of Nagoya University School of Health Sciences (No. 10-608), had three groups of participants. The S-group consisted of thirty-six outpatients who met DSM-IV-TR criteria for schizophrenia (S-patients). The PDD-group consisted of forty-four outpatients (PDD-patients) who met DSM-IV-TR criteria for PDD [i.e., Asperger's disorder, autistic disorder, and PDD not otherwise specified (PDDNOS)]. The Control-group consisted of 101 adults (Controls).

S- and PDD- patients were recruited through public hospitals (n=3), private hospitals (n=3), and psychiatry clinics (n=5) in Nagoya, and diagnosed by their attending psychiatrists. Controls were selected randomly from eighteen facilities (theaters, sport facilities, factories, welfare facilities, etc.) in Nagoya.

The inclusion criteria for S- and PDD- groups were (1) male, (2) 20-39 years of age, (3) patient lives in Nagoya, (4) has been not hospitalized for more than 6 months continuously, (5) has accessed the Internet once or more in the last week, (6) has adequate communication skills to answer our questionnaire about Internet usage, (7) has agreed to participate in this study, (8) is an outpatient of a hospital or clinic in Nagoya, and (9) has been judged to have no severe intellectual disability by his attending psychiatrist. The inclusion criteria for the Control-group were (1)-(7) noted above.

We constructed an original self-administered questionnaire for assessing Internet usage. The questionnaire consists of 21 questions: (1) age, (2) family structure, (3) educational background, (4) average number of people (including family) with the participant communicated face-to-face (off-line) in the last week, (5) year when participant used the Internet for the first time, (6) devices used to access the Internet [PC (including notebook PC and tablet PC) and/or mobile phone (including PHS and smart phone)], (7) the number of persons the participant e-mailed in the last month: [ a) family and relatives (Related-persons), b) known off-line friends and acquaintances (Off-persons), c) strangers contacted only online and has not met directly (On-persons)], (8) the amount of time spent on-line per day through PC, (9) through mobile phone, (10)-(19) attitudes and opinions about Internet (Table. 1), (20) the frequency of Internet communication through PC, (21) and through mobile phone. In (20) and (21), the use of Internet communication was divided into 5 services: e-mail, bulletin board system (BBS), blogs, micro blogs, and social networking service (SNS). Each service was then subdivided into expressing (sending, writing, etc.) and receiving (getting, reading, etc.). Point scales (i.e., a four-point scale, a six-point scale, or an eight-point scale) were used for responding to (4) and (7)-(21).

Positive symptoms were assessed using the positive items of the Positive and Negative Symptom Scale [PANSS(P)] for the S- and PDD- groups. The attending psychiatrists scored the PANSS(P). In the S- and PDD- groups, autistic traits were also assessed using the Autism-Spectrum Quotient Japanese version (AQ-J, Wakabayashi et al., 2004) [2], which is a self-administered questionnaire consisting of 50 items rated on a 4-point scale.

We showed comparisons of scores among the S-, PDD-, and Control-groups. The scores of point scales were compared among the three groups using Kruskal-Wallis test and between two groups using Mann-Whitney test (Bonferroni multiple comparison). P-values less than 0.05 were considered to be significant.

Table 1: Ten questions regarding attitudes and opinions about the Internet from the original self-administered questionnaire consisted of twenty-one questions for assessing Internet usage. A four-point scale (1 = definitely agree, 2 = slightly agree, 3 = slightly disagree, and 4 = definitely disagree) was used for responding to each question.

Question (Recognition to the Internet)

- (10) I regard the worldwide spread of the Internet as desirable.
- (11) I regard the worldwide spread of the Internet as dangerous.
- (12) I think it is difficult to protect privacy in the present Internet.
- (13) For me, it is beneficial to use the Internet under anonymous or fictitious names.
- (14) When I communicate with people whom I have not met directly on the Internet, I regard almost all of them as trustworthy.
- (15) When I communicate with people whom I have not met directly on the Internet, I can discriminate trustworthy people and untrustworthy ones.
- (16) Emotional troubles arise more frequently from the Internet communication than from face-to-face-communication.
- (17) I can say more clearly what I want to say with the Internet communication than with face-to-face communication.
- (18) I frequently hurt other people's feelings without intending to through Internet communication.
- (19) I am frequently hurt when communicating on the Internet.

#### Results

The number of valid responses were thirty-two in S-, forty-three in PDD-, and ninety-seven in the Control-group. PDD-patients who had a score of 3 or more on at least one of the PANSS(P) items assessing "delusions" or "hallucinatory behavior" were excluded (n = 8), and those who had a score of 25 or less on AQ-J were also excluded (n = 6) [3], in order to

diagnose pervasive developmental disorders more correctly. Twenty-nine PDD-patients remained.

There were no significant differences among the three groups in (1) age [one-way analysis of variance (ANOVA), F = 1.34, p = 0.266], (3) educational background (chi-square test,  $x^2 = 2.71$ , p = 0.258) or (5) the first year of having used Internet (F = 0.79, p = 0.924).

Twenty-seven (84.4%) S-patients, nineteen (65.5%) PDD-patients, and forty-three (44.3%) Controls were living with their parents, and a significant difference was found between S- and Control- groups ( $x^2 = 15.55$ , p = 0.000). Thirty-six (37.1%) Controls were living with their wives and/or children, but S- and PDD- patients were not. Four (12.5%) S-patients, nine (31.0%) PDD-patients, and twenty-one (21.6%) Controls were living alone, but there was no significant difference ( $x^2 = 3.40$ , p = 0.183)

The average number of people (including family) communicating face-to-face (off-line) in the last week was highest in the Control-group. There were significant differences between the S- and Control- groups (U=1,087.0, p=0.009), and between the PDD- and Control- groups (U=835.5, p=0.001).

Twenty-nine (90.6%) S-patients, twenty-seven (93.1%) PDD-patients, and ninety (92.8%) Controls accessed the Internet through a PC ( $x^2=0.18,\ p=0.912$ ). However twenty-eight (87.5%) S-patients, twenty-three (79.3%) PDD-patients, and ninety-five (97.9%) Controls accessed the Internet through a mobile phone, and there was a significant difference between the PDD- and Control- groups ( $x^2=13.03,\ p=0.000$ ).

The number of Related-persons and Off-persons e-mailed to in the last month were significantly lower in S- than in the Control-group (U = 1,040, p = 0.002, U = 867.0, p = 0.000). Those numbers were also significantly lower in PDD- than in Control-group (U = 968.0, p = 0.002, U = 936.5, p = 0.005). There was no significant difference among the three groups in the number of On-persons e-mailed to in the last month (H = 0.75, p = 0.689).

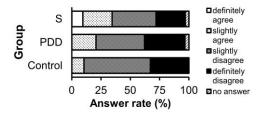
The amount of time spent online a day through a PC was highest in the PDD-group, which was significant by different from the Control-group (U = 652.0, p = 0.002). Also, the amount of time spent online a day through a mobile phone was lowest in the PDD-group, and there was a significant difference between the PDD- and Control-groups (U = 531.0, p = 0.002).

In questions (10) to (19), there were significant differences in (14), (17), and (19). The answer rates of (14), (17), and (19) in each group are shown in Fig. 1.

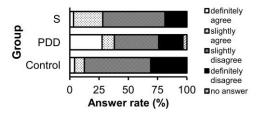
There were five significant differences between the PDD-and Control- groups regarding frequency of Internet communication. PDD-patients expressed themselves in BBS (U = 87.0, p = 0.16), and received from BBS (U = 361.5, p = 0.007) and blogs (U = 381.5, p = 0.015) significantly more frequently than Controls using PCs. On the other hand, PDD-patients significantly less frequently sent (U = 422.0, p = 0.000) and received e-mail than Controls (U = 474.5, p = 0.000) using mobile phones. There was no significant difference between S- and Control- groups, or between S- and PDD- groups in the frequency of Internet communication.

#### **Discussion and Conclusion**

The present study investigated attitudes and opinions, and the frequency of Internet communication among patients with schizophrenia or pervasive developmental disorders. (14) When I communicate with people whom I have not met directly on the Internet, I regard almost all of them as trustworthy.



(17) I can say more clearly what I want to say with the Internet communication than with face-to-face communication.



(19) I am frequently hurt when communicating on the Internet

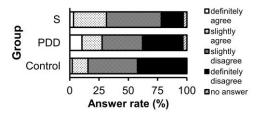


Figure 1: Answer (1 = definitely agree, 2 = slightly agree, 3 = slightly disagree, and 4 = definitely disagree) rates of (14), (17), and (19) in patients with schizophrenia (n = 32, S), individuals with pervasive developmental disorders (n = 29, PDD), and normal controls (n = 97, Control). In (14), there was no significant difference in the average ranks of the groups, but the rate of "total agree" answers ('definitely agree' and 'slightly agree') was significantly higher in S- than in the Control-group (p = 0.001). In (17), the average rank was significantly lower in PDD- than in the Control-group (p = 0.012). In (19), the average rank was significantly lower in S- than in the Control-group (p = 0.011).

Although the social ties of S- and PDD-patients were limited in size, the present study showed that: 1) S-patients had feelings of persecution when engaging in Internet communication, 2) their general trust in Internet communication was higher, and 3) the frequency of Internet communication was close to that of Controls; 4) PDD-patients regard the Internet as more useful for communicating with other people than face-to-face communication, 5) they spent more time online in a day through PCs, 6) they avoid mobile phones, 7) they more frequently use BBS and blogs to communicate, and 8) they less frequently use e-mail to communicate.

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Author's address

E-Mail: watabe.takashi@h.mbox.nagoya-u.ac.jp

# Effects of virtual reality training on upper extremity function and activities of daily living performance in acute stroke: A double-blind randomized clinical trial

Jae-Sung Kwon and Soo Hyun Park
Department of Occupational Therapy, College of Health Sciences,
Yonsei University, Gangwon-do, Republic of Korea

**INTRODUCTION:** The aim of this investigation was to examine the effects of conventional therapy (CT) combined with intensive and repetitive virtual reality (VR) program on upper extremity function and activities of daily living (ADL) performance in individuals in the acute stage of stoke.

METHODS: Twenty-six individuals in the acute stage of stroke were recruited. All subjects were randomly assigned to either the control or experimental group. In this double-blind randomized clinical trial, the control group received CT alone for 70 minutes per day, 5 days per week for 4 weeks, while the experimental group received 30 minutes of VR training in addition to CT on the same day. CT consisted of routine physical and occupational therapy such as gait training, balance training, table-top activities, strengthening exercise of upper limb, and ADL training. VR intervention was conducted using the IREX VR system. This VR system consisted of a television monitor, a video camera, cyber gloves and virtual objects, and scenes displayed on a large back screen. In this study, five VR games that were deemed to induce reaching and lifting motor skills of the upper limb at various angles were selected. Fugl-Meyer Assessment and Manual Function Test were used to measure improvement of functioning in the affected limb and the Korean version of the Modified Barthel Index was conducted to evaluate ADL performance for each group at pre- and post-intervention periods.

**RESULTS:** In tests of upper extremity functioning, VR group showed significant improvement on the Fugl-Meyer Assessment and the Manual Function Test (p < 0.05). In the CT group, a significant change was observed only on the Fugl-Meyer Assessment (p < 0.05). ADL performance showed a significant improvement pre- and post-intervention in both groups (p < 0.05). There were no significant differences between the two groups in upper extremity function and ADL performance (p > 0.05).

**CONCLUSION:** This study observed that while both CT and VR training improves upper extremity function and ADL performance, VR may hold the additional advantage of providing an individualized intensive and repetitive training while maintaining a high degree of motivation for individuals in the acute stage of stroke.

# Neck and shoulder muscle activation in farm workers performing simulated orchard work with and without neck support

In-Gyu Yoo, Jin Lee, Min-Ye Jung, and No-Yul Yang.
Department of Occupational Therapy, College of Health Sciences,
Yonsei University, Gangwon-do, Republic of Korea

**INTRODUCTION:** Work-related musculoskeletal disorders (WMSDs) have become an increasing problem in agricultural society. Activities related to harvest work include climbing ladders, picking fruit, and carrying fruit-laden bags. Such activities lead the worker to assume several awkward postures. Those who perform orchard work frequently report symptoms of musculoskeletal strain. In particular, repeated and sustained work with elevated arms is known to lead to neck and shoulder pain. However, there have been only a few studies focusing on protective ergonomic devices for such activities. The purpose of this study was to hence detect differences in electromyographic (EMG) activity in the neck and shoulder muscles while performing simulated orchard work movements with and without neck support.

**METHODS**: Fourteen healthy orchard harvesters (eight men and six women) who had no functional disorder of the neck or upper limbs and who had never received orthopedic surgery were recruited. A repeated-measures design was used. The participants were asked to perform simulated orchard work movements with and without neck support. The order of condition under which the participants performed the trials was randomly assigned for each participant. The simulated orchard work selected in our study involved reaching up with the arms while holding a 1kg dumbbell in each hand, and to maintain this posture for 1 minute. It is similar to a simple task that is often performed in harvesting apples and pears during orchard work. In the neck support condition, the UPGUARD 3000 (IMPACTO<sup>TM</sup> Protective Products Inc.) was worn by each participant. This device includes a strap attachment while it rests on the upper thorax, and approaches the neck when the head is extended or tilted backwards. With the support resting on the upper back, the extension range of motion can be limited. The EMG activities of the anterior deltoid, middle deltoid, upper trapezius, and triceps brachii (lateral head) muscles during the two conditions were analyzed using paired *t*-tests.

**RESULTS:** The EMG activity of the anterior deltoid and middle deltoid muscles increased significantly (p < .05) and that of the upper trapezius muscles decreased significantly when engaging in work movements with neck support compared to conditions without neck support (p < 0.05).

**CONCLUSION:** Wearing a neck support may prevent overuse of the upper trapezius muscles by encouraging shoulder elevation and activating the deltoid muscles. The activation of these muscles may in turn decrease scapular movement, resulting in greater stabilization of scapulohumeral rhythm. The results of the present study thus indicate that the appropriate application of neck support may ultimately be helpful in preventing disorders of the neck and shoulder muscles resulting from long-term intensive orchard work.

# Computer-based cognitive training improves cognitive function and instrumental activities of daily living in individuals with schizophrenia

<u>Duk-Youn Cho</u> and Ji-Hyuk Park Department of Occupational Therapy, College of Health Sciences, Yonsei University, Gangwon-do, Republic of Korea

INTRODUCTION: Schizophrenia is a complex brain disorder, characterized by positive and negative symptoms. Negative symptoms such as anhedonia are thought to impair cognitive functioning. Such cognitive impairment in turn negatively affect instrumental activities of daily living (IADL) and result in difficulty returning to home and the community. Cognitive rehabilitation training is commonly provided to improve such cognitive skills deficits. Recently, effects of computer-based cognitive training has shown positive effects in improving memory, attention, and executive functioning in individuals with schizophrenia. However, extant research has only shown the benefits of such training on cognitive functioning although improvement in cognitive function may also affect individuals' capacity for engaging in IADL. As such, the present study examined the effects of computer-based cognitive training on both cognitive functions and IADL.

**METHODS**: Twelve clinically stable outpatients diagnosed with schizophrenia based on the DSM- IV who also demonstrated predominance of negative symptoms were recruited. Exclusion criteria were individuals with a comorbid medical and/or psychiatric disorder based on the DSM-IV. Word list memory and word list recall tests were used to measure memory. Word list memory test requires participants to recall from a list of 10 nouns. Word list recall test asks participants to recall the 10 nouns after a given lapse of time. Attentional capacity was measured by the 8 attention tasks on the attention subtest of the Korean-Dementia Rating Scale (K-DRS). Time to completion on the Trail Making Test Forms A and B were used as the measure of executive function. To assess individuals' IADL, the Seoul-Instrument Activities of Daily Living (S-IDAL) was used. This test consists of 15 items evaluated on a 3-point scale with, 0 indicating complete independence and 3 indicating complete dependence. With a total possible score of 45, lower scores indicate greater capacity for independence in conducting IADL. REHACOM computer-based cognitive training (HAZOMED Co.) was provided as the cognitive training component. In this program, memory of words program, divided attention and vigiliance programs, and shopping and planning programs were selected to target memory, attention, and executive function, respectively.

**RESULTS:** Overall, participants' memory, attention, and executive function improved post-cognitive training. While there was no significant improvement in word list memory score (t=-.816, p>.05), improvement in word list recall was significant (t=-2.524, p<.05). A significant improvement in attention was also observed (t=-2.930, p<.05). In regards to executive function, time to completion on the Trail Making Test B significantly decreased following computer-based cognitive training (t=2.634, p<.05). IADL score significantly decreased (t=2.792, p<.05), indicating greater independence. A significant correlation between tests of memory and IADL were also found (p<.05).

**CONCLUSION:** The results of the present study demonstrated the effectiveness of computer- based cognitive training on improving not only cognitive functions but also instrumental activities of daily living in individuals with schizophrenia.

# The effects of home environment modification on occupational performance and fall efficacy in rural community dwelling elderly

<u>Han-Sol Kim</u> and Soo Hyun Park Department of Occupational Therapy, College of Health Sciences, Yonsei University, Gangwon-do, Republic of Korea

**INTRODUCTION:** The concept of "aging in place" highlights the significance of identifying the constellation of factors that place older people with physical ailments and/or impairments at risk or factors that may threaten their ability to manage day-to-day living at home. Home modification intervention is provided by occupational therapists to enhance the fit between the older adult with functional limitations and their home environment by reducing the influence of environmental barriers, thereby increasing (1) occupational performance within the home environment and (2) potential for safety by minimizing fall hazards. This study was designed to investigate the effects of home environment modification on occupational performance and fall efficacy in a sample of rural community dwelling elderly.

METHODS: The sample consisted of 15 elderly participants 65 years and older who are residing in a rural community, who also reported a minimum 5-year farming experience and who had been diagnosed with back pain or musculoskeletal disorders such as arthritis. Researcher used a home environment checklist before deciding on the specifics of the required home modification. Home environment checklist consisted of items from the Home Modification Guideline of the Korea Housing Institution. The researcher met with each participant to discuss environmental hazards and assessed potential target of home modification procedures beginning with the home entrance, then the living area, bedroom(s), kitchen, and the bathroom. Following the assessment, home modification ensued for each household. The degree of satisfaction with the home modification procedure and participants' pre- and post-intervention occupational performance was assessed using the Canadian Occupational Performance Measure (COPM). The participants' degree of fall efficacy was assessed using the Korean Version of the Fall Efficacy Scale (K-FES).

**RESULTS:** A total of 92 environmental barriers were identified in the homes of the participants. The most common place with reported and observed problems were the bathroom (38 problems), home entrance and toilet arrangement (22 problems each), followed by the living room and bedroom (5 problems each). After home modification, a significant change in the participants' capacity for occupational performance, satisfaction with home modification, and fall efficacy was found following the intervention (p<.001).

**CONCLUSION:** The results of the present study demonstrated the effectiveness of client-centered and occupational therapy-based home modification on improving occupational performance, satisfaction, and fall efficacy in a community of rural-dwelling elderly participants.

# Abstracts Biomedical Laboratory Science

# Comparative Effect of Amlodipine and Cilnidipine on Cardiac Remodeling and Diastolic Function in Dahl Salt-Sensitive Rats

Miwa Takatsu<sup>1)</sup>, Takuya Hattori<sup>1)</sup>, Tamayo Murase<sup>1)</sup>, Masafumi Ohtake<sup>1)</sup>, Miki Kato<sup>2)</sup>, Keigo Nashima<sup>2)</sup>, Chieko Nakashima<sup>2)</sup>, Keiji Takahashi<sup>1)</sup>, Kazumi Niinuma<sup>3)</sup>, Shizuka Aritomi<sup>3)</sup>, Toyoaki Murohara<sup>4)</sup>, Kohzo Nagata<sup>2)</sup>

- 1) Department of Pathophysiological Laboratory Sciences, Nagoya University Graduate School of Medicine, Nagoya, Japan
- 2) Department of Medical Technology, Nagoya University School of Health Sciences, Nagoya, Japan
- 3) Research Center, Ajinomoto Pharmaceuticals Co. Ltd., Kawasaki, Japan
- 4) Department of Cardiology, Nagoya University Graduate School of Medicine, Nagoya, Japan

#### Introduction

The L/N-type calcium channel blocker (CCB) cilnidipine suppresses sympathetic nerve activity and has a superior renoprotective effect compared with L-type CCBs such as amlodipine. The cardioprotective action of cilnidipine has remained largely uncharacterized, however. We have now investigated the effects of cilnidipine, in comparison with amlodipine, on cardiac pathophysiology in rats with salt-sensitive hypertension.

#### **Materials and Methods**

Animals and experimental protocols: Dahl salt-sensitive (DS) rats fed a high-salt diet (8% NaCl) from 6 weeks of age were treated with vehicle (LVH group), amlodipine (3 mg/kg per day), or cilnidipine (3 mg/kg per day) from 7 to 11 weeks (n = 6, 10, and 10, respectively). DS rats maintained on a 0.36% NaCl diet after 6 weeks of age served as age-matched controls (CONT group, n = 6). At 11 weeks of age, all rats were anesthetized and were subjected to echocardiographic and hemodynamic analyses.

Blood pressure measurement and echocardiography: Systolic blood pressure (SBP) was measured weekly in conscious animals by tail-cuff plethysmography (BP-98A; Softron, Tokyo, Japan). At 11 weeks, rats were subjected to transthoracic echocardiography as previously described [1]. After echocardiography, cardiac catheterization was performed as described previously [2]. Left ventricular (LV) end-diastolic pressure (LVEDP) was determined and the time constant of isovolumic relaxation (tau) was calculated by the derivative method of Raff and Glantz, as described previously [3].

Histology and immunohistochemistry: LV tissue was fixed with ice-cold 4% paraformaldehyde for 48 to 72 h, embedded in paraffin wax, and processed for histology as described [4]. To evaluate macrophage infiltration into the myocardium, we performed immunostaining for the monocyte-macrophage marker CD68 with frozen sections (thickness, 5 μm) that had been fixed with acetone.

Measurement of biochemical parameters: Plasma renin activity, plasma angiotensin II concentration, and serum aldosterone concentration were determined by radioimmunoassay as described previously [5]. Urinary norepinephrine concentration was measured by high-performance liquid chromatography, and urinary norepinephrine excretion over 24 h was calculated as described previously [6].

Assay of superoxide production: NADPH-dependent superoxide production by homogenates of freshly frozen LV tissue was measured with an assay based on lucigeninenhanced chemiluminescence as described previously [7]. Superoxide production in tissue sections was examined by

staining with dihydroethidium (Sigma, St. Louis, MO, USA) as described [8].

Assay of myocardial norepinephrine levels: Norepinephrine levels in heart tissue were measured by high-performance liquid chromatography with electrochemical detection, as described previously [9].

Quantitative RT-PCR analysis: Total RNA was extracted from LV tissue and treated with DNase with the use of a spin-vacuum isolation kit (Promega, Madison, WI). Complementary DNA was synthesized from 2 µg of total RNA by reverse transcription (RT) with random primers (Invitrogen, Carlsbad, CA) and MuLV Reverse Transcriptase (Applied Biosystems, Foster City, CA). Real-time polymerase chain reaction (PCR) analysis was performed as previously described [10].

Western blot analysis: Protein levels in LV tissue were analyzed by Western blotting using specific antibodies as previously described [11].

Statistical analysis: Data are presented as means  $\pm$  SEM. Differences among groups of rats at 11 weeks were assessed by one-way factorial analysis of variance (ANOVA); if a significant difference was detected, intergroup comparisons were performed with Fisher's multiple-comparison test. The time course of SBP was compared among groups by two-way repeated-measures ANOVA. A P value of < 0.05 was considered statistically significant.

#### Results

SBP was similar in all groups of rats at 6 weeks, but it was significantly higher in the vehicle-treated (LVH) group than in the CONT group at 7 weeks and thereafter. SBP was significantly reduced in the amlodipine (Aml)- and cilnidipine (Cil)-treated groups at 8 weeks and thereafter compared with that in the LVH group, but it did not differ between the Aml and Cil groups at any age. The ratios of heart or LV weight to tibial length, indices of cardiac and LV hypertrophy, respectively, were significantly increased in the LVH group compared with the CONT group at 11 weeks, and these effects were similarly attenuated in the Aml and Cil groups. Salt loading reduced plasma renin activity as well as the plasma angiotensin II and serum aldosterone concentrations in the LVH group, and these changes were not affected by treatment with either drug. Urinary norepinephrine excretion was markedly increased in the LVH group compared with the CONT group at 11 weeks, and this effect again was not influenced by drug treatment. Myocardial norepinephrine content was significantly decreased in the LVH group compared with the CONT group, but this change was reversed by both drugs. None of these measured parameters differed significantly between the Aml and Cil

Echocardiography revealed that both LVDd and LVDs were decreased, and that IVST, LVPWT, LVFS, LV mass, and

relative wall thickness (RWT) were increased, in the LVH group compared with the CONT group. The increase in LV mass in the LVH group was similarly attenuated by both drug treatments, whereas that in RWT was inhibited to a greater extent in the Cil group than in the Aml group. The IRT, DcT, and tau, all of which are indices of LV relaxation, as well as the ratio of LVEDP to LVDd, an index of diastolic stiffness, were all increased in the LVH group compared with the CONT group. All of these changes were attenuated to a greater extent in the Cil group than in the Aml group.

Azan-Mallory staining revealed that fibrosis in perivascular and interstitial regions of the LV myocardium was increased in the LVH group compared with that in the CONT group. These increases in the extent of LV fibrosis were partially attenuated by treatment with amlodipine and were completely inhibited by treatment with cilnidipine. The abundance of collagen type I mRNA and the ratio of collagen type I to type III mRNA abundance, which correlates with myocardial diastolic stiffness, were increased in the left ventricle of rats in the LVH group, and this effect was attenuated to a greater extent in the Cil group than in the Aml group.

The amounts of TGF- $\beta$ 1 and CTGF mRNAs in the LV were significantly increased in the LVH group compared with the CONT group, and these effects were attenuated by amlodipine and to a greater extent by cilnidipine. Expression of the ACE gene was also significantly up-regulated in the LVH group compared with the CONT group, whereas that of the AT<sub>1A</sub> receptor gene did not differ between these two groups. The overload-induced up-regulation of ACE gene expression was inhibited to a greater extent in the Cil group than in the Aml group, whereas expression of the AT<sub>1A</sub> receptor gene was down-regulated in the Cil group but not in the Aml group. The abundance of the AT<sub>1</sub> receptor protein in the left ventricle showed a pattern similar to that of the AT<sub>1A</sub> receptor mRNA in the four experimental groups.

Immunostaining for the monocyte-macrophage marker CD68 revealed that macrophage infiltration in the LV myocardium was increased in the LVH group compared with that in the CONT group and that this effect of salt loading was partially attenuated by treatment with amlodipine and was prevented by that with cilnidipine. The expression of inflammation-related genes in the left ventricle was also increased in the LVH group compared with the CONT group, and these effects were inhibited to a greater extent in the Cil group than in the Aml group.

Superoxide production in myocardial tissue sections revealed by staining with dihydroethidium as well as the activity of NADPH oxidase in LV homogenates were both markedly increased in the LVH group compared with the CONT group, and these effects were inhibited to a greater extent by cilnidipine than by amlodipine. The expression of genes for the components of NADPH oxidase was also upregulated in the left ventricle of rats in the LVH group compared with the CONT group, and these effects were inhibited to a greater extent in the Cil group than in the Aml group.

#### Discussion

We have shown that both amlodipine and cilnidipine similarly attenuated hypertension and LV hypertrophy in DS rats, whereas cilnidipine ameliorated LV concentricity, fibrosis, and diastolic dysfunction to a greater extent than did amlodipine. The superior cardioprotective effects of cilnidipine were associated with more effective inhibition of cardiac oxidative stress and inflammation. In addition, whereas the suppression of the systemic renin-angiotensin

system (RAS) by salt loading was not affected by cilnidipine or amlodipine, both the expression of ACE and  $AT_{1A}$  receptor mRNAs and that of  $AT_1$  receptor protein in the heart of DS hypertensive rats were inhibited by cilnidipine but not by amlodipine, suggesting that the cardiac RAS was inhibited only by cilnidipine. However, the present study did not clarify whether the superior cardioprotective effects of cilnidipine are directly related to its N-type  $Ca^{2^+}$  channel–blocking action in the heart. Further studies are required to determine the possible role of the N-type CCB activity, and thus of the sympatholytic effect, of cilnidipine in cardioprotection.

#### **Conclusions**

Cilnidipine attenuated LV fibrosis and diastolic dysfunction as well as LV concentricity to a greater extent than did amlodipine in DS rats. The superior cardioprotective action of cilnidipine is likely attributable, at least in part, to the greater antioxidant and anti-inflammatory effects associated with inhibition of cardiac RAS gene expression observed with this drug.

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#### **Author address**

E-Mail: takatsu.miwa@f.mbox.nagoya-u.ac.jp

#### **HO-1-Independent Anti-Allergic Action of Chrysin**

Ayaka Teranishi<sup>1)</sup>, Miyoko Matsushima<sup>1, 2)</sup>, Akemi Mori<sup>1)</sup>, Haruka Nose<sup>2)</sup>, Nanako Ogasawara<sup>1)</sup>, Yukiko Yamamoto<sup>1)</sup>, Takehiro Yamaguchi<sup>2)</sup>, Tsutomu Kawabe<sup>1, 2)</sup>

- 1) Department of Pathophysiological Laboratory Sciences, Nagoya University Graduate School of Medicine, Nagoya, Japan
- 2) Department of Medical Technology, Nagoya University School of Health Sciences, Nagoya, Japan

#### Intoroduction

Flavonoids are a group of polyphenolic compounds that are found in many fruits, vegetables, and beverages, including wine and tea. Flavonoids possess anti-oxidant, anti-tumor, anti-angiogenic, anti-inflammatory, anti-allergic, and anti-viral activities, and more than 4,000 different flavonoids have been identified to date. Flavonoids consist of two aromatic rings (A and B rings) that are joined by three carbons (C ring) [1].

We previously demonstrated that one of the flavonoids, quercetin exerted anti-allergic activity via heme oxygenase (HO)-1 activity in mast cells [2]. HO is the rate-limiting enzyme in the catabolism of heme. It breaks down the porphyrin ring to yield equimolar amounts of biliverdin, free iron (Fe<sup>2+</sup>), and carbon monoxide (CO) [3]. In mammals, biliverdin is rapidly converted by biliverdin reductase into bilirubin. HO-1 is induced ubiquitously in response to oxidative stress and is involved in a multitude of signaling pathways [4].

Chrysin is a natural flavonoid contained in fruits and honey and exerts anti-allergic [5] and anti-tumor [6] activities although their precise mechanisms of action are unclear. Several studies have been reported that chrysin was not involved in the modification of mitogen-activated protein kinases (MAPKs) signaling pathway in IgE-stimulated mast cells whereas quercetin inhibited phosphorylation of MAPKs [7, 8]. These observations suggested that chrysin and quercetin might exert inhibitory effects through a different mechanism on signal transduction pathways.

In this study, we investigated the mechanism by which chrysin could exhibit an anti-allergic activity in murine mast cells. We also investigated the involvement of HO-1 in the inhibitory effect of chrysin on mast cell activation in murine mast cells.

#### **Materials and Methods**

Animals: Balb/c mice were maintained in a temperature-(22-24°C), humidity-(55±5%) and light-(12 hour light-dark cycle; lights on at 7:00) regulated room with food and water ad libitum. All procedures were performed with the approval of the Animal Experimentation Committee, Graduate School of Medicine, Nagoya University in accordance with the Guidelines for Animal Experimentation of Nagoya University.

Cell Culture: RBL-2H3 cells were maintained in MEM supplemented with 10% fetal calf serum, 100 U/ml penicillin, and 100 μg/ml streptomycin. For preparation of bone marrow-derived mast cells (BMMC), bone marrow cells were obtained from the female of 7-week-old Balb/c mice, and cultured for 6 weeks in RPMI 1640 supplemented with 10% FCS, 20 ng/ml mouse IL-3, 100 U/ml penicillin, and 100 μg/ml streptomycin.

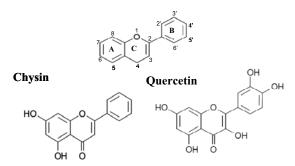


Fig. 1. Basic structure of flavonoids and the structure of chrysin and quercetin.

*Cell Activation*: Cells  $(2\times10^5 \text{ cells/ml})$  were plated and treated with chrysin for the indicated times and then stimulated with thapsigargin  $(10 \ \mu\text{M})$  or A23187  $(5\times10^{-7} \ \text{M})$  for 15 min. For IgE-mediated stimulation, cells were incubated with 0.1  $\mu\text{g/ml}$  of mouse anti-dinitrophenyl IgE  $(\alpha DNP\text{-IgE})$  for 2 h and then stimulated with 0.1  $\mu\text{g/ml}$  of DNP-bovine serum albumin (BSA) for 30 min.

*β-hexosaminidase Release Assay*: The equal volume of supernatant and 1 mM p-nitrophenyl-N-acetyl- $\beta$ -D-glucosaminide were added and incubated for 1 h at 37°C. After adding 0.1 M carbonate buffer, pH 10.5., the absorbance at 405 nm was measured.  $\beta$ -hexosaminidase release was expressed as a percentage of the total  $\beta$ -hexosaminidase activity, and the spontaneous release was subtracted from stimulated cell release.

Western Blotting: 20 μg of protein was subjected to SDS-PAGE and transferred to polyvinylidene difluoride membranes. The membrane was incubated with 4% skim milk for 1 h at room temperature. The membrane was then incubated with primary antibodies overnight at 4°C. Subsequently, the membrane was incubated with either anti-rabbit IgG or antimouse IgG antibodies conjugated with horse radish peroxidase for 1 h at room temperature. The specific protein bands on the membrane were visualized using the Enhanced Chemiluminescence Kit (GE Healthcare Bioscience, Buckinghamshire, UK) according to the recommendations of the manufacturer.

**RT-PCR, Quantitative real-time PCR:** Total RNA was isolated using TRIZOL reagent and reverse-transcribed to cDNA using random hexamers and SuperScript II according to the manufact -ufacturer's instructions. cDNA was amplified with Taq polymerase using 28 cycles for b-actin, 30 cycles for HO-1, 35 cycle for TNF-a and IL-4 under the following conditions: denaturation at 94°C for 30 s, annealing at 55°C (β-actin) or 60°C (HO-1, IL-4) or 58°C (TNF-α) for 30 s, and extension at 72°C for 30 s.

Quantitative real-time PCR was performed on the ABI 7000 Sequence Detector (Applied Biosystems, FosterCity, CA,

USA). Primersand probes for HO-1, TNF- $\alpha$  and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) were obtained from TaqManGene Expression Assays (Applied Biosystems, FosterCity, CA, USA).

#### Results

#### Chrysin inhibited degranulation in RBL-2H3 cells

Exposure of cells for 15 min to chrysin resulted in a concentration-dependent inhibition in degranulation from RBL-2H3 cells after stimulation with A23187, thapsigargin, or IgE. Chrysin strongly inhibited thapsigargin-induced degranulation whereas the extent of inhibition on A23187- or IgE-mediated degranulation by chrysin was much weaker. Quercetin, which is known to exhibit HO-1-dependent antiallergic activity, also inhibited A23187-, thapsigargin-, or IgE-mediated degranulation. The extent of inhibition on A23187- or IgE-mediated degranulation by quercetin was more pronounced than chrysin. Chrysin and quercetin did not affect spontaneous degranulation and had no significant cytotoxicity in RBL-2H3 cells at the concentrations used.

## Chrysin suppressed TNF-a and IL-4 mRNA expression in RBL-2H3 cells

We examined the effect of chrysin on tumor necrosis factor (TNF)- $\alpha$  and IL-4 mRNA expression stimulated with A23187 or IgE. The expression of TNF- $\alpha$  and IL-4 mRNA was increased in A23187- or IgE -stimulated RBL-2H3 cells, and robust inhibition was observed by chrysin treatment although chrysin showed weak inhibition of degranulation in A23187- or IgE-stimulated RBL-2H3 cells. These findings suggest that the inhibitory effect of chrysin could be superior to cytokine production rather than degranulation.

#### HO-1 expression induced by chrysin in RBL-2H3 cells

We previously demonstrated that quercetin exhibited antiallergic action via induction of HO-1. We next examined expression levels of HO-1 mRNA and protein in RBL-2H3 cells cultured with chrysin by quantitative real-time PCR and western blot. Unexpectedly, the expression levels of HO-1 were not increased after exposure to chrysin. At the concentration of 50  $\mu M$  of chrysin, significant decrease of HO-1 expression was observed, as compared with that of control.

## Effect of HO-1 on degranulation in RBL-2H3 cells after exposure to chrysin

To investigate the involvement of HO-1 in the inhibitory activity of chrysin, we used tin protoporphyrin IX (SnPP), an HO-1 inhibitor. RBL-2H3 cells were exposed to SnPP for 1 h with a 15-min incubation of chrysin before stimulation. The inhibition of degranulation by chrysin was maintained despite the addition of SnPP, suggesting that the inhibition of degranulation by chrysin might be mediated via HO-1-independent pathway.

## Effect of chrysin on HO-1 induction by hemin or quercetin in RBL-2H3 cells

Since we observed the reduction of HO-1 expression after exposure to chrysin at the concentration of 50  $\mu$ M, we hypothesize that chrysin might transcriptionally regulate the expression of HO-1. We next investigated the effect of chrysin on HO-1 induction induced by quercetin or hemin, a HO-1 inducer, in RBL-2H3 cells. Chrysin decreased both quercetin- and hemin-induced HO-1 expression at the mRNA and protein levels.

#### Discussion

In this study, we demonstrated that the anti-allergic effect of chrysin was mediated via HO-1-independent pathway in murine mast cells. We also demonstrated that chrysin was able to decrease the expression of HO-1 induced by quercetin or hemin.

First, we investigated the inhibitory effect of chrysin on degranulation and the expression of TNF- $\alpha$  and IL-4 mRNA stimulated by A23187, thapsigargin, or IgE. Chrysin strongly inhibited thapsigargin-induced degranulation whereas the inhibition of A23187- or IgE-induced degranulation was weak. Since thapsigargin, an endoplasmic reticular Ca<sup>2+</sup>-ATPase inhibitor, activates mast cells due to the elevation of cytosolic calcium levels, suggesting that chrysin might affect the calcium mobilization in mast cells.

Nuclear factor erythroid 2-related factor 2 (Nrf2) is involved in cellular protection against oxidative stress through antioxidant response element (ARE) -directed induction of several phase 2 detoxifying and antioxidant enzymes, including HO-1. HO-1 is also under the control of the transcription factor, broad complex-tramtrack-bric-a-brac (BTB) and Cap'n'collar (CNC) homology (Bach) 1, which repress the transcription HO-1 [9]. We have previously reported that quercetin upregulated HO-1 expression with the translocation of Nrf2, leading to antiallergic effect in rodent mast cells [2]. We observed the reduction of quercetin- or hemin-induced HO-1 expression by chrysin, suggesting that chrysin might regulate the activation of Bach1 or Nrf2. It has been reported that genistein, also one of the flavonoids, blocked nuclear export of Bach1, thus allowing Nrf2 stays in cytoplasm [10]. This finding leads us to consider the possibility that chrysin might regulate Nrf2-Bach1 interaction. Further studies have to be elucidated how chrysin negatively regulates the expression of HO-1.

#### Conclusion

In the present study, our results demonstrated that chrysin mediated anti-inflammatory effects via HO-1-independent pathway in mast cells. To elucidate the molecular mechanism of anti-allergic effect by chrysin may well lead to promising new therapeutic strategies for promoting not only anti-allergic but also a wide range of anti-inflammatory therapy.

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#### **Author address**

E-Mail: teranishi.ayaka@a.mbox.nagoya-u.ac.jp

# (-)-Epigallocatechin-3-gallate prevents doxorubicin-induced overexpression of P-glycoprotein through inhibition of MEK/ERK signaling pathway in HepG2 Cells

Hana Satonaka, Kumiki Ishida, Yuki Komori, Sakiko Arisawa, Jun Ueyama, Shinya Wakusawa

Department of Medical Technology, Nagoya University Graduate School of Health Sciences

#### Introduction

(-)-Epigallocatechin-3-gallate (EGCG) is the most abundant component of tea catechins, and it reportedly has various biological and pharmacological actions such as antioxidative and iron chelating activities. Additionally, EGCG has been suggested to inhibit the transport function of P-glycoprotein (P-gp) via direct action on it or antioxidative action [1,2]. P-gp is an efflux pump that extrudes chemotherapeutic agents out of the cells, decreasing their intracellular concentrations, and causing multidrug resistance (MDR) against anti-tumor chemotherapy. Therefore, modulations of the function and/or expression of P-gp are expected to improve the effect of anticancer chemotherapy.

In this study, we investigated whether EGCG acts as an inhibitor of the overexpression of P-gp in HepG2 cells. Further, to elucidate its mechanisms, we investigated the signal transduction system involved in the inhibitory action of EGCG on the up-regulation of P-gp induced by doxorubicin (DOX).

#### **Materials and Methods**

Cell culture. Human hepatoma HepG2 cells were cultured in Dulbecco's modified Eagle's medium (Sigma) supplemented with 5% (v/v) heat-inactivated fetal calf serum (BioWest) and 100 U/mL of penicillin, 100  $\mu$ g/mL of streptomycin, and 0.25  $\mu$ g/mL of amphotericin B (Invitrogen).

Rhodamin 123 (R123) uptake assay. After cells were incubated for 30 min with 3μM R123, intracellular R123 was extracted with ethanol and its fluorescence intensity was measured Ex; 480 nm, Em; 538 nm).

RT-PCR. After total RNA was isolated using TRIzol Reagent (Invitrogen), cDNA was prepared using RNA reverse transcriptase (ReverTra Ace, TOYOBO, Japan). Then, polymerase chain reaction (PCR) was carried out using specific PCR primers for MDR1 and GAPDH obtained from Hokkaido System Science (Sapporo, Japan).

Western blotting. P-gp was detected with the C219 anti-MDR1 P-gp mouse monoclonal antibody (Centocor). Total-and phosphorylated-proteins of ERK, p38 MAP kinase, and Akt were detected using respective specific antibodies obtained from Cell Signaling Technology.

Statistical analysis. Data are expressed as the mean  $\pm$  S.D. Statistical analyses were performed using Student's t-test after a test for equality of variance. P < 0.05 was considered statistically significant

#### Results

Inhibition of DOX-induced MDR1 gene expression and P-gp expression by EGCG.

MDR1 gene expression was significantly induced by 24-hr treatment with DOX. While EGCG did not influence MDR1 gene expression by itself, it significantly suppressed the

induction by DOX. The expression of P-gp was significantly increased by DOX, and the induction was markedly suppressed by EGCG (Figure 1).

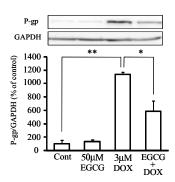


Figure 1. EGCG inhibits DOX-induced overexpression of P-gp in HepG2 cells.

HepG2 cells were exposed to 3  $\mu$ M DOX in the presence or absence of 50  $\mu$ M EGCG for 24 h. Then, whole cell lysates were used for Western blot analysis of P-gp. The photograph is typical of three independent experiments. Column graph data are expressed as the mean  $\pm$  S.D. (n=3). \*P<0.05, \*\*P<0.01.

Reversal of R123 uptake in cells pretreated with EGCG and DOX

To evaluate the effect on P-gp function in cells pretreated with DOX and EGCG, we examined the effect of combined pretreatment with EGCG and DOX on the uptake of R123. While the uptake of R123 was significantly decreased in DOX-pretreated cells, the uptake in the cells pretreated with EGCG combined with DOX was partially reversed.

Effects of inhibitors for MAP kinases and PI3K/Akt signaling on the DOX-induced MDR1 gene expression.

DOX-induced up-regulation of MDR1 mRNA was significantly suppressed by LY294002 (a PI3K inhibitor) and SB202190 (a p38 MAPK inhibitor), and slightly-suppressed by U0126 (a MEK1/2 inhibitor). SP600125 (a JNK inhibitor) barely influenced the levels in basal and stimulated conditions.

Effects of LY294002, SB202190, U0126 and SP600125 on P-gp level.

SB202190 and U0126 significantly decreased P-gp levels by combined treatment with DOX. On the other hand, LY294002 and SP600125 did not affect P-gp levels in combination with DOX (Figure 2).

Effects of EGCG on the phosphorylation of ERK, Akt, and p38 MAPK..

DOX significantly induced the phosphorylation of ERK, Akt, and p38 MAPK against the total level. EGCG inhibited DOX-induced phosphorylation of ERK and Akt, though it did not

affect the total level. On the other hand, EGCG did not affect DOX-induced phosphorylation of p38 MAPK (Figure 3).

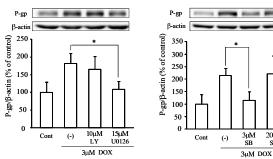


Figure 2. Effects of LY294002, U0126, SB202190, and SP600125 on DOX-induced overexpression of P-gp in HepG2 cells.

20µM SP

HepG2 cells were exposed to 3  $\mu$ M DOX in the presence or absence of LY294002 (LY, 10  $\mu$ M), U0126 (15  $\mu$ M), SB202190 (SB, 3  $\mu$ M), and SP600125 (SP, 20  $\mu$ M) for 20-24 h. Then, whole cell lysates were used for Western blot analysis of P-gp. The photograph is typical of three independent experiments. Column graph data are expressed as the mean  $\pm$  S.D. (n=3). \*P<0.05.

#### Discussion

The results showed that EGCG inhibited P-gp overexpression in DOX-treated cells through inhibiting the induction of MDR1 gene expression. Our results also indicated that MDR1 gene overexpression by DOX depended on the activation of PI3K/Akt, MEK/ERK, and p38 MAPK signaling systems. However the P-gp expression was not affected by a PI3K/Akt inhibitor and therefore it was suggested that it is not directly dependent on the PI3K/Akt signaling system. Further, although EGCG inhibits both Akt phosphorylation and MDR1 gene overexpression, its inhibitory action on the PI3K/Akt pathway seemed to scarcely contribute to the suppression of P-gp overexpression. As for MEK/ERK signaling, EGCG partially inhibited DOXinduced activation of the MEK/ERK pathway along with decreasing the expression of MDR1 gene and P-gp. Then it was suggested that EGCG may prevent P-gp overexpression through the inhibitory action on MEK/ERK activation. As for p38 MAPK, several studies reported that EGCG inhibited its activity [3-5] and its negative effect has also been reported [6]. In the present study, as EGCG did not affect the activation of p38 MAPK by DOX in HepG2 cells, it clearly indicated that the effect of EGCG on P-gp overexpression is independent of the inhibitory action on p38 MAPK signaling pathway. Thus, it was suggested that EGCG partially inhibits the acquisition of P-gp-dependent multidrug resistance through the inhibition of MEK/ERK signaling pathway.

#### Conclusion

We showed that EGCG antagonized induction of P-gp in DOX-treated cells through inhibiting MDR1 gene overexpression. As the molecular bases of the phenomenon, we showed that EGCG inhibited DOX-induced activation of PI3K/Akt and MEK/ERK pathways and that P-gp induction by DOX was dependent on MEK/ERK and p38 MAPK. Therefore, it was suggested that EGCG suppressed DOX-induced P-gp overexpression partially through the inhibition of MEK/ERK signaling pathway.

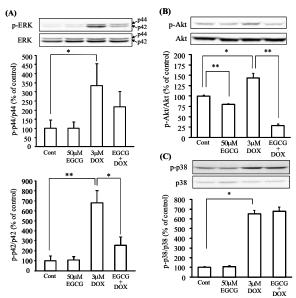


Figure 3. Effects of EGCG on the phosphorylation of ERK, Akt, and p38 MAPK in DOX-treated HepG2 cells.

HepG2 cells were exposed to 3  $\mu$ M DOX in the presence or absence of 50  $\mu$ M EGCG for 20-24 h. Then, whole cell lysates were used for Western blot analysis of phosphorylated ERK (p-ERK) (A), phosphorylated Akt (p-Akt) (B), and phosphorylated p38 MAPK (p-p38) (C). Total protein level was also detected with each specific antibody. The photograph is typical of three independent experiments. Column graph data are expressed as the mean  $\pm$  S.D. (n=3). \*P<0.05, \*\*P<0.01.

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#### **Author address**

E-Mail: satonaka.hana@f.mbox.nagoya-u.ac.jp

# THE POSITIVE ROLE OF C-MYB IN SPHK1 OVEREXPRESSION OF MOUSE ERYTHROLEUKEMIA CELLS

Misa Kobayashi<sup>1)</sup>, Hiromi Ito<sup>1)</sup>, Kazumi Hagiwara<sup>1)</sup>, Asuka Hoshikawa<sup>1)</sup>, Naoki Mizutani<sup>1)</sup>, Keiko Tamiya-Koizumi<sup>1)</sup>
Akira Takagi<sup>1)</sup>, Tetsuhito Kojima<sup>1)</sup>, Motoshi Suzuki<sup>2)</sup>, Mitsuhiro Nakamura<sup>3)</sup>, Yoshiko Banno<sup>4)</sup>,
and Takashi Murate<sup>1)</sup>

- 1) Department of Medical Technology, Nagoya University Graduate School of Health Sciences, Nagoya, Japan 2) Division of Molecular Carcinogenesis, Nagoya University Graduate School of Medicine, Nagoya, Japan
  - 3) Department of Drug Information, Gifu Pharmaceutical University, Gifu, Japan
  - 4) Department of Dermatology, Gifu Graduate School of Medicine, Gifu, Japan

#### Introduction

Sphingolipid (SPL) is a complex lipid containing an amidelinked fatty acid and sphingoid base. Recently, SPLs such as ceramide, sphingosine and sphingosine 1-phospahte (S1P), and ceramide 1-phosphate are considered as intracellular or intercellular signaling molecules in numerous biological processes (1). Sphingolipid rheostat model, where he balance between ceramide and S1P determines cell's fate has been proposed (2). Ceramide acts as a signaling molecule leading to apoptosis, growth arrest, cell differentiation and inflammation, whereas S1P mostly works as an inhibitor of apoptosis and stimulator of cell proliferation.

S1P is produced by sphingosine kinases 1 and 2. SPHK1 expression not only stimulates proliferation and protects from apoptosis, but also induces tumor formation in some cases. On the contrary, overexpression of SPHK2 suppresses cell growth and induces apoptosis. Thus, SPHKs play an important role in cancer growth and survival. Previous reports including ours have shown increased SPHK1 expression of various cancer and leukemia cells. Considering the role of sphingolipid metabolic enzymes as the chemotherapy sensor, the elucidation of SPHK1 expression mechanism is clinically important.

The mouse erythroleukemia cell line caused by the Friend virus (Friend cells) has been extensively studied, because of the suitable model of virus oncogenesis (3) and also because of high inducibility toward erythroid lineage by chemical inducers. The sequential changes of protooncogenes (*c-Myb*, *Fli-1 and Pu.1*) and cell cycle regulators (CDK2,4 and 6) have been reported.

Recently, le Scolan *et al.* reported that overexpression of SPHK1 is an oncogenic event in Friend cell lines (4). However, it remains to be determined how this overexpression is induced and whether HMBA-induced differentiation affects this overexpression. We approached these issues by establishing wild-type (WT) and dominant negative (DN) SPHK1- and SPHK2-transfected Friend cells and HMBA-resistant Friend cells (R cells). We further analyzed mouse *Sphk1* transcription mechanism in Friend cells. Our analysis revealed that the c-Myb as the major transcription factors of *Sphk1* gene and that Sphk1 at least partially plays a role in modulating differentiation sensitivity byHMBA.

#### **Materials and Methods**

<u>Cell lines:</u> Mouse Friend erythroleukemia cell line (original Friend cells) was reported previously (5), and its HMBA-resistant subline (Friend R) was established by continuous treatment with HMBA.

<u>Erythroid differentiation:</u> Chemical induction was performed with 5mM Hexamethylene-bisacetamide (HMBA). Hemoglobin-positive cells were detected by liquid benzidine staining.

Sphk enzyme activity was measured as described previously (6). Real time RT-PCR was previously described previously (7). Western Blotting: Anti-SPHK2, anti-FLI-1, anti-PU.1, anti-c-MYB, anti-GATA-1, and anti-GATA-2 antibody were purchased from Santa Cruz Biotechnology. Anti-β-actin antibody was purchased from BioVision. Anti-mouse SPHK1 antibody was described before (8).

Sphk1 promoter analysis: To determine the transcription initiation point of Sphk1 in Friend cells, RNA ligase-mediated rapid amplification of 5'-cDNA ends (5-RACE) was performed. Based on these data, the 1.7-kb 5'-promoter region of mouse SPHK1 gene was obtained by PCR methods and inserted into pGL3 basic vector. Eight deletion mutants and 4 mutation-inserted vectors were prepared.

Electrophoresis mobility shift assay (EMSA): Nuclear extract was prepared from original Friend cells or Friend R cells with or without HMBA treatment for 48 h. EMSA was performed according to the method previously described previously (9). Chromatin immunoprecipitation (ChIP) assay was carried out as described previously (10).

<u>Transient transfection of siRNA</u>: Friend cells were transfected with siRNA against c-Myb, nonspecific siRNA or c-Myb expression vector by the lipofection method.

#### Results

SPHK1 and SPHK2 expression of various mouse cell lines
Sphk1 mRNA of Friend cells was much higher than other
mouse cell lines analyzed, whereas Sphk2 mRNA did not. This
tendency was also demonstrated in Western blotting.
Effects of SPHK1 and SPHK2 overexpression

To examine the role of Sphks in Friend cell survival, proliferation and differentiation, we established several subclones of Friend cells. SPHK1-wild-type (SPHK1-WT) demonstrated higher proliferation and resistance against serum depletion-induced cell death. Furthermore, erythroid differentiation was delayed as compared with original Friend cells. On the contrary, SPHK1-dominant-negative (SPHK1-DN) showed lower proliferation in culture with FCS and higher apoptosis in serum-depleted culture. We also established WT-and DN-SPHK2 transfectants. Cell proliferation was delayed in SPHK2-WT and apoptosis induced with serum depletion was reduced in SPHK2-DN cells.

<u>HMBA-induced erythroid differentiation of Friend cells and its resistant clone, Friend R</u>

We examined HMBA-induced differentiation of original Friend cell and the resistant clone, R cells. After 4 days incubation with 5mM HMBA, Friend cells demonstrated almost 100 % hemoglobin positive, whereas Friend R did not show any hemoglobin positivity. Friend cells gradually decreased cell proliferation during HMBA treatment, whereas R cells continued to proliferate even in HMBA (+) medium. R cells showed higher Sphk1 mRNA and delayed and much milder decrease of Sphk1 enzyme activity by HMBA compared with

original cells. To prove the positive effects on *Sphk1* expression by proto-oncogenes, we examined FII-1 and Pu.1 proteins. c-MYB expression was also examined because it has been reported that differentiation-resistant Friend cell lines can not completely down-regulate c-MYB expression with DMSO. Interestingly, c-MYB protein stayed high in HMBA-treated R cells, whereas FLI-1 and PU.1 decreased in HMBA-treated Friend R cells, suggesting the positive relationship between HMBA resistance and *Sphk1* overexpression stimulated by c-Myb transcription factor. 5' promoter analysis

Promoter analysis using various lengths of reporter vector revealed that the region between – 53 and -4 bp from the first exon is sufficient for the promoter activity of Friend cells. We further analyzed this region by inserting several mutations to the putative transcription factor binding sites. Results revealed that the proximal Myb-binding site was the most important within this area, through other Myb- and Ets-binding site also demonstrates some promoter activity. *EMSA* 

The promoter region containing three Myb-binding sites and one Ets-binding site was used as the biotin-labeled probe for EMSA. Nuclear extracts of Friend cells produced 3 bands. Bands 2 and 3 were competed with the same non-labeled probe, suggesting the specificity of these band formation. Anti-c-Myb antibody decreased band 3, although not completely. We produced c-Myb protein from GST-c-MYB fusion protein. It clearly shows that band 3 contained c-Myb protein. Intriguingly, HMBA treated Friend cells but not HMBA-treated Friend R cells demonstrated the reduction of band 3. Furthermore, Band 1 increased its intensity in both HMBA-treated Friend cells and Friend R cells, and increased band 2 appeared only in HMBA-treated Friend R cells, suggesting the complex occupation of these binding sites with multiple transcription factors.

<u>ChIP assay and siRNA for c-MYB or c-MYB expression</u> <u>vector transfection</u>

We performed the ChIP assay covering this region. In vivo binding of c-MYB was clearly shown. Inhibition and overexpression of c-MYB using siRNA for c-MYB and c-MYB expression vector,. Thus, we proved that c-MYB level could affect SPHK1 expression significantly.

#### Discussion

In the present study, we analyzed the sequential change and the pathophysiological roles of SPHK family proteins during HMBA-induced differentiation of Friend cells. Our analyses confirmed the previous paper by le Scolan et al. (4) reporting high *Sphk1* expression of Friend cells. Moreover, in our current study, *Sphk1* rapidly decreased during HMBA-induced differentiation of original Friend cells, whereas its HMBA-resistant variant, R cells, did not, suggesting the important role of *Sphk1* in leukemic proliferation of Friend cells and the sensitivity to chemical inducers. By using stable transformants of wild type and dominant negative SPHK1 and SPHK2, we also provided the evidence that *Sphk1* and *Sphk2* play different roles in Friend cells and the validity of proposed sphingolipid rheostat model.

Our present results including the comparison of cellular proteins of HMBA-treated original Friend cells and R cells, the promoter analysis of *Sphk1*, EMSA, and ChIP assay revealed that *Sphk1* expression was mostly regulated by c-Myb and Myb-binding sites of the 5'-*Sphk1* promoter. Moreover, our EMSA exhibiting the binding of Myb protein binding in vivo and the decrease of Myb binding in HMBA-

treated original Friend cells but not in HMBA-treated R cells strongly suggest that Myb/SPHK1 signaling modulates the differentiation induction sensitivity of Friend cells.

#### Conclusions

In Friend cells, c-Myb plays a major role in *Sphk1* transcription and that Sphk1 level can modulates HMBA-induced commitment to terminal cell differentiation.

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#### **Author address**

E-Mail: kobayashi.misa@a.mbox.nagoya-u.ac.jp

#### A SIGNAL PEPTIDE MUTATION OF ENDOGLIN ASSOCIATED WITH HHT

Atsuo Suzuki<sup>1,6)</sup>, Yuhri Miyawaki<sup>1)</sup>, Junko Fujita<sup>1)</sup>, Asuka Maki<sup>1)</sup>, Eriko Okuyama<sup>1)</sup>, Moe Murata<sup>1)</sup>, Akira Takagi<sup>1,2)</sup>, Takashi Murate<sup>1,2)</sup>, Masaaki Teranishi<sup>3)</sup>, Tadashi Matsushita<sup>4)</sup>, Hidehiko Saito<sup>5)</sup> and Tetsuhito Kojima<sup>1,2)</sup>

- 1) Department of Pathophysiological Laboratory Sciences, Nagoya University Graduate School of Medicine
- 2) Department of Medical Technology, Nagoya University School of Health Sciences
- 3) Department of Otorhinolaryngology, Nagoya University Graduate School of Medicine
- 4) Division of Transfusion Medicine, Nagoya University Hospital
- 5) National Hospital Organization Nagoya Medical Center
- 6) Japan Society for the Promotion of Science Research Fellow

#### Introduction

Hereditary hemorrhagic telangiectasia (HHT), also known as Osler-Rendu-Weber syndrome, is an inherited autosomal dominant vascular dysplasia with a frequency of 1 in 10,000 and exhibits age-related penetrance with variable expressivity [1-3]. The most common clinical manifestations involve the development of vascular abnormalities seen as telangiectases on skin and lesions in nasal mucosa that readily bleed. Further clinical manifestations are pulmonary, cerebral, hepatic and, in rare cases, spinal cord arteriovenous malformations. These may cause serious complications such as stroke, brain abscess, hemorrhage, or venous thromboembolism [4-6].

HHT type 1 (HHT1) is caused by a mutation in the gene encoding endoglin (ENG) located on the long arm of chromosome 9 (9q34) [7-9]. HHT type 2 (HHT2) is caused by a mutation in the activin-like kinase receptor 1 (ALK1) gene (ACVRL1) located on the long arm of chromosome 12 (12q13) [10-12]. Endoglin is a homodimeric integral membrane glycoprotein that interacts with signaling receptor complexes for several members of the transforming growth factor-β (TGF-β) superfamily, and composed of disulfidelinked 90-kDa subunits [13-15]. It is expressed primarily in the vascular endothelial cells of capillaries, arterioles, and activated venules, as well as in monocytes. syncytiotrophoblasts, and some leukemic cells. ALK1 is also expressed on endothelial cells, and is a type I receptor of the TGF-β superfamily [16]. TGF-β family cytokines are multifunctional proteins that regulate proliferation, differentiation, migration, adhesion and apoptosis of various cell types [5].

To date, 282 different mutations have been reported in the *ENG* gene and 246 distinct mutations in the *ACVRL1* gene (human gene mutation database: HGMD [17]). Some missense mutations in the signal peptide region of endoglin have been reported, but their molecular basis has yet to be investigated in detail. In this study, we analyzed the *ENG* gene in a Japanese patient with HHT, and found a novel missense mutation in the signal peptide region of endoglin. We further investigated the molecular basis of HHT in the patient through expression analyses of the mutant endoglin in COS-1 cells.

#### **Materials and Methods**

Sample preparation

Ethical approval for this study was obtained from the Ethics Committee of the Nagoya University School of Medicine. Citrated blood samples were obtained from the patient and his sister with informed consent. Genomic DNA was isolated from the peripheral leukocytes by phenol extraction.

Polymerase Chain Reaction (PCR) and DNA sequencing

The protein-coding exons and exon-intron boundaries of *ENG* and *ACVRL1* were amplified by the polymerase chain reaction (PCR) using gene-specific primers.

#### Cell culture

African green monkey kidney COS-1 cells were purchased from the American Type Culture Collection. Human endothelium-like EAhy926 cells were generously donated by Dr. Cora-Jean S. Edgell (University of North Carolina). The cells were cultured in Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% fetal bovine serum (FBS).

#### Transient transfection

COS-1 cells were seeded, and the respective vector was transfected using Lipofectoamine2000 reagent according to the manufacturer's directions. Following experiments were performed at 48 h after transfection.

#### Western Blot analysis

The transfected cells were lysed with or without  $\beta$ -mercaptoethanol ( $\beta$ -ME), boiled, and subjected to 10% SDS-PAGE followed by Western blotting.

#### Flow cytometry analysis

COS-1 cells were transiently transfected with  $1\mu g$  of pL-ENGWT or pL-ENGLI3Q, and harvested using 1mM EDTA in PBS after 48hr. The cells were washed, and incubated with antiendoglin antibody or isotype-matched rabbit IgG ( $10\mu g/mL$ ). Anti-rabbit IgG-Alexa488 antibody was incubated and the cells were analyzed by flow cytometer.

#### Immunofluorescence microscopy

The transfected COS-1 cells were replated and grown on 18x18mm cover glasses that were coated with collagen I. Fortyeight hours after transfection, the cells were fixed in cold methanol, and permeabilized with cold acetone. Antibodies used in immunofluorescence were as follows; rabbit antiendoglin antibody, mouse anti-alpha 1 sodium potassium ATPase antibody, anti-protein disulfide isomerase (PDI) antibody, anti-rabbit IgG-Alexa488 antibody, anti-mouse IgG-Alexa555 antibody.

#### Results

Case report

The patient was a 61-year-old Japanese man, and showed epistaxis, telangiectases, lung arteriovenous malformations and familiar bleeding history, he was diagnosed with HHT according to Curação criteria [5].

#### Sequencing of ENG and ACVRL1

Direct sequencing of the proband's *ENG* and *ACVRL1* genes revealed a novel missense mutation in exon 1 of *ENG* as a heterozygous form, but no mutation in *ACVRL1*. The mutation was a T-to-A transversion at nucleotide 38 in the coding sequence of *ENG* (c.38T>A), replacing leucine 13 (CTG) with a glutamine (CAG) (p.Leu13Gln) in the hydrophobic core region of the endoglin signal peptide.

Western blot analysis of recombinant endoglins expressed in COS-1 cells

To examine the effects of the L13Q missense mutation on the structure and function of endoglins, we expressed the mutant and wild-type endoglins (long-form; L-ENG, shortform; S-ENG) in COS-1 cells, and compared them by Western blotting. Under reducing conditions, the recombinant wild-type L- and S-ENG showed 3 bands, whereas the L13Q mutant showed only a smaller band. The endogenous endoglin from EAhy926 cells possessed a single band equal in size to a larger band of recombinant L-ENG. Under non-reducing conditions, Western blotting revealed that the wild-type L-ENG showed two bands representing a protein dimer, which were similar in size to the endogenous endoglin from EAhy926 cells. However, the L13Q mutant mostly retained a smaller 60kDa band at 72hr after transfection, indicating that the L13Q mutation impaired the dimerization of recombinant endoglin.

#### Impaired cell surface expression of the L13Q mutant

To analyze whether recombinant endoglins express on the cell surface, we performed flow cytometry using antiendoglin antibody. The results showed that over 25% of the cells transfected with wild-type endoglin-expression vector were positive for endoglin expression on the cell surface, whereas less than 3% of the cells transfected with L13Q mutant endoglin-expression vector were positive.

We tested the cell-surface expression of recombinant endoglins by immunofluorescence analysis for Na-K-ATPase using as a trasnmembrane marker. As a result, wild-type endoglin was detected all over the cell bodies and colocalized with Na-K-ATPase on a part of the cell surface, but we could detect no positive endoglin signal of L13Q mutant.

#### Distribution of recombinant endoglins

To investigate the intracellular distribution of the recombinant endoglins, we performed immunofluorescence microscopy for endoglin, together with that for endoplasmic reticulum (ER) by using an antibody against protein disulfide isomerase (PDI). In the COS-1 cells, wild-type endoglin signals were detected in the entire area of the cell and colocalized with ER marker PDI in the peri-nuclear region. Meanwhile, the L13Q mutant endoglin was stained in a scattered pattern and almost never co-localize with PDI.

#### Discussion

In this study, we investigated the molecular basis of HHT in a Japanese patient, and identified a novel missense mutation in the *ENG* gene (c.38T>A, p.Leu13Gln), located in the hydrophobic core of the endoglin signal peptide. There are some reports of missense mutations in the endoglin signal peptide [3, 18-22], but their molecular basis has yet to be investigated in detail.

To examine effects of the L13Q mutation on the structure and function of endoglin, we performed transient expression experiments for the recombinant endoglins in COS-1 cells. In

Western blotting under non-reducing conditions, the wild-type recombinant endoglins appeared to be expressed as a protein dimer, whereas the L13Q mutant remained as a non-glycosylated precursor. It was speculated that the L13Q mutation might impair post-translational processing of endoglin such as glycosylation and dimerization, probably due to a destroyed function of the signal peptide. Flow cytometry and immunofluorescent microscopy analyses of the recombinant endoglins also demonstrated that the wild-type endoglins were expressed on the cell surface and co-localized with the ER, but the L13Q mutant did not. These results suggested that the L13Q mutation might severely impair endoglin expression on the cell surface.

#### Conclusions

We identified a novel missense mutation in the hydrophobic core of the endoglin signal peptide (p.Leu13Gln), which is suggested to be responsible for HHT in the patient.

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#### **Author address**

E-mail: suzuki.atsuo@d.mbox.nagoya-u.ac.jp

#### Anthocyanin inhibits CagA and VacA toxins via SecA suppression in *Helicobacter pylori*

Sa-Hyun Kim<sup>1</sup>, Min Park<sup>1</sup>, Gyusang Lee<sup>1</sup>, Woo-Duck Seo<sup>2</sup>, Sang-Ick Han<sup>2</sup>, and Jong-Bae Kim<sup>1</sup>

Department of Biomedical Laboratory Science, College of Health Science, Yonsei University, Wonju, Korea

<sup>2</sup>Department of Functional Crop, NICS, Miryang, Korea

**INTRODUCTION:** Anthocyanin from various crops and fruits are known as an antioxidant, antibacterial and antiviral agent. It was reported as a potential anti-microbial agent in *Helicobacter pylori*. However it has never known that anthocyanin is a toxin inhibitor for *H. pylori*. We examined that the biosynthesis of cytotoxin associated protein A (CagA) and vacuolating toxin A (VacA) can be suppressed by anthocyanin in vitro.

**METHODS:** *H. pylori* reference strain (ATCC 49503, CagA+/VacA+) was used in this examination. Bacteria were subcultured in the Brucella agar medium with 10% fetal bovine serum at  $37\,^{\circ}$ C/ 10% CO<sub>2</sub> incubator. And cultured *H. pylori* cells were incubated in the Mueller-Hinton broth with or without anthocyanin 3.4 days. Anthocyanin was administrated to the culture broth as the concentration of 100 micromoles. Next, the two dimensional electrophoresis (2DE) was performed to compare the changed protein profiles of *H. pylori* without and with anthocyanin. This 2DE data were confirmed by western blotting, and the anti-CagA mouse monoclonal antibody, the anti-VacA rabbit polyclonal antibody, and anti-*H. pylori* polyclonal rabbit antibody which we produced were used in immunoblottings. To examine the start points of the inhibition for CagA and VacA toxins, the RT-PCR and PCR were performed, these data were compared with the data of western blotting.

**RESULTS:** Two dimensional electrophoresis (2DE) profiles of *H. pylori* reference strain (ATCC 49503, CagA+/VacA+) demonstrated that anthocyanin can inhibit the expression of SecA which regulates type IV, and V secretion systems of *H. pylori*. The biosynthesis of CagA and VacA can be suppressed via SecA inhibition because CagA and VacA is regulated by type IV, and V secretion system, respectively. Immunoblotting was performed and confirmed the biosynthesis of CagA and VacA were suppressed in *H. pylori* with the treatment of anthocyanin, also.

**CONCLUSION:** For the first time, our data demonstrate that anthocyanin can be an inhibitor for *H. pylori* toxons, CagA and VacA via SecA suppression. Further study should be needed whether anthocyanin might be effective in the suppression of the biosynthesis of CagA and VacA toxin of *H. pylori* in vivo. If so, anthocyanin could be used to reduce the gastric inflammation or stomach cancer due to *H. pylori* infection.

#### Molecular Diagnostic Approach for Screening Latent Tuberculosis Infection (LTBI)

Sunghyun Kim<sup>1+</sup>, Young Keun Kim<sup>2+</sup>, Hyejon Lee<sup>3</sup>, Jang Eun Cho<sup>4</sup>, Young Mi Kim<sup>3</sup>, Hyunjung Kim<sup>3</sup>, Sang-Nae Cho<sup>3</sup>, and Hyeyoung Lee<sup>1\*</sup>

**INTRODUCTION:** Tuberculosis (TB) continues to be one of the most critical infectious disease and causes three million deaths annually. About one-third of world population is latently infected with *Mycobacterium tuberculosis* (MTB). Recently, new immunodiagnostic tests for detection of latent TB infection (LTBI) called interferon gamma release assay (IGRA) have been developed. Commercially available IGRA tests have showed higher specificity and sensitivity than conventional tuberculin skin test (TST). However, IGRA tests have some limitations. In order to overcome these limitations, we developed alternative IGRA using reverse transcriptase (RT)-PCR.

**METHODS**: Total of 101 TB suspects were enrolled for this study. All suspects were diagnosed by various clinical laboratory tests (AFB sputum smear, mycobacterial culture, chest radiographs, histopathologic technique, TB/NTM real-time PCR). Whole bloods of all suspects were collected for performing IGRA using QuantiFERON®-TB Gold In-Tube ELISA kit (Cellestis, Victoria, Australia) and *IFN-y mRNA RT-PCR*.

**RESULTS:** In active pulmonary or extrapulmonary TB patients, IGRA (90%, 100%) showed higher positivity than IFN-γ mRNA RT-PCR (both 80%). However, in previous TB patients, IFN-γ mRNA RT-PCR (83.3%) showed higher positivity than IGRA (50%). In latent TB or non-TB suspects, IFN-γ mRNA RT-PCR (46.6%) also showed higher positivity than IGRA (30.1%). In patients who have infected with nontuberculous mycobacteria (NTM), both IFN-γ mRNA RT-PCR and IGRA have shown 100% negativity. Furthermore, IFN-γ mRNA RT-PCR was also able to distinguish between MTB infection and NTM infection. In 6 previous TB patients, IGRA showed 1 (16.7%) indeterminate result, however, it was positive when performed with IFN-γ mRNA RT-PCR. And also among 73 latent TB or non-TB subjects, IGRA showed 7 (9.6%) indeterminate results, among them 3 (42.9%) were positive and 4 (57.1%) were negative when performed with IFN-γ mRNA RT-PCR.

**CONCLUSION:** Although IFN- $\gamma$  mRNA RT-PCR has shown lower sensitivity in detection of active TB cases, it showed higher sensitivity in detecting latent TB suspects than IGRA. The assay developed in this study reduces turn-around time, cost for test, volume of blood and is not affected by the number of samples.

<sup>&</sup>lt;sup>1</sup> Department of Biomedical Laboratory Science, College of Health Sciences, Yonsei University,

<sup>&</sup>lt;sup>2</sup> Department of Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Gangwon,

<sup>&</sup>lt;sup>3</sup> Department of Microbiology, College of Medicine, Yonsei University, Seoul,

<sup>&</sup>lt;sup>4</sup>Department of Biomedical Laboratory Science, Daegu Health College, Daegu, Republic of Korea

#### Target-specific gene delivery by anti-EGFR immunonanoparticles to tumor cells

Jung Seok Kim, Yeon Kyung Lee, Hwa Yeon Jung, Young Eun Shin and Young Serk Park.
Department of Biomedical Laboratory Science, College of Health Sciences,
Yonsei University, Wonju, Republic of Korea

**INTRODUCTION:** Gene therapy has been considered as a promising approach in the treatment of varied disease as the understaing of genetic basis of diseases is expanded. The epidermal growth factor receptor (EGFR) has been recognized as a therapeutic target molecule for cancer treatment. Elevated levels of EGFR are found on varied types of tumors and have been proposed as a prognostic marker for cancer progression and survival. Therefore, antibodies recognizing EGFR such as Cetuximab and Panitumumab have been widely applied for targeting of vehicles carrying therapeutic genes (pDNA or siRNA) to EGFR-expressing cancer cells. In this study, we have developed EGFR-targeted gene delivery systems (immunolipoplexes and immunoviroplexes) by conjugating anti-EGFR antibodies (Cetuximab) to liposomal surface. The plasmid DNA was effectively complexed with those nanoparticles and then efficiently transferred to varied EGFR-positive cancer cells (A549 and SK-OV-3). In this report, we would like to introduce preparation of anti-EGFR immunonanopaticles containing pDNA and their effectiveness in pDNA transfection to EGFR-positive cells *in vitro* and *in vivo*.

**METHODS**: Immunolipoplexes and immuniviroplexes were prepared by conjugation of Cetuximab molecules to cationic lipoplexes and cationic Sendai F/HN viroplexes, respectively. Their EGFR-mediated cell bindings and gene transfection were tested in EGFR-positive A549 human lung cancer cells and SK-OV-3 human ovarian cancer, using flow cytometry, fluorescence microscopic analysis, and assay of transgene (luciferase) expression. The anti-EGFR immunoliplexes and immunoviroplexes were intravenously administered to SK-OV-3-xenografted nude mice. Their cellular uptake and *in vivo* gene transfection were assessed by assay of transgene expression and fluorescence microscopic examination.

**RESULTS:** Anti-EGFR immunonanoparticles showed selective binding to EGFR-positive cells (A549 and SK-OV-3) and also exhibited higher gene expression in EGFR-positive cells than in EGFR-negative cells. Especially, the anti-EGFR immunoviroplexes exhibited more efficient pDNA transfection than the anti-EGFR immunolipoplexes. The anti-EGFR immunonanoparticles were able to enhance transfection to EGFR-positive SK-OV-3 tumor cells xenografted in nude mice, compared with the bare lipoplexes. Under the same transfection conditions, the anti-EGFR immunonanoplexes and immunoviroplexes induced 100-fold and 400-fold higher gene expression in the tumor than the bare cationic lipoplexes, respectively. At the same time, the anti-EGFR immunonanoplexes showed higher accumulation in the tumor tissues. Among the two systems, the anti-EGFR immune-viroplexes appeared to be more effective in EGFR-mediated *in vivo* pDNA transfection than the anti-EGFR immunolipoplexes.

**CONCLUSION:** Anti-EGFR immunonanoparticles were able to transfer pDNA more efficiently and selectively to EGFR-expressing tumor cells. Especially, the anti-EGFR immunoviroplexes exhibited higher *in vitro* and *in vivo* pDNA transfection than the anti-EGFR immunolipoplexes. This study suggests that anti-EGFR immunonanoparticles can be a useful system for therapeutic gene delivery to EGFR-overexpressing cancer cells.

#### Molecular Detection of Circulating Tumor Cells in Peripheral Blood of Breast Cancer Patients

<sup>1</sup>Park Sangjung, <sup>2</sup>Han Hyunju, <sup>2</sup>Kim Seung II and <sup>1</sup>Lee Hyeyoung.

<sup>1</sup>Department of Biomedical Laboratory Science, College of Health Sciences, Yonsei University, Gangwon <sup>2</sup>Yonsei Cancer Center, College of Medicine, Yonsei University, Seoul, Republic of Korea

**INTRODUCTION:** Breast cancer is considered as a systemic disease because it has higher metastatic property than other types of cancer. Metastasis of cancer is the leading cause of cancer-related deaths. In metastatic stage of cancer, cancer cell departs from primary tumor site and moves to other organs through the blood stream. Thus, detection of circulating tumor cells (CTC) in peripheral blood of cancer patients is very important for prognostic and predictive significance. The presence of CTCs in the blood of a cancer patient is associated with a worse prognosis. Therefore, diagnosis of CTC in early stage of breast cancer patients is important to predict prognosis of patients. In this study, we identified specific genetic markers useful for CTC detection in peripheral blood of early breast cancer patients using Real-time RT-PCR, which will be valuable for monitoring the metastatic stage and to predict prognosis of patients.

**METHODS**: A total of 20 female patients with metastatic breast cancer being treated at the Yonsei Severance Hospital between 2010 and 2011 were enrolled in this study. Peripheral blood was collected from the patients during surgical therapy. Peripheral blood (10ml in EDTA) was obtained from breast cancer patients and healthy donor. Blood cell lysis reagent removed RBC in blood. Total RNA was extracted from blood samples and cell lines using Trizol according to the manufacturer's protocol. Real-time RT-PCR targeting cytokeratin (CK19), Ki67 and Human Epithelial Growth Factor Receptor (HER-2) were performed in final volume of 20 ul. Each gene expression normalized using TBP gene. The cut-off value of each assay was determined based on the results of healthy donors.

**RESULTS:** The sensitivities of real-time RT-PCR for detection of each marker were performed. Sensitivity of real-time RT-PCR for targeting CK19 was 100 cells, while those of HER-2 and Ki67 were 10 cells. The cut-off values for each assay were decided based on the expression levels of normal controls. Subsequently, the real-time RT-PCRs targeting CK19, HER-2, and Ki67 were performed using blood samples derived from 20 female patients with metastatic breast cancer. The results showed that among 20 patients, 20 percents (4/20) had CK19 positive rates and another 20 percents (4/20) had HER-2 positive rate. On the other hand, 70 percents (14/20) had Ki67 positive rate. Patients who were only single marker expression were 10: 8 patients expressed only Ki67 and 2 patients expressed only HER2. Six patients expressed two markers together, and 4 patients expressed CK19 and Ki67. Two patients were HER2 and Ki67 co-expression. Lastly, 4 patients did not express any markers.

**CONCLUSION:** Among 20 patients, 16 patients (80 %) were detected to contain multiple markers by using real-time RT-PCR. Therefore, real-time RT-PCR employing multiple CTC markers seems to be more effective than single marker for diagnosis of CTC.

# Real-time nucleic acid sequence based amplification (NASBA) for detection of influenza A virus subtypes

Jaewon Lim¹, Yoonjung Cho¹, In Soo Lee², Hyeeun Bang¹, Hyeyoung Lee¹ and Tae Ue Kim¹

¹Department of Biomedical Laboratory Science, College of Health Science,

Yonsei University, Wonju, 220-710

<sup>2</sup>Department of Clinical Laboratory Science, Hyejeon College, Hongseong, 350-702

**INTRODUCTION:** Influenza A virus of the *Orthomyxoviridae* family is a contagious respiratory pathogen that continues to evolve and burden in the human public health. It is able to spread efficiently from human to human have the potential to cause pandemics with significant morbidity and mortality. It has been estimated that every year about 500 million people are infected with this virus, causing about approximately 0.5 million people deaths worldwide. Influenza A viruses are classified into different subtypes by Antigenicity base on their hemagglutinin (HA) and neuraminidase (NA) proteins. The sudden emergence of influenza A virus subtypes and access for epidemiological analysis of this subtypes demanded a rapid development of specific diagnostic tools. Also, rapid identification of the subtypes can help to determine the antiviral treatment, because the different subtypes have a different antiviral drug resistance patterns.

**METHOD:** In this study, our aim is to detection of influenza A virus subtypes by using real-time NASBA which has high sensitivity and specificity through molecular beacon. Real-time NASBA is the method that able to shorten the time compare to other molecular diagnostic tools and is performed by isothermal condition. We selected major pandemic influenza A virus subtypes H3N2 and H5N1. Then, three influenza A virus gene fragments were targeted, heamgglutinin (HA) gene, neuraminidase (NA) gene and Matrix protein (M) gene, respectively. M gene is distinguished influenza A virus from other influenza virus. We designed specific primers and molecular beacons for each targeted RNA segments.

**RESULT:** We performed RT-PCR with each of subtype reference genes specific primer to confirm specificity and quantify the amplicons. M gene, H3N2 and H5N1 genes primer have good specificity; however H3N2 NA2 gene primer has shown lower specificity. PCR product which has amplified by H5N1 gene primer has shown lower relatively sensitivity then others. To confirm the optimal condition of real-time NASBA, we tested with positive control and negative control. It was confirmed that optimal cut-off signal value was 2, and then the amplification signals of each gene have rise up since 21 to 41 minutes. We performed each of subtype HA/NA gene specific molecular beacon to confirm the specificity. As a result, molecular beacon detecting all subtypes of HA/NA genes have higher specificity.

**CONCLUSION:** the real-time NASBA was able to detect and distinguish H3N2/H5N1 subtypes from other subtypes of influenza A virus. Also, the specificity and the sensitivity of the method using real-time NASBA were higher then that of RT-PCR. This study suggests that rapid detection of neo-appearance pandemic influenza A virus using real-time NASBA has the potential to determine the subtypes of respiratory pathogen.

# List of Participants - Yonsei

Department	Name (Korean)	Name (English)	Position	e-mail
Biomedical Engineering	신태민	Tae Min Shin Professor		tmshin@yonsei.ac.kr
Nursing	신윤희	Yun Hee Shin	Professor	yhshin@yonsei.ac.kr
Nursing	안양희	Yang Heui Ahn	Professor	ahn 57@yonsei.ac.kr
Nursing	허혜경	Hea Kung Hur	Professor	hhk0384@yonsei.ac.kr
Nursing	임영미	Young Mi Lim	Professor	youngmi@yonsei.ac.kr
Nursing	박소미	So Mi Park	Associate Professor	somi@yonsei.ac.kr
Nursing	김기연	Gi Yon Kim	Associate Professor	gykim@yonsei.ac.kr
Nursing	김기경	Ki Kyong Kim	Associate Professor	kyongkk@yonsei.ac.kr
Physical Therapy	유승현	Sung Hyun You	Professor	neurorehab@yonsei.ac.kr
Physical Therapy	전혜선	Hye-SeonJeon	Professor	hyeseonj@yonsei.ac.kr
Physical Therapy	신헌석	Heon-Seock Cynn	Professor	cynn@yonsei.ac.kr
Occupational Therapy	유은영	Eun-young Yoo	Professor & Chair	splash@yonsei.ac.kr
Occupational Therapy	정민예	Min-Ye Jung	Associate Professor	minye@yonsei.ac.kr
Occupational Therapy	박수현	Soo Hyun Park	Assistant Professor	parksoohyun@yonsei.ac.kr
Occupational Therapy	박지혁	Ji-Hyuk Park	Assistant Professor	otscientist@yonsei.ac.kr
Biomedical Lab. Science	오옥두	Ok-doo Awh	Professor	immunoch@yonsei.ac.kr
Biomedical Lab. Science	김태우	Tae-ue Kim	Professor & Dean	kimtu@yonsei.ac.kr
Biomedical Lab. Science	김종배	Jong-bae Kim	Professor	kimjb70@yonsei.ac.kr
Biomedical Lab. Science	박용석	Yong-serk Park	Professor	parkys@yonsei.ac.kr
Biomedical Lab. Science	이혜영	Hye-young Lee	Professor & Chair	hyelee@yonsei.ac.kr
Biomedical Lab. Science	김윤석	Yoon-suk Kim	Associate Professor	yoonsukkim@yonsei.ac.kr
Biomedical Lab. Science	이기종	Ki-Jong Rhee	Assistant Professor	kjrhee@yonsei.ac.kr
Nursing	최지혜	Ji Hea Choi	Fellow	jiheachoi@yonsei.ac.kr

최경옥	Gyeong Ok Choi	Teaching Assistant	cgo119@hanmail.net
최영주	Young Ju Choi	MSN	kochipin@nate.com
문학희	Hak Hee Moon	Graduate student	hhpia@hanmail.net
강혜원	Hye Won Kang	Graduate student	angle9991002@hanmail.net
전희정	Hee Jeong Jeon	Graduate student	heej1339@naver.com
함정숙	Jeong Suk Ham	Graduate student	onyou153@hanmai.net
백지은	Ji Eun Baek	Graduate student	anaba100@hanmail.net
송정희	Jung Hee Song	Graduate student	leesong713@naver.com
정지수	Ji Soo Jung	Graduate student	papaya1978@hanmail.net
신동은	Dong Eun Shin	Graduate student	adel0408@hanmail.net
이근숙	Geun Sook Lee	Graduate student	eormsdl00@naver.com
김소영	So Young Kim	Graduate student	atom522@naver.com
노지희	Ji Hee Noh	Graduate student	redfoxjh@hanmail.net
이승금	Seung Geum Lee	Graduate student	lsg3017@hanmail.net
이원휘	Won-Hwee Lee	Graduate student	kema97@yonsei.ac.kr
김수정	Su-Jung Kim	Graduate student	ssambac1@hotmail.com
홍지아	Ji-A Hong	Graduate student	ptjia@hanmail.net
임원빈	One-Bin Lim	Graduate student	onebin7942@hotmail.com
김태진	Tae-jin Kim	Graduate student	xowlszzzz@naver.com
박경미	Kyung-Mi Park	Graduate student	motiveS2@yonsei.ac.kr
신윤겸	Yoon-Kyum Shin	Graduate student	kyum309@naver.com
이재진	Jae-Jin Lee	Graduate student	cymdyb@naver.com
이희원	Hee-Won Lee	Graduate student	vichw@hanmail.net
강선영	Sun-YoungKang	Graduate student	rloveush@hanmail.net
권재성	Jae-Sung Kwon	Graduate student	kkoombo@yonsei.ac.kr
유인규	In-Gyu Yoo	Graduate student	ig0623@empas.com
	최영주 문학희 강혜원 전희정 함정숙 백지은 송정희 정지수 신동은 이근숙 김소영 노지희 이승금 이원휘 김수정 홍지아 임원빈 김태진 박경미 신윤겸 이재진 이희원 강선영 권재성	최영주 Young Ju Choi  문학희 Hak Hee Moon  강혜원 Hye Won Kang  전희정 Hee Jeong Jeon  함정숙 Jeong Suk Ham  백지은 Ji Eun Baek  송정희 Jung Hee Song  정지수 Ji Soo Jung  신동은 Dong Eun Shin 이근숙 Geun Sook Lee  김소영 So Young Kim  노지희 Ji Hee Noh 이승금 Seung Geum Lee 이원휘 Won-Hwee Lee 김수정 Su-Jung Kim  홍지아 Ji-A Hong 임원빈 One-Bin Lim  김태진 Tae-jin Kim  박경미 Kyung-Mi Park  신윤겸 Yoon-Kyum Shin 이재진 Jae-Jin Lee 이희원 Hee-Won Lee  강선영 Sun-YoungKang 권재성 Jae-Sung Kwon	최영주 Young Ju Choi MSN  문학회 Hak Hee Moon Graduate student  강혜원 Hye Won Kang Graduate student  한정숙 Jeong Suk Ham Graduate student  박지은 Ji Eun Baek Graduate student  성정희 Jung Hee Song Graduate student  청지수 Ji Soo Jung Graduate student  신동은 Dong Eun Shin Graduate student  리스숙 Geun Sook Lee Graduate student  보지희 Ji Hee Noh Graduate student  나지희 Ji Hee Noh Graduate student  이승금 Seung Geum Lee Graduate student  이원휘 Won-Hwee Lee Graduate student  공지어 Ji-A Hong Graduate student  김대진 Tae-jin Kim Graduate student  나윤경 Yoon-Kyum Shin Graduate student  신윤경 Yoon-Kyum Shin Graduate student  기해진 Jae-Jin Lee Graduate student  강선영 Sun-YoungKang Graduate student  건재성 Jae-Sung Kwon Graduate student

Occupational Therapy	조덕연	Duk-Youn Cho	Graduate student	guylian77@naver.com
Occupational Therapy	김한솔	Han-Sol Kim	Graduate student	soriyam@nate.com
Occupational Therapy	조현경	Hyun-Kyung Jo	Graduate student	hyun073022@nate.com
Occupational Therapy	유지은	Ji-Eun Yoo	Graduate student	ujeeun@nate.com
Occupational Therapy	김지예	Ji-Yea Kim	Graduate student	toryjiye0918@gmail.com
Occupational Therapy	최윤미	Yoon-Mi Choi	Graduate student	chymym@gmail.com
Occupational Therapy	조은미	Eun-Mi Jo	Graduate student	hopeotem@naver.com
Biomedical Lab. Science	임재원	Jae-won Lim	Graduate student	jaewon330@hanmail.net
Biomedical Lab. Science	조윤정	Yun-jung Cho	Graduate student	black5579@naver.com
Biomedical Lab. Science	이규상	Kyu-sang Lee	Post-doctoral Fellow	innkeepers@hanmail.net
Biomedical Lab. Science	김사현	Sa-hyun Kim	Graduate student	kimsh@yonsei.ac.kr
Biomedical Lab. Science	박민	Min Park	Graduate student	xowkdvk@naver.com
Biomedical Lab. Science	김정석	Jung-suk Kim	Graduate student	blue6749@naver.com
Biomedical Lab. Science	이연경	Yeon-kyung Lee	Graduate student	yunni8011@hanmail.net
Biomedical Lab. Science	정화연	Hwa-yeon Jung	Graduate student	cca1987@hanmail.net
Biomedical Lab. Science	신영은	Yeong-eun shin	Graduate student	1pororo9@naver.com
Biomedical Lab. Science	진현우	Hyun-woo Jin	Post-doctoral Fellow	jjinhw@nate.com
Biomedical Lab. Science	최연임	Yeon-im Choi	Post-doctoral Fellow	poohlike80@hanmail.net
Biomedical Lab. Science	박상정	Sang-jung Park	Graduate student	wva276sj@naver.com
Biomedical Lab. Science	김성현	Sung-hyun Kim	Graduate student	ksungh 20@hotmail.com
Biomedical Lab. Science	김현정	Hyun-jung Kim	Graduate student	betomeet@naver.com
Biomedical Lab. Science	백아름	Ah-reum Baek	Graduate student	greenchoa27@nate.com
Biomedical Lab. Science	하형종	Hyung-jong Ha	Graduate student	imhotjay@naver.com
Biomedical Lab. Science	이경홍	Kyung-hong Lee	Graduate student	bighong7@hanmail.net
Biomedical Lab. Science	이민호	Min-ho Lee	Graduate student	lmh77777@naver.com
Biomedical Lab.	강여울	Yeo-ul Kang	Graduate student	yy1006@naver.com

# List of Participants - Nagoya

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ya-u.ac.jp

Radiological Technology	林 大貴	HAYASHI, Daiki	Graduatestudent MC1	hayashi.daiki@g.mbox.nagoya-u.ac.jp
Radiological Technology	杉本成人	SUGIMOTO, Naruto	Graduatestudent MC2	sugimoto.naruto@h.mbox.nagoya-u.ac.jp
Radiological Technology	林 結伊	HAYASHI, Yui	Graduatestudent MC2	hayashi.yui@b.mbox.nagoya-u.ac.jp
Medical Technology	小林美沙	KOBAYASHI, Misa	Graduatestudent MC2	kobayashi.misa@a.mbox.nagoya-u.ac.jp
Medical Technology	里中 華	SATONAKA, Hana	Graduatestudent MC2	satonaka.hana@f.mbox.nagoya-u.ac.jp
Medical Technology	髙津美和	TAKATSU, Miwa	Graduatestudent MC2	takatsu.miwa@f.mbox.nagoya-u.ac.jp
Medical Technology	寺西彩香	TERANISHI, Ayaka	Graduatestudent MC2	teranishi.ayaka@a.mbox.nagoya-u.ac.jp
Medical Technology	鈴木敦夫	SUZUKI, Atsuo	Graduatestudent DC2	suzuki.atsuo@d.mbox.nagoya-u.ac.jp
Physical Therapy	入谷直樹	IRITANI, Naoki	Graduatestudent MC1	iritani.naoki@h.mbox.nagoya-u.ac.jp
Physical Therapy	萩原悠太	HAGIWARA, Yuta	Graduatestudent MC1	hagiwara.yuta@h.mbox.nagoya-u.ac.jp
Physical Therapy	北野貴之	KITANO, Takayuki	Graduatestudent MC2	kitano.takayuki@a.mbox.nagoya-u.ac.jp
Physical Therapy	村瀬数馬	MURASE, Kazuma	Graduatestudent MC2	murase.kazuma@c.mbox.nagoya-u.ac.jp
Physical Therapy	平川倫恵	HIRAKAWA, Tomoe	Graduatestudent DC2	hirakawa.tomoe@a.mbox.nagoya-u.ac.jp
Physical Therapy	石田章真	ISHIDA, Akimasa	Graduatestudent DC3	ishida.akimasa@c.mbox.nagoya-u.ac.jp
Physical Therapy	河野裕治	KONO, Yuji	Research Assistant	kono.yuji@h.mbox.nagoya-u.ac.jp
Occupational Therapy	黒田真梨	KURODA, Mari	Graduatestudent MC2	kuroda.mari@f.mbox.nagoya-u.ac.jp
Occupational Therapy	田中将裕	TANAKA, Masahiro	Graduatestudent MC2	tanaka.masahiro@a.mbox.nagoya-u.ac.jp
Occupational Therapy	中川与四郎	NAKAGAWA, Yoshiro	Graduatestudent DC2	nakagawa.yoshiro@d.mbox.nagoya-u. ac.jp
Occupational Therapy	渡部貴史	WATABE, Takashi	Graduatestudent DC2	watabe.takashi@h.mbox.nagoya-u.ac.jp
Occupational Therapy	山川ひとみ	YAMAKAWA, Hitomi	Graduatestudent MC1	yamakawa.hitomi@b.mbox.nagoya-u.ac.jp
Occupational Therapy	山下紗代	YAMASHITA, Sayo	Graduatestudent MC1	yamashita.sayo@a.mbox.nagoya-u.ac.jp

## Reflections on the 2010 Meeting

## 2010 Nagoya-Yonsei University Research Exchange Meetings on Health Science 참관기

(Nagoya, Japan, 22~24 October 2010)

연세대학교 보건과학대학 임상병리학과 분자진단학연구실 김성현

2010년 10월 22일, 일본의 나고야대학 다이코 캠퍼스에서 열릴 나고야대학교 보건과학대학과 연세대학교 보건과학대학간의 연구 학술교류에 참가하기 위해 연세대학교 보건과학대학 5개 학과 인 물리치료학, 보건행정학, 방사선학, 임상병리학, 작업치료학과 그리고 연세대학교 원주의과대학 간호학과의 대표 교수님들과 대학원생들이 인천공항에서 모여 인사를 나눈 뒤 일본으로 향했다. 약 두 시간 후 일본 나고야 공항에 도착하였고, 입국심사를 하고 나오자마자 연세대학교 방문단 을 환영하는 팻말을 들고 일본나고야대학에서 오신 안내자 분들께서 환영을 해주셨다. 일본어를 잘 하지 못하는 우리 방문단을 위해 나고야대학에서 능숙하진 않지만 어느 정도 한국어 대화가 가능한 안내자 분을 보내주셔서 보다 편하게 일정이 시작되었다. 약 한 시간 정도 셔틀버스를 타 고 호텔로 향했다. 공항에서는 한국어 안내판이 있고, 사람들의 생김새도 비슷해 일본에 왔다는 실감을 느낄 수 없었지만, 공항에서 호텔로 향하는 길에 일본식 주택과 일본어 간판, 좌우가 반대 로 된 차로 등을 보면서, 일본에 왔음을 실감할 수 있었다. 나고야 시는 산업도시여서 그런지 많 은 굴뚝들과 공장들을 주위에서 쉽게 볼 수 있었다. 호텔에 도착한 우리 연세대학교 방문단은 짐 을 풀고 모여 나고야 대학 병원으로 향했다. 얼마 전 새롭게 증축되고, 리모델링된 나고야 대학병 원은 실내가 매우 깨끗하게 정돈되어 있었고, 규모 또한 국내의 지방대학병원 규모에 비해 컸다. 나고야대학병원에 도착하자마자, 나고야와 나고야 대학의 홍보책자, 그리고 이번 학술교류에 대한 안내책자와 명찰들을 받았고, 나고야대학의 소개와 역사에 대한 설명을 들었다. 우리방문단을 위 해 서투른 한국말 인사들을 발표자들마다 준비해와 적극적으로 홍보하고 환영해주는 나고야대학 측 교수님들과 관계자 분들께 감동과 고마움을 느꼈다. 나고야대학 및 대학병원에 대한 설명을 듣고 우리는 병원 투어를 하였다. 관련 검사실과 치료실 등 병원 내부를 구경하였다. 규모나 시설 들 면에서는 연세대학교 원주기독병원과 큰 차이는 없었지만, 앞으로의 노령화 사회에 대비한 치 료, 검사시설들 면에서는 우리가 더욱 보완해 나가야 될 필요성이 있음을 느낄 수 있었다. 병원투 어를 마친 뒤 우리 방문단은 저녁식사를 위해 연회장으로 향했다. 연회장에는 나고야대학의 관련 학과의 모든 교수님, 연구교수님들 및 관련학과의 교직원 분들이 모두 나와 우리를 기다리고 있 었고, 연회는 시작 되었다. 우리대학에 대한 환영사로 연회는 시작되었고, 나고야대학의 각 학과 의 교수님들, 그리고 우리 방문단 측 교수님들과 대학원생이 각자 자기소개와 인사를 나누었고, 다음날 있을 학술교류 행사에 앞서 미리 친해질 수 있는 좋은 기회가 되었다. 나고야의 야경이

한눈에 들여다보이는 나고야대학병원 가장 위층에 있는 연회장은 아주 인상이 깊었고, 연회를 위해 맛있는 음식들이 준비되어 있었다. 간단한 소개 및 인사 후에 연회를 나누는 동안 나고야대학의 교수님들과 함께 연구 및 각 나라의 현재 상황들에 대한 대화를 나눌 수 있어 좋은 정보교류의 장이 될 수 가 있었고, 무엇보다도 서로 상대방나라의 언어는 하지 못하지만 영어라는 공통언어로써 대화가 연결이 되고, 서로의 공감대를 나누고, 좋은 정보교류를 할 수 있다는 점에서 신기하기도 하고, 많은 도움이 되었던 것 같다. 약 두 시간 정도의 연회를 마친 뒤 아쉬움을 뒤로하고, 다음날 일정을 위해 숙소로 향했고, 휴식을 취했다.



두 번째 날(10월23)은 호텔에서 일본식 아침식사로써 시작이 되었다. 일본식 아침식사를 한 뒤 나고야대학교 보건과학대학이 있는 다이코 캠퍼스로 향했다. 보건과학대학 대학원 대형 강의실에 우리대학 측 방문단과 나고야대학 보건과학대학의 모든 교수님들, 대학원생들의 참여가운데 2010년도 두 대학간의 학술교류 행사가 시작 되었다. 생각보다 많은 학생들과 교수님들께서 참가한 가운데 행사가 시작 되었다. 오전에는 우리대학 측 보건행정학과 교수님과 대학원생의 프레젠테이션으로 학술 교류가 시작이 되었다. 두 나라의 전체적인 보건 의료분야에 대한 비교와, 상황들을 알 수 있는 좋은 기회가 되었고, 각자 서로의 다른 입장과 의견이 서로 토의되고 서로 조언을 나누는 등 좋은 시간 이었다.



오전 세션이 끝난 뒤 단체 사진촬영을 하고, 두 대학의 각 과별로 모여 일본식 도시락인 밴 또를 먹었다. 점심을 먹으면서 나고야대학교 임상병리학과의 교수님들과 대학원생 발표자들과 많

은 이야기를 나누고 각 대학의 대학원생에 대한 학교와 정부의 지원 등 실질적인 대학원생활에 대한 각자의 이야기를 나눌 수 있는 좋은 계기가 되었다. 맛있는 점심식사 후 각 학과별로 연구교류 발표가 시작 되었다. 우리 측 대표단 2명의 연구발표와 나고야대학의 4명의 대학원생의 연구발표가 이어졌고, 서로에게 많은 질문과 조언이 이어졌다.

특히 우리대학은 일본 나고야대학에 비해 분자진단 및 유전자치료 분야에서는 보다 앞서 있고, 일본의 나고야대학은 생리학, 병리학, 면역학, 혈액학과 생화학적인 기초학문분야에서 우리 대학에 비해 월등한 연구시설 및 연구활동을 하고 있었다. 따라서 두 대학간의 연구교류를 통해 기초연구와 응용분야가 잘 어우러진다면, 서로에게 보다 많은 도움이 될 수 있을 것으로 예상된다. 특히 일본의 나고야 대학은 우리대학과는 달리 임상병리학과에 약 17명 정도의 교수님 및 연구교수님이 계시고, 그 중 8명이 medical doctor로써, 우리대학에 비해 실질적인 임상의와의 의사소통과 연구교류가 보다 쉽게 잘 이루어 지고 있는 것으로 보였다. 그리고 특히 생리학과 병리학, 혈액학 교육을 위한 병원과 동일한 실습시설들과 연구를 위한 연구시설들이 따로 준비가 되어있어, 두 대학간의 교류를 통해 현재 우리나라에는 부족한 생리학, 병리학, 혈액학 분야의 인재 및 전문가를 키워내는 데에 많은 도움이 될 것으로 생각이 되고, 이러한 우리나라에서 부족한 분야에서도 앞서 나감으로써 다른 대학들에 비해 차별화된 인재를 키워내고 미래에도 경쟁력이 있는 국내 최고의 연세대학교 임상병리학과로 거듭날 수 있을 것으로 예상된다.





모든 연구발표들을 마친 뒤 나고야대학 임상병리학과의 각 연구실 투어를 시작했다. 교수님들 마다 현재의 진행중인 연구과제들과 본인들의 연구실실적들을 연구실 복도의 벽과 교수님연구실 벽에 붙여놓고 하나하나 자세히 설명해주시고, 자신들의 연구실에서 나온 논문들을 하나하나 인쇄해서 선물로 주시는 등의 배려와 자신들의 연구에 대한 자부심과 적극적인 설명 등을통해 또 한번 감동을 받았고, 본받아야 할 점으로 생각 되었다. 랩투어를 마친 뒤 학과별 단체사진 촬영을 하였다. 나고야 대학의 교수님들께서는 우리측 방문단을 위해 가장 좋은 자리를 대학원생들에게 양보하시는 등 많은 배려를 해주셨다. 모든 일정이 마친 뒤 각 학과별 연회 장소로이동을 했고, 우리는 일본식 음식들과, 회를 먹으며 더욱 깊은 이야기들을 나눌 수 있어 좋은 시간이 되었다. 연회장에서 많은 이야기를 나누면서 많은 정보들 또한 함께 얻을 수 있었다.



특히 나고야대학에서는 현재 4명의 노벨상 수상자가 있고, 오카자키 프레그먼트를 발견해 낸 오카자키 교수님이 나고야대학의 교수님이었다는 사실 또한 알 수 있었고, 매우 신기하기도 하였다. 함께 사진도 찍고, 서로의 명함을 나누며 앞으로의 교류를 기약했고, 아쉽지만 둘째 날일정도 모두 마치게 되었다. 마지막 날은 나고야의 도심을 둘러보며, 마무리 할 수 있었다. 2박3일간의 짧은 시간 동안 많은 일정들을 소화해 내느라 많이 피고하고 힘들기도 하였지만, 한국으로돌아오는 비행기를 타면서 많은 아쉬움과 앞으로 좋은 교류가 될 수 있다는 가능성의 희망 또한가질 수 있었다. 짧은 시간 동안 이었지만, 교류 행사를 위한 적극적이면서도 많은 준비와 배려를해주신 일본 나고야대학 측 관계자들께 감사를 드리고, 무엇보다도 대학원생들에게 이런 좋은 학술 교류의 기회와 보다 넓은 시야를 갖고 미래지향적인 생각을 한번 더 할 수 있도록 좋은 기회를 가질 수 있도록 도와주신 연세대학교 보건과학대학과, 관련 교수님들께도 진심으로 감사의 마음을 드린다. 비록 첫 연구교류 행사였지만, 처음의 시작은 미미했지만, 이번 교류가 보다 발전하고 매년 이어져서, 앞으로 우리나라와 세계를 이끌어 나갈 선두주자인 연세대학교 보건과학대학 이 되기 위한 계기가 되었으면 좋겠다.



### 2010 Nagoya-Yonsei University Research Exchange Meetings on Health Sciences 참관기

임상병리학과 석.박사 통합과정 박상정

2010 년 10월 22일 금요일 아침 낮 12시 30분 비행기 시간을 맞추기 위해 원주에서 아침 일찍출발하여 약속된 시간 보다 한 시간 정도 빠르게 공항에 도착하였다. 공항에 도착 하니 평일오전이라 그런지 생각보다는 한산하다는 생각이 들었다. 일본에 다녀 온지 2 달여 정도 밖에지나지 않아서 인지 두 번째 방문하는 일본은 무엇인가 익숙하다는 생각이 들었다.

드디어 사람들이 다 모이고 면세점에서 우리와 교류할 학과에 드릴 선물을 구입한 후 12 시 30 분 나고야 공항을 향하는 비행기에 몸을 실었다. 같이 향하는 일행들은 모두 보건과학대학 소속의 학생들 이었지만 우리 학과는 현재 미래관에 있다는 위치적 특성상 다른 학과 사람들을 많이 알지는 못했다. 비행기 옆자리에 앉은 학생은 방사선학과의 이영진 학생 이었는데 당일처음 만났지만 비행하는 동안 이것저것 물어 보면서 어색하지 않은 시간을 보냈다. 그렇게이야기를 나누던 중 약 한 시간 반 정도 후에 어느덧 비행기는 나고야 공항에 들어섰다. 나고야 공항은 특이하게도 활주로 바로 옆에 바다가 있어서 비행기가 착륙하면서부터 마음이 시원해지는 것을 느낄 수가 있었다.

나고야 공항에 도착하니 나고야 대학 쪽에서 우리를 맞이하러 두 분이 나오셨고, 우리는 그 분들의 안내를 받아 공항에서 한 시간 정도 떨어진 호텔로 향했다. 호텔에 도착 후 나고야 대학 병원에서 간단한 병원 tour 가 예정 되어있어 간단하게 짐을 푼 후 우리는 나고야 대학 병원으로 향했다. 나고야 대학 병원은 Bed 수가 약 900 Bed 정도 되는 규모의 병원 이었고, 나고야 시내 중심에 위치하여 접근성이 매우 용이 한 것을 알 수 있었다. 병원의 기본 방침은 최고의 의료 수준을 제공하고 최고의 의료인을 양성하여 지역사회에 공헌하자는 방침을 가지고 있었다. 간단하게 병원의 역사와 현재 의료진 학생의 현황을 설명 듣고 본격적으로 병원 tour 를 시작하였다. 우선 특이 한 점은 이 병원에는 2, 3 층에 대 부분의 진료 과가 모여 있다는 것이었다. 우리나라 에서는 같은 성격을 지닌 진료 과가 한 곳에 모여 있기 마련인데 이곳에는 진료 과의 구분이 모호하게 모두 같은 곳에서 기다리게 되어있었다. 환자를 관리하는 측면에서는 매우 좋아 보였으나, 어떠한 질환을 가진 환자들을 같은 공간 속에 둔다는 것은 원내 감염 관리에 있어서 문제가 생길 수도 있겠다는 생각을 하였다. 아무래도 병원을 돌아보면서 중점적으로 보게 된 것은 이곳의 진단검사의학과 시설이 우리나라의 그것과 어떤 것이 같고, 어떤 것이 다른지를 비교해 보는 것이었다. 이곳의 진단 검사 의학과도 우리나라의 시설과 마찬가지로 대부분의 검사가 자동화 설비를 이용한 검사를 진행하고 있었다. 하지만 그 규모가 우리나라의 진단검사 의학과의 규모보다 훨씬 작게 느껴졌다. 6 년 전 실습을 나갔던 신촌 세브란스 병원의 진단 검사 의학과 보다 규모가 약 1/3 정도 밖에 되지 않아서 약간은 의아하게 생각 하였다. 또한 인상 깊게 본 것은 재활치료 시설이 매우 잘 되어있다는 점이었는데, 이 도시의 특성상 여러 가지 산업이 발달한 도시 로서 산업재해로 인한 환자나 나이가 드신 어르신들을 위하여 이러한 시설이 발달 한 것이 아닐까라고 생각을 하였다.

병원 투어가 끝나고 병원의 맨 위층에 있는 식당에서 간단한 환영식이 이루어졌다. 그 자리에서 내일 교류하게 될 Dept. of Medical Technology 교수님들을 몇 분 만나게 되었다. 비록 나는 영어를 잘하지는 못 하였지만 하는 일이 비슷하고, 같은 분야에 관심을 가지는 사람들끼리의 만남이어서 그런지 재미있는 시간을 보낼 수가 있었다. 약 한 시간 반 정도의 환영행사를 마치고 우리는 숙소로 돌아 왔고 그렇게 나고야에서의 첫날이 끝이 났다.

둘째 날에는 호텔 식당에서 일본식 아침을 먹고 시내에서 조금 외각으로 떨어진 나고야 대학 Daiko 캠퍼스로 향하였다. 오전 10 시부터 11 시 20 분까지 진행된 Keynote Address 에서는 나고야 대학의 Yohshie Kodera 교수님께서 "Present and Future of Health Science Research in Japan" 이라는 주제를 가지고 강연을 하셨다. 강연 초반부에서는 나고야 대학의 역사와 어떤 분야가 발달하였는지를 설명해 주셨는데, 이 대학에서만 노벨상 수상자가 무려 4 명이나 된다는 사실을 알게 되었다. 나중에 학과 교류시간에 알게 된 사실이지만 Okazaki Fragment 를 발견한 Okazaki 교수도 이 대학 출신이라는 것을 알게 되었다. 또한 이곳의 보건과학 대학은 총 5 개의 학부로 구성되어있다는 것도 알 수 있었다. 또한 이어지는 강연에서는 서영준 교수님께서 "The Present and Future of Korean Healthcare Industry" 라는 주제를 가지고 강연을 해 주셨다. 이 강연에서는 현재 우리나라의 Healthcare industry 의 현 실태에 대해 말씀해 주셨고, 또한 앞으로 병원에서는 어떤 방향을 추구해 나가야 하는 지에 대해서 설명해 주셨다. 이쪽으로 관련된 분야는 처음 듣는 내용이라 생소한 면이 적지는 않았지만 흥미 있게 강연을 들을 수 있었다. 이어 두 번째 Session 이 끝나고 그 후로는 학과별 시간을 가지게 되었다. 먼저 점심식사를 하면서부터 학과별로 만나게 되었는데 그 자리에서 어제 뵈었던 교수님들도 다시 만나게 되었고, 오늘 발표를 할 나고야 대학의 학생들도 만날 수가 있었다. 점심을 먹으면서 이런 저런 얘기가 오고 갔는데, 우리나라와 이곳이 많이 비슷하다는 것을 알 수가 있었다. 특히 나고야 대학 학생은 나와 같이 간 학생과 나보다 한 살이 적었는데 벌써 박사과정 중이라는 말을 하였고, 우리는 현재 전문연구요원으로 군 복무 중이라는 얘기를 하였고, 그 사실에 어느 정도 놀라는 눈치였다. 이어 오후 1 시 30 분부터는 우리가 속한 Medical Technology Session 을 시작 하였다. 우리학교에서는 나와 김성현 박사과정 학생이 각각 "Mycobacterium tuberculosis-induced Expression of Granulocyte-Macrophage Colony Stimulating Factor is Mediated by Erk1/2 MAPK or PI3-K/Akt Signaling pathway"란 주제와 "Comparison of REBA HPV-ID with DNA Chip Based Assay for HPV genotying"이라는 주제를 가지고 발표를 진행하였다. 발표를 진행하면서 매우 긴장이 되어 몇몇 작은 실수를 하였지만 무사히 발표를 마칠 수 있었다. 나고야 대학 측에서도 석사과정 학생 1 명, 박사과정 학생 1 명 그리고 Post Doc. 과정 1 명 이렇게 총 세 명이 각자 연구 하고 있는 분야에 대해서 발표를 하였다. 이어지는 자유 토론 시간에서 우리가 발표 했던 내용에 대한 여러 가지 질문들을 받을 수가 있었다. 특히 나고야 대학 교수님 중에서는 우리가 발표했던 내용과 비슷한 분야를 연구하시는 교수님들이 몇몇 분 계셨기 때문에 그 분들이 관심을 많이 가져 주시고 질문도 많이 해주셨다. 영어를 뛰어나게 잘하는 것이 아니었기 때문에 성심성의껏 대답은 해 드렸지만 내용을 다 이해하셨는지 참 궁금하긴 하다. 이렇게 Session 을 마친 후 우리는 Dept. of Medical Technology 의 실험실을 둘러 볼 수 있는 기회가 마련되어 있었다. 이곳은 우리 학과와는 다르게 같은 학과의 실험실이 한 곳에 모여 있는 것이 아니라 두 세 개씩 따로 따로 다른 곳에 위치하고 있었다. 특히 인상적이었던 것은 각 실험실이 위치하고 있는 곳

마다 각자 실험실의 세포를 배양할 수 있는 시설과 동물을 키울 수 있는 시설을 가지고 있다는

사실에 놀랐다. 또한 생리학 연구실의 경우에는 우리나라 어느 임상병리학과에도 가지고 있지 않은 심전도와 뇌파 검사 기계를 가지고 있어서 학부 학생들이 학부 과정에서 이미 기계에 대한 전반적인 이해와 그 사용법을 어느 정도 익힐 수 있다는 사실이 매우 놀라 놀랐다. 다른 실험실은 우리학교 실험실 시설과 어느 정도 비슷한 정도의 규모를 가지고 있었고, 가지고 있는 기자재도 비슷하였다. 여러 실험실을 돌면서 이곳 학과에 대한 설명을 들었는데 정식으로 교수님으로 계신 분은 총 8 분이고, Assistant Professor 가 9 명이 계셨다. 각 대학원에는 실험실별로 많게는 8 명에서 적게는 2 명 까지 있어서 많은 사람들이 있는 것을 알 수 있었다. 우리나라 임상병리학과에는 임상병리학 전공이나 일반 화학 및 생물학을 전공하신 분 들이 대부분 교수를 하고 있는데, 나고야 대학에는 Assistant Professor 를 포함하여 총 6 분의 Medical Doctor 가 계셨고, 그 분들이 모두 의과대학 소속이 아닌 보건과학대학 소속이라는 점도 무척이나 흥미로웠다.

이렇게 학과별 Session 및 실험실 tour 를 마치고 저녁식사 하는 곳으로 향하였다. 저녁식사는 우리 숙소 부근에서 하기로 되어있어서 우리는 지하철을 이용하여 이동하였다. Daiko 캠퍼스가 일본 프로야구 팀인 나고야 돔 Stadium 근방에 있다는 것을 지하철을 타러 가면서 알게 되었다. Nagoya Stadium Station 으로 이동하여 지하철을 타러 가는 도중 그 날이 야구 경기가 있다는 것을 알게 되었고, 많은 팬들이 야구장으로 가는 것을 보았다. 역 벽면에는 주니치 드래곤즈의 선수들과 감독 및 코치 역대 기록을 가지고 있는 선수들로 전시가 되어있었다. 야구를 좋아하는 나에게는 특별한 경험 이었다. 일본 지하철은 우리나라와 비슷하게 되어있었는데, 우리나라와 다른 점은 지하철 광고가 정말 많다는 것이다. 물론 우리나라도 지하철 광고가 상당히 많은 것을 볼 수 있었는데, 일본의 지하철 광고는 우리나라 이상으로 되어있었다.

저녁 식사를 하러 도착한 곳은 일본 일식 전문점이었는데, 일인당 얼마만큼의 돈을 지불하면 정해진 시간 동안 음식이 코스별로 계속해서 나오고, 술은 무제한으로 얼마든지 마실 수 있는 곳이었다. 이곳에서 나고야 대학의 사람들과 처음에는 매우 서먹서먹하고, 또한 영어도 잘하지 못하기 때문에 어색하였지만 같은 분야에 종사하는 사람으로서 금방 친하게 지낼 수 있었다. 저녁 식사를 마치고 아쉬운 작별인사를 한 뒤 우리 일행은 한 학생이 추천해 준 나고야 명물이라는 야마짱이라는 곳으로 향했다. 그 곳은 나고야에서 꼭 맛보아야 할 음식인 닭 날개요리를 파는 곳이었다. 우리나라의 치킨 윙과 비슷했는데, 튀김옷이 약간 독특했고, 후추를 이용하여 약간 매콤한 맛을 내고 있었다. 그렇게 나고야에서의 둘째 날도 끝이 났다.

마지막 날에는 아침부터 바빴다. 호텔에서 나오는 일본식이 값도 비싸고, 어제 먹은 메뉴 그대로였기 때문에 다른 음식을 찾다가 편의점 도시락을 먹기로 결정을 하고 편의점으로 향했다. 일본에는 도시락 문화가 발달해서 그런지 다양한 종류의 도시락을 판매하고 있었다. 그러나 데워달라는 말이 잘 통하지 않아서 매우 고생했다. 역시 일본에서는 영어만 가지고는 대화가되지 않는 다는 것을 몸소 느끼고, 다음번에 일본에 올 시에는 반드시 일본어를 해야 갰다는 생각을 했다. 그렇게 간단하게 아침을 해결한 후 교수님들께서는 도쿠가와 이에야스 박물관으로 향했고, 대부분의 학생들은 나고야 중심부에 위치한 Takashimaya 백화점에서 이것저것을 구경했다. 그곳에는 생활용품을 저렴한 가격에 파는 Tokyu Hands 라는 상점이 층층마다 있었는데, 역시 엔고 현상 때문인지 우리나라 가격과 비교하면 물건들이 상당히 비싼 편이라는 것을 알 수 있었다. 여러 곳을 둘러 본 후 다시 숙소 앞에서 버스를 타고 공항으로 향했다. 공항에서 일본식

라멘으로 간단하게 점심을 해결 한 후 다시 인천으로 돌아오면서 길다면 길고 짧다면 짧은 2 박 3 일간의 나고야 대학 방문 일정을 마쳤다.

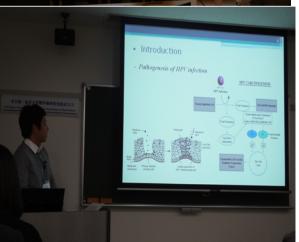
2 박 3 일 동안의 시간동안 너무 많은 것을 보고 많은 사람들을 만났다. 그러나 그 시간이 너무짧았기 때문에 일정들이 빡빡하게 짜여 있어서, 몸은 무척이나 피곤하였다. 그러나 몸은 힘든 반면 마음만은 매우 즐거웠다. 내년에 또 있을 나고야 대학과의 교류를 기대하게 만든 일정이었다.

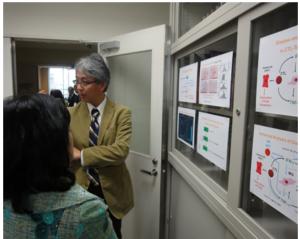














### 일본 나고야 대학의 작업치료학과와 교류를 통한 만남

연세대학교 작업치료학과 유은영 교수님, 박혜연 박사, 이주현 석사, 조덕연 석사, 김한솔 석사

2010년 10월 23일 나고야 대학교의 교류 초청을 받아 일본으로 갔다. 대학원을 들어오고 첫 외 국 방문이라 너무 설래 였다. 유은영 교수님께서 처음 일본 나고야 방문 기회가 왔는데 다 같이 가보자 라고 하셨을 때 흔쾌히 가겠다고 했던 대답이 갔다온 후 느꼈지만 대학원 생활 중에 가장 잘한 일중 하나라고 생각이 들었다. 첫 나고야 방문 날, 낯선 일본 교수님들의 나고야 대학 발표 를 듣고 병원 탐방을 하였다. 다른 병실은 잘 모르겠지만 일본의 작업치료실은 한국과 비슷하면 서도 다른점이 있었다. 특히 일상생활동작실에서 아이들을 치료하는 감각통합실의 경우 일본은 그들의 정서와 문화에 맞는 다다미 방 모형을 하였던 건 정말 신선한 부분 이었다. 작업치료는 장애를 가진 환자들을 일상생활에서 독립적인 생활을 할 수 있도록 하는 전공분야여서 그런지 각 나라의 일상생활동작실을 보면 그들의 문화를 알 수 있는 것 같다. 그 외에도 일본 작업치료실에 는 현재 가정환경수정을 할 때 사람들의 기능에 맞추어 가정환경 수정이 가능한 기계가 있었는데 이는 우리들의 발걸음을 멈추게 할 정도로 관심을 끄는 기계였다. 이렇게 작업치료 병원을 둘러 본 후 저녁 환영회에 참석을 하였다. 그 자리에서 일본 나고야 대학교와 병원을 대표하시는 분들 께서 인사를 하였는데 우리나라말로 소개를 하고자 노력 하시는 모습이 감사하였다. 저녁 환영회 에서는 각 과의 학과장 교수님들과의 대화시간이 주어졌는데 서로에 대해 잘 모르는 상황이라 어 색한 부분도 있었지만 선동렬 야구 이야기, 학과 이야기 등으로 대화를 하다 보니 금새 친해질 수 있었다.

둘째 날 발표를 맡은 박혜연 박사와 이주현 석사는 발표 준비 때문에 정신이 없으셨지만 막상 발표시간이 다가오자 언제 그랬냐는 듯 유창한 영어실력으로 발표를 무사히 잘 마무리 하였다. 일본 나고야 대학의 학부생들과 대학원생, 교수님들 사이에서 우리 학교 작업치료학 연구에 대해 발표하고 서로 연구한 분야에 대해 교류하는 시간은 다른 어떤 발표, 교류하는 시간 보다 뜻 깊 은 것 같다. 발표가 끝나고 일본 학과장 교수님께서 나고야 대학의 작업치료실을 구경 시켜 주셔 서 구경을 하였다. 이후 작업치료학과 교수님들 대학원생들간의 저녁 만찬 시간을 아주 멋진 일 본 전통 식당에서 가졌다. 일본 교수님들과 유은영 교수님, 대학원 생들은 식사 시간 동안 그 동 안 궁금했던 각 나라의 작업치료 실정 이라던지, 작업치료사 실태, 작업치료학과 학생들에 대해 많은 질문들을 하시고 이야기를 나누었다. 마지막엔 서로 인사를 나누고 단체사진을 찍으면서 이 날을 기념하고 마무리를 하였다.

이러한 학교간의 교류를 할 수 있게 기회를 주신 학교측에 깊은 감사를 전하고 싶다. 소중한 교류를 통해서 각 나라에 대한 작업치료학과 그에 따른 여러 가지 정보를 교환하고 이야기 나눌수 있어서 소중한 시간들이었던 것 같다.

## 2010 Yonsei - Nagoya University Research Exchange Meetings on Health Science 참관기

(Nagoya, Japan, 22~24 October 2010)

연세대학교 원주의과대학 간호학과 백 지 은, 안 양 희

처음으로 해외에서 발표할 기회가 주어진 것은 오랜 직장 생활과 대학원 공부에 지쳐 있던 나에게 또 다른 설렘과 즐거움을 주었다. 또한 뇌졸중 분야에 대해서 간호학적인 측면의 근거중심 접근도 한국어가 아닌 영어를 사용해서 외국 청중들 앞에서 발표해야 한다는 사실은 나로 하여금 약간의 걱정과 두려움, 새로운 기회에 대한 도전과 자극을 동시에 갖게 하였다.

나는 안양희 교수님과 매지 캠퍼스 보건과학대학에 계시는 타과 교수님 및 대학원 학생들과 함께 10월 22일부터 10월 24일까지 일본 나고야 대학교 Daiko 캠퍼스에서 열린 제 1회 '2010 Yonsei - Nagoya University Research Exchange Meetings on Health Science '학술 심포지엄에 참석하였다. 이번 학술 심포지엄은 올 4월에 MOU 체결을 한후에 개최하는 첫 모임이었다.

나고야 공항에서 숙소까지 가는 차창 너머로 'something unique to Japan'을 찾기 위해 쉴새 없이 두리번거렸지만 내가 발견한 것은 오직 운전석이 우리와 반대 방향인 차들이 도로를 질주하는 모습과 일본어로 쓰여진 간판들뿐이었다. 아마도 같은 아시아권이고 전 에 일본문화를 경험했었기에 도착 후 낯설거나 이질감은 느낄 수 없었던 건 너무나 당연 했는지 모르겠다는 생각과 더불어 오히려 대도시가 아닌 중소도시인 나고야시에 대한 친 근감마저 더 느껴졌다. 인천 공항에서 나고야 공항까지는 비행기로 2시간 정도가 소요되 었지만 그 외에 거리에서 소요되는 약 2시간이 나고야 대학교 도착 시간을 조금 지연시 켜 본격적인 만남은 오후 5시가 넘어서야 시작되었다. 호텔 체크인을 하고 제일 먼저 도 착한 나고야 대학 부속병원의 첫 인상은 주변의 커다란 녹지 공원과 넓은 부지에 큰 규 모의 대학과 병원 건물들이 긴 전통만큼 오래 되었지만 2년 전 새로 지은 건물과 리모 델링으로 전반적으로 깔끔한 상태가 지속적인 관리에 있었음을 다시 한번 알 수 있었다.

일본 나고야 대학교는 1871년에 설립된 국립대학으로 아이치현 나고야시에 위치한 일본의 우수 대학교 중 하나이며, 노벨상 수상자가 4명이나 되었음을 자랑스럽게 설명하였다. 나고야 대학교 쓰루마이 캠퍼스에 위치한 부속 병원은 건물 중앙을 중심으로 좌우날개모양을 본떠서 설계하였다고 한다. 또한 병원 내부에서 가장 눈에 뜨였던 것은 넓고다양한 공간이(휴게실, 대기실, 다양한 검사실) 환자를 위한 배려 즉 환자 중심의 공간이

라는 점에서의 동선을 잘 고려해서 시스템 배치를 위한 노력이 곳곳에서 보였다.





나고야 대학교 캠퍼스 정문

나고야 대학교 부속병원

병원의 전체적인 간략한 소개를 시작으로 각 분야의 시설과 장비를 견학하면서 병원 내부를 직접 볼 수 있는 기회를 가졌다. 국내 실정과 비교해서 일본의 강점은 무엇이고 또 우리가 배워야 할 점 그리고 우리의 강점은 무엇인가를 잠시나마 생각해볼 수 있었던 시간이었지만 사진촬영을 정중히 금하여 다소 아쉬운 점이 남아있었다. 국내 의료계가 의료 시장의 변화와 다양한 소비자들의 높은 요구도로 과도기에 있지만 각 병원마다 장점을 살려서 기존 병원운영에 혁신을 가하고 있는 실정이 일본 내 역시 비슷한 분위기임을 느낄 수 있었으며, 연세 세브란스 병원의 JCI인증을 매우 부러워하는 한편 적극적인 관심을 갖고 있다는 것도 알 수 있었다. 간호분야의 병원 내부관련 시설과 업무 시스템을 보고자 별도로 부탁을 해서 안교수님과 함께 VIP병동을 볼 수 있는 시간을 가졌다. 첫 눈에 바로 들어왔던 것은 물류관리를 위한 바코드 시스템과 전자기록, 환자 프라이버시를 위한 병실 방문 앞 전자 이름표 등 효율적이고도 체계적인 깔끔한 시스템이 단연 돋보이고 인상적이었다. 짧은 시간이라 간호사들이 직접 간호업무를 하는 모습을 자세하게 볼 수 없었지만 불필요한 시간 낭비를 줄일 수 있도록 nursing station을 중심으로 방사선 모양으로 병실배치가 되어 있는 것이 눈에 띄었다. 앞으로 EMR 도입을 준비하는 우리에게 많은 도움이 될 수 있는 부분이었다.

이날 우리 일행은 간단히 병원 내부를 보고 난 뒤 현지에서 우리를 위해 마련한 석찬에 초대되었다. 병원 내 연회장인 15층 스카이라운지에서 좀 늦은 저녁이었지만 나고야시내의 야경을 즐길 수 있었고 모두가 함께할 수 있는 멋진 저녁식사 시간이었다. 환영만찬을 통해 두 대학교의 모든 부서장 및 교수진과 학생들이 모여 각자 소개를 하고 인사를 하는 시간을 가졌다. 소개를 하면서 또 받으면서 영어로 질문을 하고 궁금했던 것들을 하나씩 풀어 놓는 긴장된 첫날을 잘 이완시켜줬던 좋은 출발을 알리는 첫만남의 시

간이었다.

다음 날은 나고야 대학교 Daiko 캠퍼스에 위치한 보건과학대학 학술장소로 이동하여 본격적인 학술 심포지움을 시작하였다. Midori ASANO교수님은 지난 4월 우리 학교를 방문하여 인사를 나눈 적이 있어 우리 일행을 너무나 반갑게 맞아 주셨다. 심포지움의 전반부는 Keynote Address와 보건행정학과의 발표가 있었다. 나고야 대학교에서 보건과학의 발전을 위한 전망설명이 있었고, 연세대학교에서는 보건행정학과 서영준 교수님의 보건의료산업 발전방향에 대한 발표가 있었다. 그리고 일본 나고야 대학교에는 보건행정학과가 개설되어 있지 않기 때문에 전체 모임에서 연세대학교 박사과정 대학원생(신정우선생님)과 일본 well-being and society 연구소에서 근무중인 정선생님이 발표를 하였다.

점심은 간단한 도시락으로 일본 대학원생들과 함께 하였다. 서로 인사할 수 있었던 시간으로 서로가 긴장되고 서먹할 수 있는 자리를 한결 부드럽게 해주었다고 본다. 개인적으로 발표를 앞둔 학생들에게 소중한 배려가 되었다는 생각이 들었다. 식사 후 간호, 물리치료, 방사선, 임상병리, 작업치료 5개 학과별로 session이 이루어졌다. 간호학과는 Midori ASANO교수님의 배려로 교수님 방에서 안교수님과 함께 짧은 티타임을 갖고 발표하기 전조금이나마 긴장을 풀 수 있는 시간을 가질 수 있었다.

간호학과 session은 나고야 대학교 간호학과를 소개로 본격적인 학술발표를 시작하였다. 이곳 나고야 대학교의 간호학과 역사는 우리와 비슷하지만 전신인 조산사 훈련기관을 시작으로 그 역사를 거슬러 가본다면 연세 간호대학교와 역사가 비슷하였다. 한국에서 나고야 대학을 방문하기 전 박사과정이 2004년 개설하였다는 정보를 듣고 우리 간호학과가 뒤쳐져 있는 것이 아닐까 하여 다소 걱정이 앞섰으나 현재 일본의 간호교육 수준을 비교해보았을 때 우리가 앞서 있음을 알 수 있었다. 다만 부럽게 느껴진 점은 일본정부의 지지와 투자가 막강하고, 선두를 달리기 위한 노력과 열의가 무척 강하다는 것이었다. 일본교수님의 자세한 나고야 대학교 간호학과 역사와 교육과정 소개를 마치고, 안양희 교수님의 발표를 시작으로 학술발표가 이루어졌다.

안교수님은 결혼이주 여성의 정신건강문제와 정책방향에 대하여 발표를 하셨는데, 부드럽고 탁월한 영어발표 실력으로 청중을 압도 하셨다. 개인적으로 멋진 교수님의 모습을 볼 수 있어 더욱 영광스럽고 뿌듯한 자리이기도 하였다. 학생발표는 나와 일본 대학원생 4명 이렇게 총 5명이 발표를 하였다. 70-80명 청중 앞에서 영어로 발표하는 것이긴장과 부담이 되었지만 또 다른 배움의 과정이 틀림 없으리란 확신을 갖고, 떨리는 마음으로 스스로를 위로하였다. 준비된 급성기 허혈성 뇌졸중 환자의 응급간호에 대한 근거중심 간호전략에 대해 자신있게 발표를 하였다. 대학원생들의 논문발표 후, 안교수님과보건행정학과 서교수님의 예상외의 날카로운 질문과 comments는 발표자들을 다소 긴장하게 만들었지만 참석한 학생 모두에게 도전이 되었으리란 생각을 해본다. Session 후 일본 간호학과 교수와 학생의 후속 질문이 이어지었고, 이러한 질문들은 다양한 견해 등을나눌 수 있는 계기가 되었으며, 다음에 더 잘 준비해서 활발한 학술교류를 해야겠다는

#### 다짐을 갖도록 해주었다.





학술대회(오전 Session)

학술대회(오후 Session)

의사소통은 영어로 이루어져 조금 답답하고, 서로가 자세한 설명을 들을 수 없었던 아쉬움이 있었지만 첫 학술교류인 점을 감안 할 때 전체적인 발표는 너무나 만족스러웠다. 물론 개인적으로 영어와 일어 공부를 좀더 하였다면 훨씬 풍부한 교류가 되지 않았을까 하는 아쉬움은 있었지만 양쪽 모두가 첫 학술교류인 만큼 충분한 만족감을 보여줬던 소중한 시간이었다. 또한 나고야 대학교내 간호학과 설립이 우리와 비슷하고 박사과정이 먼저 시작되었다고 하지만 학문적으로 우리가 월등히 앞서있음을 지속적으로 느낄수 있었다. 그곳에서 왠지 우리나라 70-80년대 초창기 간호학과의 모습이 보여졌다. 하지만 협회와 학계가 함께 움직여 교육과정을 일원화하고 국비로 석·박사 과정을 지원해주는 프로그램은 앞으로 충분히 우리나라보다 더 앞서갈 수 있으리란 조금은 우려되는점도 있었다.

학과별 학술교류가 끝나고 우리는 나고야 간호학과에서 마련해주신 주변 경치가 멋스럽고 너무나 고풍스러운 고급 프랑스식 퓨전 레스토랑에서 저녁을 대접받았다. 좀 더 친근해져 더 편안한 분위기에서 발표를 막 끝낸 홀가분한 기분으로 넉넉한 식사시간을 가지면서 그 동안 못다한 이야기를 나눌 수 있었다. 평소 일본은 간호사의 사회적 지위가우리보다 낮고 간호학적 모델도 바람직하지 않다라는 정보와 인식을 갖고 있어 궁금하기도 하고 확인하고 싶은 마음에 분위기가 편안하게 익어갈 무렵 조심스럽게 물어봤다. 의외로 그런 문제점을 모두가 인정하면서 앞으로 일본 간호계가 사회적 위상이 한국처럼되기를 소망하고 있다는 이야기를 들었을 때 우리나라 간호계 선구자들의 노고를 생각하며 그분들이 너무나 훌륭한 분들이고 더 존경스럽고 자랑스럽게 느껴졌다.

일본과 한국 간호계가 비슷하지만 약간 다른 점이 큰 문제가 될 수 없던 학술교류의 장이었다. 서로에 대한 간호계의 비교가 조금은 예민한 측면이란 생각에 조심스러웠지만 적극적이고 솔직한 그분들의 모습에 다소 무거움은 사라지고, 한류에 대한 이야기, 서로 관심 있는 문화에 대한 다양한 이야기를 나누면서 시간 가는 줄 모르고 너무나 맛있는 음식과 좋은 만남으로 이런 배움의 즐거움이 또 있을까 싶어 헤어지는 시간이 무척이나 아쉬웠다. 또한 공통적으로 간호계가 나아가야 할 방향은 무엇보다도 병원과 학교가 좀 더 유기적 관계를 갖고 함께 간호계를 발전시켜야 한다는 일치된 결론을 내리면서 새로 운 각오와 다짐을 하고 내년을 기약하며 헤어졌다. 다음에 우리 학교에서 학술 심포지움 을 할 때 우리가 이 분들의 정성스런 배려와 귀한 대접을 받은 만큼 꼭 더 잘 준비해서 이분들을 잘 대접해 드려야겠다는 생각을 하며 숙소로 돌아왔다.



학술대회 후(다과 및 차 모임)



학술대회 후(나고야 성 앞에서)



학술대회 후(저녁식사 모임)



학술대회 후(저녁식사 모임)

마지막 날 오전에 빡빡한 일정을 소화하랴 지친 우리들을 위해 일요일에 쉬지도 못하시고 오전 10시부터 박물관 견학에 대한 관광안내를 해주셨다. 박물관 견학을 통하여 일본 고유한 문화를 엿볼 수 있는 시간이었다. 공항으로 오는 차에서 점심식사 시간전이라 간단한 일본식 찹쌀떡을 나눠주시는 일본 교수님의 모습이 친근하게 느껴져서 너무나 좋았다. 이번 학술교류 발표 준비과정과 일본에서의 일정을 통해 나 개인적으로 또 다른

진보를 이룰 수 있었고 가깝지만 먼 나라라는 막연한 양가적(兩價的)인 마음을 가졌던 일본을 좀 더 구체적으로 체험할 수 있었던 기회였다. 또한 우리 학과의 학문적 수준이 아시아에선 최고이며, 세계적임을 확인할 수 있어 뿌듯하였다.

출발은 부담감으로 시작되었지만 2박 3일 일정을 무사히 마친 뒤 오는 뿌듯함과 자신 감은 나 자신을 향상시키고 발전시킬 수 있는 또 다른 멋진 경험이었다. 해외 학회 참여 경험이 2005년 싱가폴에서 열렸던 Sigma Theta Tau Co-Study 포스터 발표가 전부였던 나에게 이번 학술 심포지움은 규모는 작지만 영어 구두 발표라는 점에서 커다란 배움을 주었던 점에서 무척 영광스러운 기회였다. 대학원 공부를 하면서 연휴기간과 모든 휴일을 반납해야 하는 다소 힘든 상황에서도 첫 학술 교류의 첫 출발이라는 책임감에 열심히 준비해왔던 결실이 이것이구나 하는 보람된 시간이었다.

한편, 나고야 공항에서부터 우리를 너무나 친절하게 가이드해주신 간호학과 지역사회 Naoko ITO선생님은 서울대 한국어 학당을 다닌 경험으로 능숙하게 한국어를 잘하셔서 우리가 움직이는데 전혀 불편함 없게 해주셨다. 2박 3일의 일정 동안 많은 분들이 도움을 주셨지만 특히나 Naoko ITO선생님은 현지에서 우리에게 가장 큰 힘이 되어 주셨다. 마지막으로 발표와 준비에 격려와 도움을 주신 여러 교수님 및 선후배, 동료들에게 깊은 감사와 고마움을 전하고, 특히 학술교류 참여 기회를 주신 원주 의과대학 학장님과 학부 장님 또 많은 가르침과 배려를 베풀어 주신 안양희 교수님께 끝으로 감사 인사를 드리면서 참관기를 마치고 싶다.

# 2010 Yonsei - Nagoya University Research Exchange Meetings on Health Science 참관기

(Nagoya, Japan, 22~24 October 2010)

연세대학교 물리치료학과 최 보 람, 전 혜 선

필자는 2010년 10월 22일부터 24일까지 일본 나고야에 있는 나고야대학(Nagoya university) Daiko 캠퍼스에서 열린 '2010 Yonsei - Nagoya university Research Exchange Meetings on health science'에 참석하였다. 이 연구교류는 연세대학교와 나고 야대학간의 지속적인 학술 교류를 위한 첫 발을 디디게 되었다.

연세대학교 보건과학대학에서 참여한 인원은 보건과학대학 부학장(신태민 교수), 물리치료학과 2명(전혜선 교수 외 1명), 간호학과 2명(안양희 교수 외 1명), 방사선학과 3명(김희중 교수 외 2명), 임상병리학과 3명(이혜영 교수 외 2명), 보건행정학과 3명(서영준 교수 외 2명), 작업치료학과 5명(유은영 교수 외 4명)을 포함한 총 19명 이었다.

2010년 10월 22일 오후 1시 30분 인천국제공항에서 나고야행 비행기를 타고 2시간 정도 걸려 나고야 국제공항에 도착하였다. 나고야의 화창한 날씨는 더욱 우리를 반기는 듯 했고, 약간 더운 날씨는 한국보다 남단에 위치하고 있고, 4면이 바다로 둘려 쌓여 있는 일본의 지형적 특성을 잘 대변해 주었다. 마중 나온 나고야 대학 교수들의 안내를 받으며 공항을 빠져나왔다. 미리 준비해 온 버스를 타고 두 시간 가량 걸려 일본 메이조선 후시미(Fushimi) 역 근처에 있는 Trusty 호텔에 체크인을 하고 짐을 풀어 놓았다.

제크인을 마친 후, 30분 정도 버스를 타고 오후 5시경 나고야대학 부속병원으로 갔다. 나고야대학 부속병원의 컨퍼런스 룸에서 환영사 및 나고야대학 부속병원에 대한 간략한 소개를 받았다. 나고야대학 부속 병원은 1871년에 설립되어 약 130년의 오랜 역사를 가진 일본 3대 병원 중 하나이며 쯔루마이에 위치하고 있다. 기본방침은 최고 수준의 의료를 제공하고 뛰어난 의료인을 양성하여 지역과 사회에 공헌하자는 것이다. 나고야대학에 대해서 설명하는 동안 프리젠테이션마다 한글로 번역을 해놓아서 일본의 친절함에 대하여 다시 한 번 느낄 수 있었다. 전자 카르테, 수술 지원 로봇, 높은 정밀도의 방사선 치료 시스템과 같은 선진 기기에 대한 설명도 간략하게 들을 수 있었다.

환영사 및 나고야대학 부속 병원에 대한 소개를 마친 후 병원 내부를 구경 할 수 있었다. 병원 업무가 끝날 시간이라 환자들이 없었지만, MRI영상실, 임상병리실, 외래환자진료실, 물리치료실을 둘러 볼 수 있었다. 물리치료실은 국내 병원 시설과 거의 비슷하였으며, 한 층을 재활치료실로 지정하여 반은 작업치료실로 사용하고 나머지 반은 물리치료실로 사용하고 있어서 넓은 치료 공간을 보유하고 있었다. 실제 환자를 치료하는 모습을 보지 못한 것이 약간 아쉬웠지만, 일본의 병원 환경에 대하여 알게 되었고, 유사한 시스템을 갖추고 있어서 친근감을 느꼈다. 병원 내부 견학을 끝내고 병원의 가장 높은 층에 있는 연회실로 자리를 옮겼다. 나고야대학 보건과학대학 소속의 모든 교수님들과 함께 환영만찬 겸 저녁식사를 함께 하였다. 연세대학교 및 나고야대학 소속 교수님들과 대학원생들의 소개가 있었고, 저녁식사와 함께 각대학의 학과별 교수님과 대학원생들 간의 담소를 나누었다. 9시경 연회가 끝나고 숙소로 돌아와 나고야에서의 첫날밤을 보냈다.

둘째 날 Trusty 호텔에서 제공하는 일식으로 아침식사를 하고 나고야대학교 Daiko 캠퍼스 의 East building의 강당으로 이동하였다. 나고야대학의 학장과 연세대학교의 신태민 교수 의 개회사를 시작으로 학술발표가 시작되었다. 10시부터 11시 20분까지 진행된 기조연설에 서 나고야대학교의 Yoshie kodera교수와 연세대학교의 서영준 교수의 일본과 한국의 보건 사업에 대한 발표가 있었다. 약간의 휴식시간 뒤에 11시 30분부터 12시까지 보건행정학과 정성원, 신정우 대학원생의 한국의 보건행정에 관한 발표가 있었다. 오전의 행사를 마치고 학과별 점심식사를 한 다음,13시 30분부터 학과별 주요 연구 주 제에 대한 발표가 있었다. 연세대학교 물리치료학과 전혜선 교수와 최보람 대학원생은 5번 째와 6번째에 발표자로 참여하였다. 첫 번째 발표는 나고야대학의 Susuma ota 교수의 "Development of an instrumental for measuring patella mobility and its clinical application"에 대한 발표가 있었다. Patella mobility를 측정하기 위한 Patellofemoral arthrometer를 개발하여 patella mobility 측정의 타당도를 검증하였으며, Patellofemoral pain syndrome환자와 TKR환자에게 적용하여 정상인과 patella mobility의 차이를 연구하였 다. 두 번째와 세 번째 발표는 쥐 실험을 통하여 줄기 세포의 분화과정에 대한 연구와 쥐에 게 internal capsule hemorrhage를 유발하여 forced impaired forelimb use의 영향에 대한 연구였다. 네 번째 연구는 일본인의 Stroke 재발률에 대한 연구였고, 다섯 번째로 물리치료 학과 전혜선 교수는 "Locomotor imagery training improves gait performance in people with chronic hemiparetic stroke"에 대한 발표를 진행하였다. Imagery training을 통한 Chronic hemiparetic stroke환자의 여러 gait 변수와 평가도구의 변수의 변화에 대하여 설 명하였다. 마지막으로 최보람 대학원생은 "The effect of an isometric knee extension with hip adduction(KEWHA) exercise on selective VMO muscle strengthening"에 대하여 발표했다. Vastus medialis의 선택적인 강화를 위한 운동방법을 제시하였다. 총 6명의 발표 로 구성이 되었고, 각 발표가 끝나면 활발한 질의응답과 논의시간을 가졌다. 나고야대학의 물리치료학과에 대하여 느낀 점은 기초과학에 중점을 두고 인체 내부의 변화에 대한 연구가 활발하게 이루어지고 있다고 느꼈다. 발표자들과 이야기를 나누어 보니, 현재 실험실 내에 서 이루어지고 있는 연구가 많다고 하였고, 물리치료에 대한 과학적인 접근법을 찾기 위해 노력한다고 하였다.

오후 행사를 모두 마치고 학과별 저녁식사가 있었다. 나고야에서 최고급 식사라고 하면서 석판에 굽는 소고기를 대접해 주었고, 맥주와 사케를 마시며 교수님들과 대학원생이 어우러 지는 시간을 보냈다. 일본 대학원생들과 한국과 일본의 문화에 대한 이야기를 나누면서 많 은 공감을 가졌고, 같은 물리치료를 연구하는 사람으로서 친밀감을 더욱 더 느끼게 해주었다. 마지막 날은 예정된 일정보다 일찍 호텔을 나와서 전혜선, 유은영 교수님과 함께 호텔 주변을 산책하였다. 한국의 일요일과 같이 한산한 도시풍경을 볼 수 있었고, 공원에는 애완견과 산책 나온 사람들이 많았다. 도시 주변은 깨끗했으며 많은 사람들이 자전거를 타고 다니고, 자전거 도로 역시 어디서나 볼 수 있었다. 아침 식사를 마치고, 나고야 역 주변 및 도쿠가와 이에야스 박물관 탐방이 진행되었다. 시내관광과 박물관 관광으로 팀을 나누어서 이동하였다. 시내관광은 지하철을 타고 다카시마야 백화점에서 관광을 하였다. 백화점을 크게 세로로 이분한다면 반은 Tokyo hand라고 하는 큰 규모의 생활용품점이 층마다 있었으며 나머지 반은 한국의 백화점처럼 다양한 쇼핑시설이 갖춰져 있었다. 또한 도쿠가와 이에야스박물관 방문 팀은 버스를 타고 이동하였다. 도쿠가와 이에야스는 도요토미 가문의 마지막후손이자 우환인 도요토미 히데요시를 자결케 한 인물로서 자신의 통치체제를 250여 년간지속시키며 인내의 미학을 보여준 인물이다. 도요토미 히데요시에 대한 일화를 보며 남에게서가 아닌 나 자신 안에서 잘못을 찾아야 한다는 교훈도 얻을 수 있었다.

모든 일정을 마치고, 나고야 공항에서 인천 공항으로 돌아왔다. 이번 학술교류 참석을 통해 일본의 물리치료 분야에 대한 연구 방향과 발전 방향을 알 수 있었고, 같은 연구 분야의 여러 사람들과 많은 이야기를 나누면서 다양한 주제에 관한 논의를 나눌 수 있어서 좋은 경험이 되었다. 그리고 일본의 문화를 체험해 볼 수 있는 기회 또한 큰 즐거움으로 남았다. 앞으로 지속적인 관계유지를 가지기 위해 노력해야겠으며, 내년 11월에 예정인 원주에서 진행되는 연세대학교와 나고야대학의 학술교류가 또한 잘 치러지기 바라며, 이상으로 연세대학교와 나고야대학의 학술교류 참관기를 마친다.

# 2010 Yonsei - Nagoya University Research Exchange Meetings on Health Science 참관기

(Nagoya, Japan, 22~24 October 2010)

연세대학교 방사선학과 MPIL 연구실 이 영 진, 조 효 민, 김 희 중

필자는 2010년 10월 22일부터 2010년 10월 24일까지 일본 나고야에 있는 나고야대학교 Daiko 캠퍼스에서 열린 '2010 Yonsei - Nagoya University Research Exchange Meetings on Health Science'에 참석하였다. 이 연구교류는 보건과학 분야의 각 나라를 대표하는 연세대학교와 나고야대학교 간의 지속적인 학술 / 연구 교류를 위해 만들어졌다. 2010년 10월 22일 오후 1시 30분 인천국제공항에서 나고야행 비행기를 타고 2시간 정도 걸려 나고야 국제공항에 도착하였다. 주위의 풍경은 일본어로 기술되어있는 것을 제외하고는 한국과 비슷하여 친근한 느낌이었다. 또한 나고야의 날씨는 한국의 서울, 원주와 비슷하거나 조금 높았고 시차는 전혀 없어서 적응에 큰 문제가 없었다. 나고야는 아이치 현의 현청 소재지로서 일본 전국에서 네 번째로 인구가 많은 도시이며, 도쿠가와 집안이 나고야성을 중심으로 이 지역을 지배하였다고 전해진다. 연세대학교 보건과학대학에서 금번 학술교류에 참여한 인원은 보건과학대학 부학장(신태민 교수), 방사선학과 3명(김희중 교수 외 2명), 임상병리학과 3명(이혜영 교수 외 2명), 작업치료학과 5명(유은영 교수 외 4명), 물리치료학과 2명(전혜선 교수 외 1명), 보건행정학과 3명(서영준 교수 외 2명), 간호학과 2명(안양희 교수 외 1명)을 포함한 19명 이었다. 22일에는 도착 후 나고야대학교 부속 병원을 소개받고 23일에는 나고야대학교 Daiko 캠퍼스에서 보건과학분야 및 각 학과별 학술교류를 하였으며 24일에는 나고야 시내를 탐방하며 문화를 경험할 수 있었다. 첫 날 오후 3시경 나고야 국제공항에 도착하여 픽업나온 나고야 대학교 교수 및 학생들의 안내에 따라 일본 메이조선 후시미 역 근처에 있는 호텔에 체크인을 하고 오후 5시경 나고야대학교 부속 병원으로 갔다. 오후 5시 45분부터 환영사 및 나고야대학교 부속 병원에 대한 간략한 소개를 받았다. 나고야대학교 부속 병원은 1871년에 설립되어 약 130년의 오랜 역사를 가진 일본 3대 병원 중 하나이며 쯔루마이에 위치하고 있다. 기본방침은 최고 수준의 의료를 제공하고 뛰어난 의료인을 양성하여 지역과 사회에 공헌하자 는 것이다. 현재에는 365일 24시간 동시에 대규모로 진료 상황을 유지할 수 있는 System인 전자카르테와 수술지원로봇, IMRT 등을 병원의 자랑으로 내세우고 있다. 특히 전자카르테는 개인정보보호를 고려하여 고도의 보안 System을 구축하고 있고, 지문으로 Login하게 되어있어 안정성과 신뢰성을 높일 수 있는 System으로 설명하였다. 더불어 한국과 비교하여 방사선 검사 시 접수기가 있다는 것은 특이할 만한 점이다. 병원의 전체적인 소개가 끝나고 병원의 각 보건과학분야 시설에 대한 설명 및 직접 눈으로 볼 수 있는 시간을 가졌다. 본관 2층에 있는 MRI, CT 영상실 보면서 한국의 대학병원과 구성, 장비 수 등을 비교해 볼 수 있는 좋은 기회가 되었다. 환영만찬 겸 저녁식사는 병원 내 연회장에서 진행되었으며, 연세대학교 및 나고야대학교 보건과학대학의 모든 교수진, 학생들이 모여 서로 인사하고 소개하는 시간이병행되었다. 방사선학과는 연세대학교 김희중 교수와 나고야대학교 Yoshie Kodera 교수 주관으로 하여 서로 안부를 묻고 서로의 관심 분야 및 현재 진행하고 있는

일에 대해 소개하였다.

둘째 날 호텔에서 제공하는 일식으로 아침식사를 하고 나고야대학교 Daiko 캠퍼스에 위치한 보건과학대학 학술장으로 이동하였다. 10:00부터 11:20분까지 진행된 Keynote Address에서 나고야대학교의 Yoshie Kodera 교수는 나고야대학교의 소개를 위주로 발표를 진행하였다. 주요 내용으로는 1980년 방사선 기술학과가 개설되고 학교의 노벨상 수상자는 총 4명, 보건과학대학의 학부는 총 5개로 구성되어 운영된다는 것이었다. 이 후 점심식사를 하고 다음 학술발표 전까지 나고야대학교 방사선 기술학과 보유 장비 및 연구실을 소개받았다. 주목할 점은 이곳에 CT, 일반촬영장비, C-arm, Densitrometer, Mammo촬영장비 등 여러장비를 보유하고 있는데 관리가 철 저하다는 점이었다. 30년이 넘은 장비를 보유하면서도 1주일에 1번 이상 기술검사 및 안전도검사를 실시하여 유지가 가능하도록 하는 점은 관리분야에 있어 우리가 배워야할 점이라는 생각이 들었다. 13:30분부터는 각 전공별 Session이 개설되어 우리는 Radiological Technology 학술장으로 이동하여 참여하였다. 연세대학교 방사선학과 김희중 교수와 박사과정의 조효민 연구 원이 각각 2번째, 5번째 발표자로 참여하였다. 김희중 교수는 "Advancement of Medical Imaging and Instrumentation in Radiological Science"라는 주제로 연세대학교 및 보건과학대학의 소개와 동시에 방사선학과, 그리고 각 연구실별 연구내용을 소개하였고 앞으로의 비젼과 발전방향 도 제시하였다. 또한 조효민 연구원은 "Multi-material Decomposition Imaging in the Photon Counting Detector"라는 주제로 현제 진행하고 있는 원자력기초공동연구소 사업인 BAERI 과제와 연계한 연구내용을 발표하였다.

또한 나고야대학교 방사선 기술학과의 몇몇 교수와 학생들은 방사선 치료, CT, Mammography 등 자신의 연구 분야를 발표하였다. 현재 나고야대학교 는 Monte Carlo Simulation에 대한 관심도가 높았으며, 이에 대한 질문 및 Discussion도 활발히 진행되었다.

학술제를 마치고 연세대학교와 나고야대학교의 방사선학과는 서로간의 Scientific Collaboration을 위한 MOU(Memorandum of understanding for a Joint Research Agreement On Medical Imaging Physics) 협약식을 진행 하였다. 연세대학교 보건과학대학 부학장인 신태민 교수도 참석하였으며 협 약문서 사인을 통하여 공식적인 학술교류, 연구분야에 대해 서로 협력하고 함께 발전해 나갈수 있는 출발점이 되었다.

저녁식사는 전공별 따로 진행되었다. 방사선학과는 나고야 사카에역 주변 에 있는 선술집에서 진행하였으며 주요 교수진과 대학원 연구원들이 함께모여 친목도모의 시간을 가졌다. 연세대학교의 김희중 교수는 "너무 좋은 자리를 마련해주고 하나하나 배려해주어 너무나 감사드리며 내년 11월에 한국 방문시 더욱 특별하게 모시겠다. 또한 특히 MOU 체결은 연세대학교와 나고야대학교 모두 너무 특별하고 소중한 일이며 기쁜일이다."라고 전했으며 이에 Yoshie Kodera 교수는 "나고야에 방문해주어 너무 감사드리고 발표도 너무 훌륭하여 많이 배울수 있었으며 내년 뿐만 아니라 지속적인 서로간의 협력도 기대된다."라고 답변하였다. 저녁식사를 마치고 우리는 사카에역 주변 나고야 시내를 관광하였다. 나고야 도심을 관통하는 도로인 히사야오도리의 중앙에 위치한 '나고야 TV타워'를 보았다. 이는 1954년에 건설된 일본 최초의 텔레비전 중계탑으로 전해진다. 또한 일본이 자랑하는 후시미역 근처에 라면집에 들려 라면을 먹었고, 마루에이 백화점 내에 있는 100엔샵에 들려 여러 가지 일본 제품을 구경하였다.

마지막 날에는 나고야 역 주변 및 도쿠가와 이에야스 박물관 탐방이 진행되었다. 각각 팀으로 나누어져 관광을 시작하였으며 나고야 역 주변 관광팀은 사카에 역에서 히가시야미선 지하철을 타고 2정거장을 지나 나고야 역에 내려 다카시마야 백화점을 관광하였다. 여기에 있는 Tokyu Hands는 정말 규모가 거대하였으며 주방용품, 패션잡화 등 다양한 제품을 소개하고 판매하고 있었다. 또한 도쿠가와 이에야스 박물관 방문팀은 버스를 타고 이동하였다. 도쿠가와 이에야스는 도요토미 가문의 마지막 후손이자 우환인 도요토미 히데요리를 자결케 한 인물로서 자신의 통치체제를 250여년간 지속시키며 인내의 미학을 보여준 인물이다. 박물관을 보며 남에게서가 아닌 나 자신 안에서 잘못을 찾아야 한다는 교훈도 얻을 수 있었다.

이번 학술교류 참석을 통해 일본의 방사선학 분야의 연구동향 및 발전방향을 알 수 있었고, 일본의 문화를 보고 체험할 수 있었다. MOU 체결을 통해 서로간의 신뢰를 쌓았고 협력의 출발점이 되었다. 또한 지속적인 관계유지를 위해 많은 노력을 기울여야 하겠으며, 내년 11월 3일부터 5일까지 원주에서 진행되는 학술교류에도 많은 관심을 가져야겠다고 다짐하며 본 참관기를 마친다.