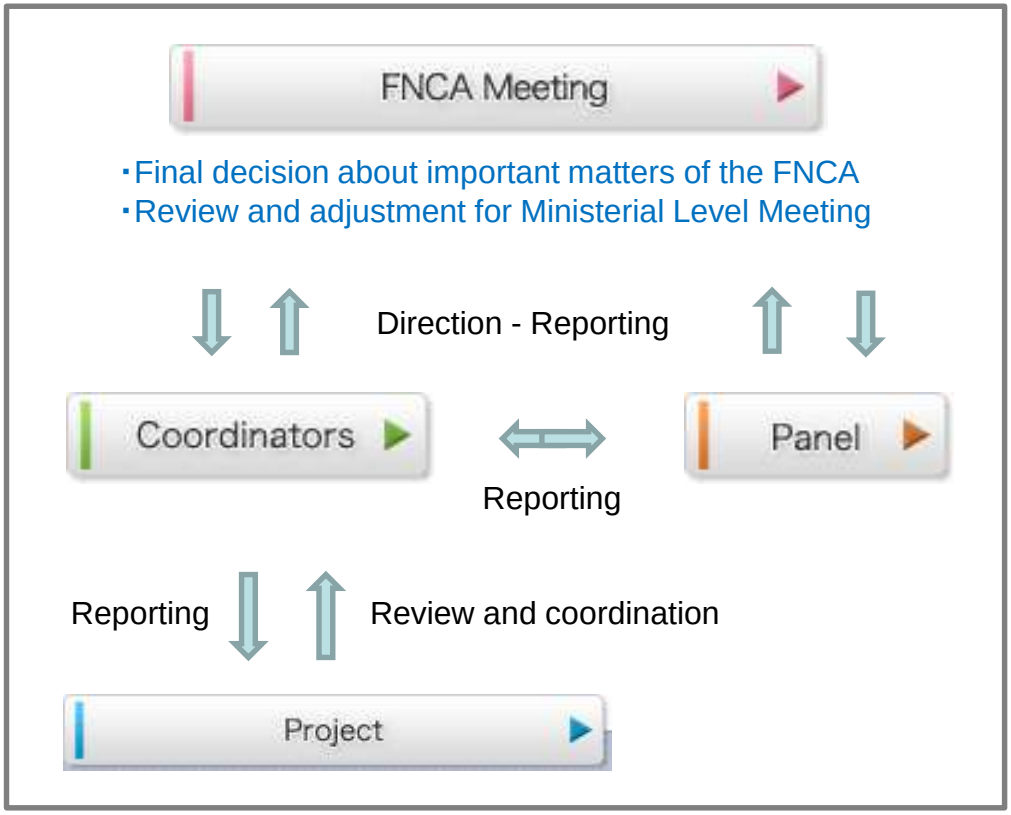
Forum for Nuclear Cooperation in Asia (FNCA)

- Radiation Oncology Project-

Shingo Kato M.D. Ph.D.
FNCA Radiation Oncology Project Member
Saitama Medical University
International Medical Center

Forum for Nuclear Cooperation in Asia (FNCA)

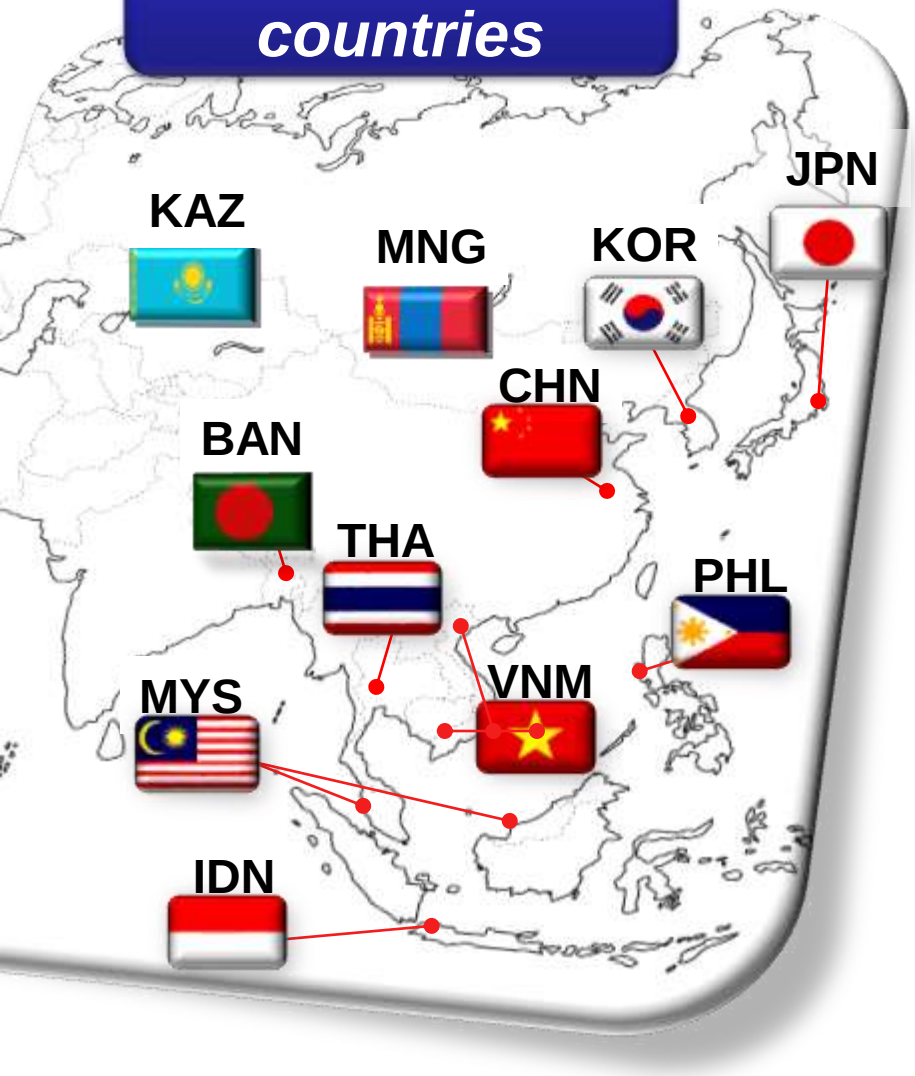
FNCA is a Japan-led cooperation framework for peaceful use of nuclear technology in Asia.
The cooperation consists of FNCA meetings and 10 project activities with the participation of 12 countries; AUS, BAN, CHN, IDN, JPN, KAZ, KOR, MYS, MON, PHL, THA, and VNM.



http://www.fnca.mext.go.jp/

FNCA Radiation Oncology Project (since 1993)

Participating countries



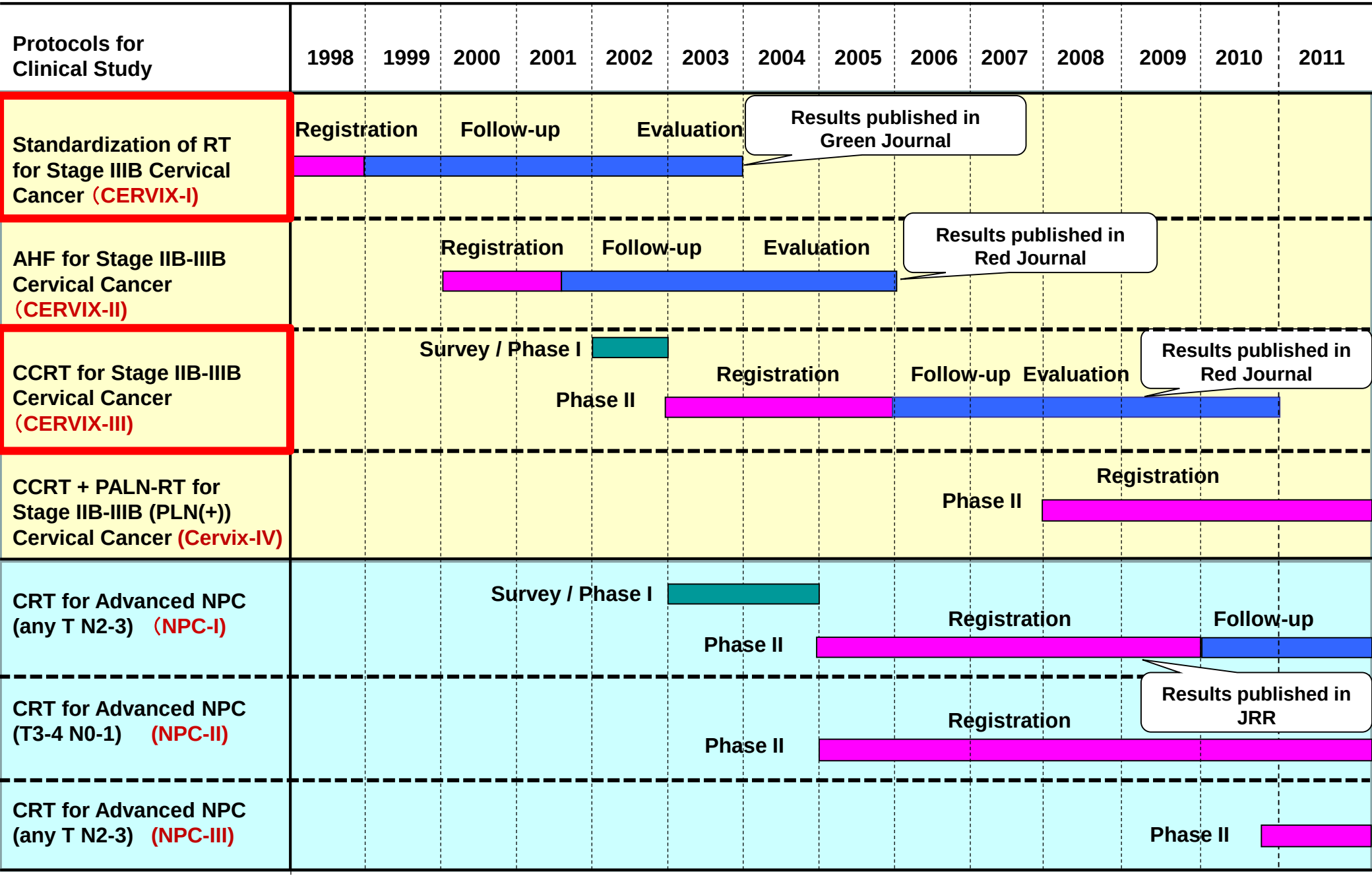
Purpose

To establish safe and effective treatments for predominant cancers in Asia.

Activities

- **Clinical trials for cervix cancer, NPC, and breast cancer**
- **Physical QA/QC of RT**
- **Workshops/ Open lectures/ Technical visits/ etc.**

FNCA Clinical Studies of RT and CCRT



Cervix-I

Standardization of RT for stage IIIB cervical cancer among FNCA countries

Patient accrual: 1995.1-1998.12
Sample size: 210 cases

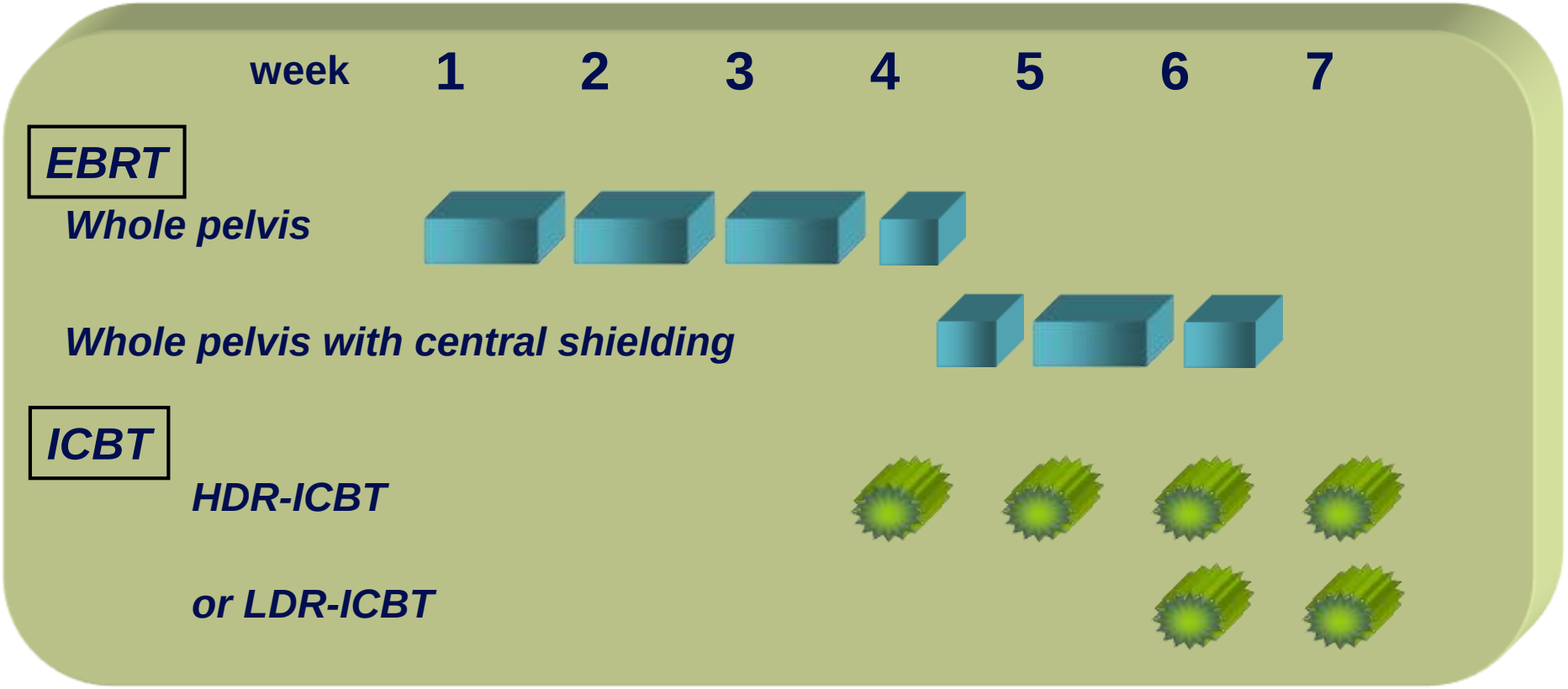
Objectives

1. To evaluate the efficacy of standardized RT protocol for stage IIIB cervical cancer in FNCA countries

2. To evaluate the acute and late toxicities of this treatment

Primary endpoint:	**2-y overall survival**
Secondary endpoint:	**2-y local control**
	Acute and late toxicity

Standardized Protocol of Radiation Therapy (Cervix-I)



EBRT: 1.8-2Gy/fr, Whole Pelvis: 30-40Gy + Central Shielding: 10-20Gy

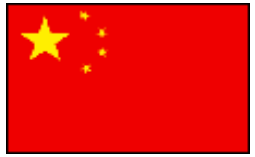
ICBT: HDR treatment: 20-28Gy/4fr (5-7Gy/fr)

LDR treatment: 40-45Gy/1-2fr

Registered patients & Follow-up status

Patient accrual: 1995.1-1998.12 total 210 cases

5-year follow-up rate: 71%



CHN
34
88%

IDN
24
29%

JPN
33
100%

KOR
20
100%

MYS
12
42%

PHL
22
96%

THA
37
73%

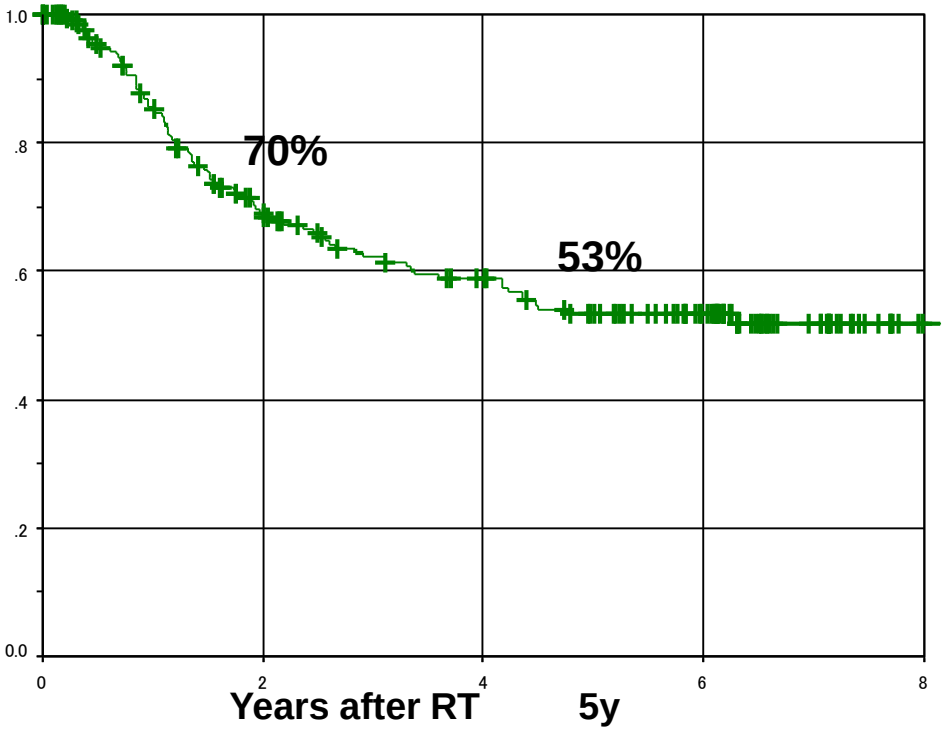
VNM
28
36%

Compliance with the protocol

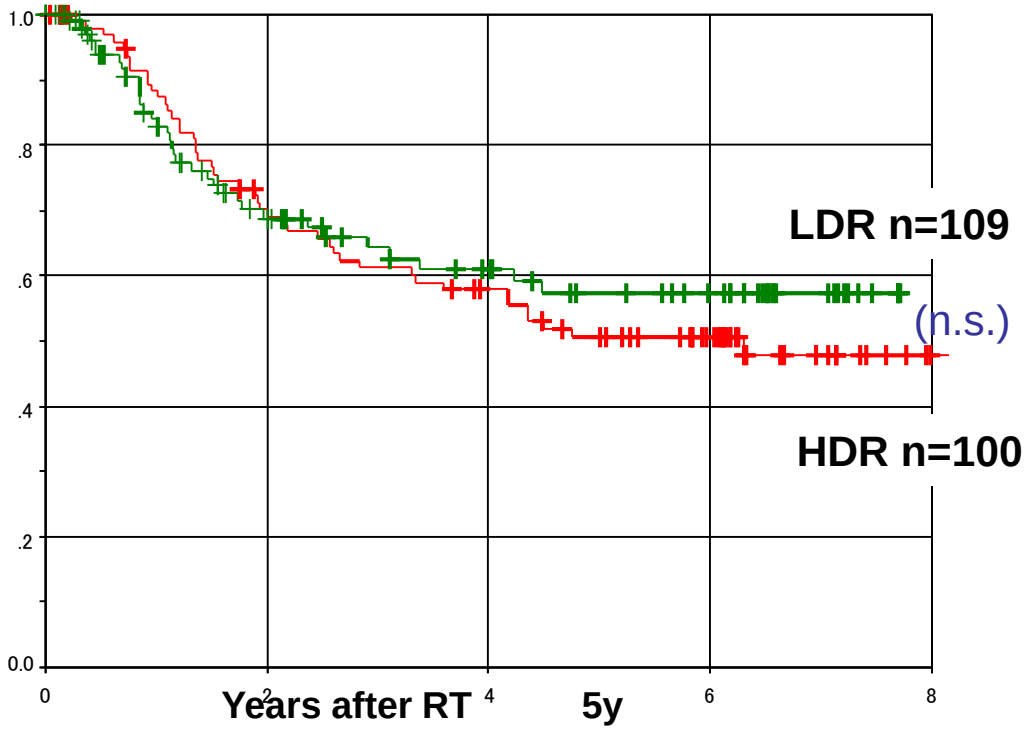
EBRT	
Total dose	50 Gy (22 – 60 Gy)
Whole Pelvis	36 Gy (15 – 60 Gy)
Central Shielding	24 Gy (0 – 33 Gy)
	(Compliance: 71%)
ICBT point A dose	
HDR (100 pts)	24 Gy (12 – 32 Gy)
	(85%: 20 – 28 Gy)
LDR (110 pts)	30 Gy (26 – 52.7 Gy)
	(61%: 30 – 45 Gy)
OTT	47 d (32 – 96 d)
	(72%: $\leq$ 50 d)

Results (Cervix-I)

Overall survival



Overall survival by dose rate



Late Radiation Morbidity

(at 5 years of follow-up)

RTOG/EORTC Grade	0	1	2	3	4
Rectum/Sigmoid colon (%)	74	18	5	3 (3%)	0
Urinary Bladder (%)	78	13	5	2 (4%)	2
Small Intestine (%)	94	4	1	1 (1%)	0

Summary of Cervix-I

210 patients (stage IIIB cervical cancer) were treated with the "standardized RT protocol".
The 5-year OS of 53% was favorable.
The rate of severe late complication (3-4%) was acceptable.

We experienced a number of problems and difficulties.
- diagnostic imaging (use of CT: 30%)
- treatment compliance (violation: 30-40%)
- follow-up rate (5-y: 71%)

These factors may have affected the reliability of the results.

This study provided an important opportunity for mutual understanding the status of RT in the respective countries.
This mutual understanding was important to plan the following clinical studies.

Cervix-III

CCRT for locally advanced cervical cancer

Patient accrual: 2003.4-2006.3
Sample size: 120 cases

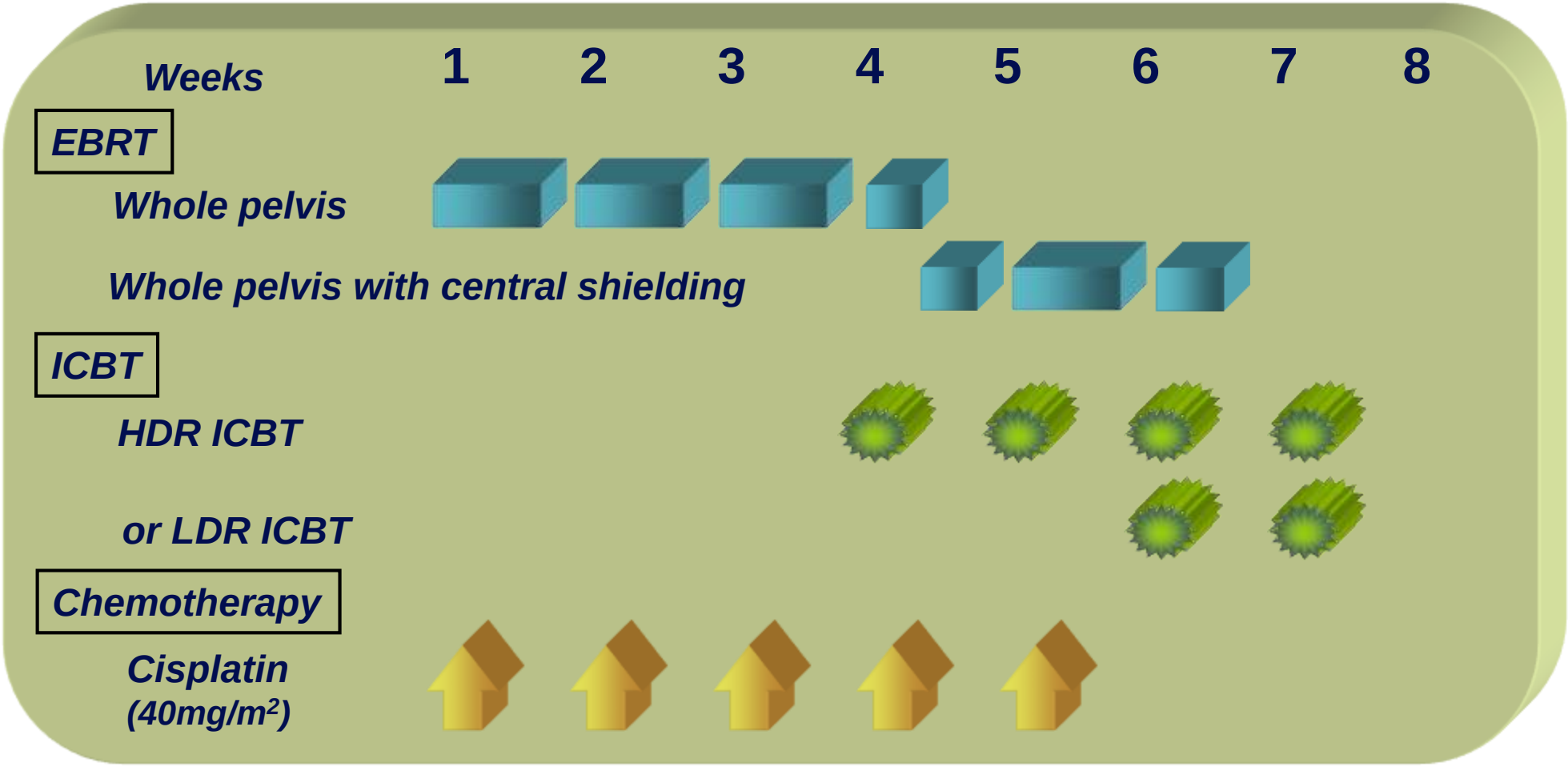
Objectives

1. **To evaluate the efficacy of CCRT using CDDP (40mg/m^2/week) in the patients with locally advanced cervical cancer**

2. **To evaluate the acute and late toxicities of this regimen**

Primary endpoint:	**2-y overall survival**
Secondary endpoint:	**2-y disease-free survival**
	2-y local control
	Acute and late toxicity

Protocol treatment (Cervix-III)

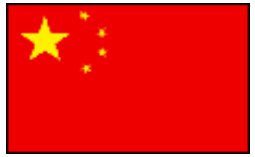


EBRT: 1.8-2Gy/fr, Whole Pelvis: 30-40Gy + Central Shielding: 10-20Gy
ICBT: HDR treatment: 24-28Gy/4fr (6-7Gy/fr)
LDR treatment: 40-45Gy/1-2fr
Cisplatin: 40 mg/m^2/weekly, week 1- week 5

Registered patients & Follow-up status

Patient accrual: 2003.4-2006.3 total 120 cases

Follow-up rate : 117/120=97%!!



CHN
18
100%

IDN
5
100%

JPN
32
100%

KOR
10
100%

MYS
14
79%

PHL
12
100%

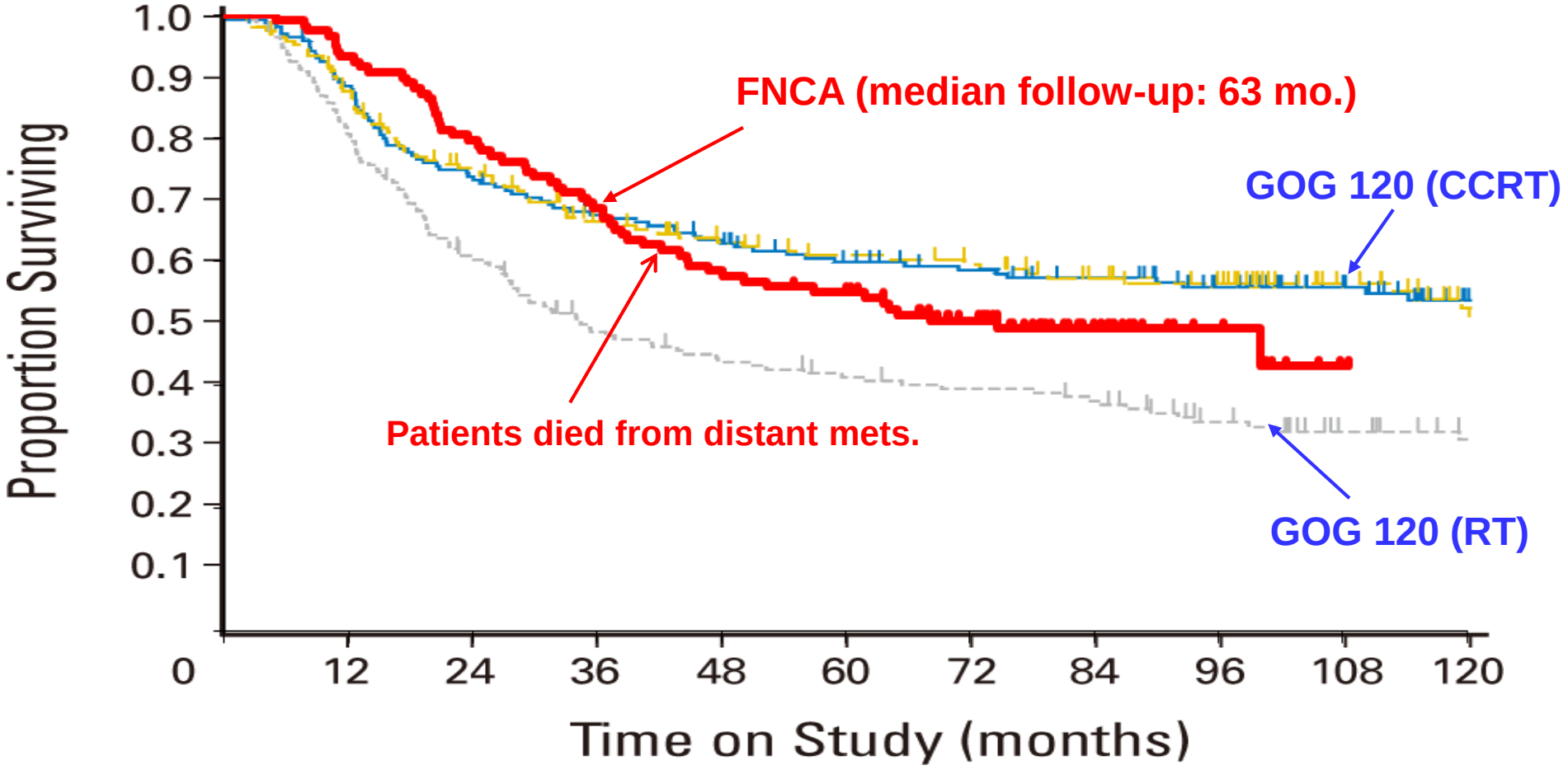
THA
19
100%

VNM
10
100%

Compliance with the protocol

EBRT	**median**	
Total Dose	**50 Gy**	**(50-65.6 Gy)**
Whole Pelvis	**36 Gy**	**(30-50.4 Gy)**
Central Shielding	**14 Gy**	**(0-20 Gy)**
	(No protocol violation)	
ICBT		
Dose rate	**HDR : 88, MDR : 5, LDR : 27**	
Point A dose	**HDR : 26 Gy/4fr**	**(20-30 Gy/3-5fr)**
	MDR : 29 Gy/1fr	**(26-30 Gy/1fr)**
	LDR : 45 Gy/2fr	**(35-50 Gy/1-2fr)**
Median BED at point A	**86.3 Gy_{10} (71.7-110.5 Gy_{10})**	
	(HDR: 84 Gy_{10}, LDR: 102 Gy_{10})	
OTT (median)	**49 days (≤ 60 days: 97/120 patients)**	
Cycles of Chemo.	**1 cycle : 2**	
	2 : 6	**(median: 5 cycles)**
	3 : 12	**(≥ 4 cycles: 83%)**
	4 : 19	
	5 : 81	

Overall survival curves in GOG 120 and FNCA Cervix-III



Rose PG, et al. JCO 25: 2804-2810, 2009.
Kato S, et al. IJROBP 87: 200-205, 2013.

Comparison of the results of RT/CCRT

Study	Eligible stage	Treatment	No. of Pts.	5-y LC (%)	5-y OS (%)
GOG 85[1)]	IIB-IVA IIB:61.0-62.8% III: 33.5-36.1% VIA: 2.8-3.7%	RT+CDDP/5FU	177	-	63
		RT+HU	191	-	50
GOG 120[2)]	IIB-IVA IIB: 46.2-57.4% III: 40.3-50.2% VIA: 2.3-3.5%	RT+CDDP	176	78	60
		RT+CDDP/5FU/HU	173	79	61
		RT+HU	177	66	40
FNCA[3)]	IIB-IIIB IIB: 50% IIIB:50%	RT+CDDP	120	77	55

1) Whitney CW, et al. JCO 17: 1339-1348, 1999. 2) Rose PG, et al. JCO 25: 2804-2810, 2009.
3) Kato S, et al. IJROBP 87: 200-205, 2013.

GOG studies; PALN was surgically staged, PALN (+) patients were excluded.
FNCA study; No surgical staging. 81% were staged by CT.
(Patients in FNCA study could have more advanced disease.)

Toxicities of CCRT for Advanced Cervical Cancer

Study (references)	Treatment	Acute hemat. Grade 3-4 (%)	Acute GI Grade 3-4 (%)	Late overall Grade 3-5 (%)
RTOG 9001 1, 2)	**1) RT + CDDP+5FU**	**37**	**17**	**13**
	2) Extended-field RT	**1**	**2**	**12**
GOG 85 3)	**1) RT + CDDP+5FU**	**4**	**8**	**16.2**
	2) RT + HU	**24**	**4**	**16.5**
FNCA 4)	**1) RT + CDDP**	**21**	**6**	**7.8**

1) Morris et al, NEJM, 1999. 2) Eifel et al, JCO, 2004. 3) Whiteney et al, JCO, 1999.
4) Kato S, et al. IJROBP 87: 200-205, 2013.

Summary of Cervix-III

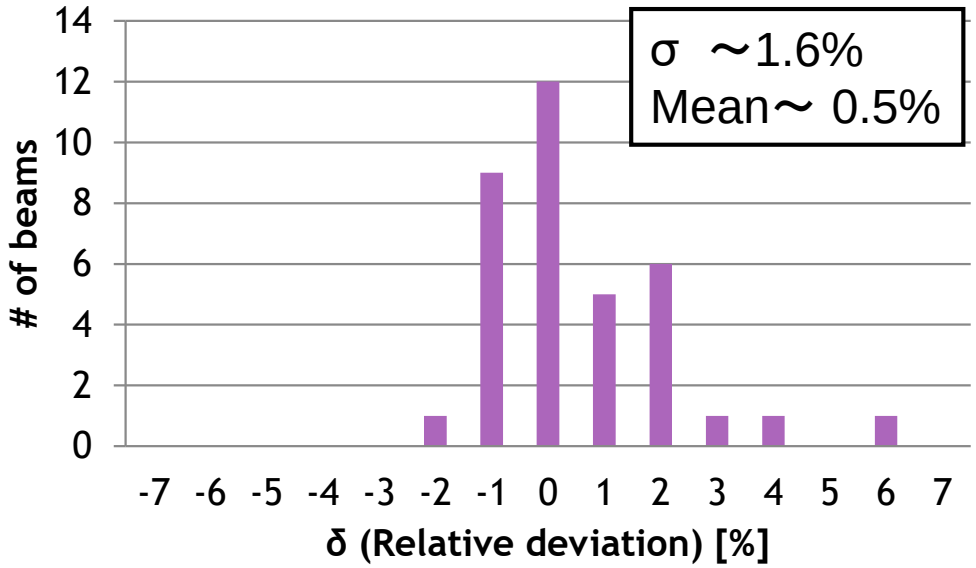
In the 3rd clinical study, 120 patients were treated with CCRT.
The 5-year LC and OS of 77% and 55% were favorable.
The rate of severe late complications (7.8%) was acceptable.
To improve long-term survival outcome, it was considered important to prevent distant metastasis.

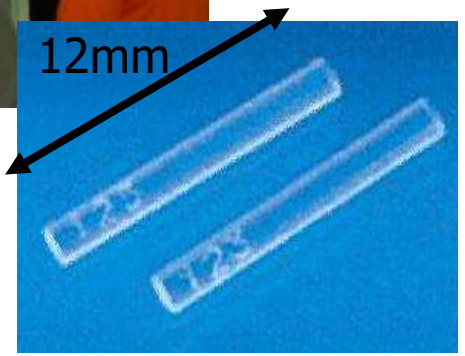
The quality of clinical study was improved dramatically.
- diagnostic imaging (use of CT: 81%)
- treatment compliance (no major violation)
- follow-up rate (5-y: 97%)

This treatment protocol has become a standard protocol for advanced cervical cancer in the FNCA countries.

QA/QC in External Beam Therapy

1. 36 beams (4-18MV) from 12 hospitals in 9 countries were surveyed using glass dosimeters (Dose Ace).
2. **The results of the survey were almost favorable.**
3. Only 1 beam exceeded the tolerance level (< +/-5%).
   We already solved the problem. (Reported in 2009.)





δ (Relative deviation) [%]
= 100 x (user stated value –measured value)/measured value

QA/QC in Brachytherapy

Measurement of source intensity
Calibration of source activity
Checking of source movement & positional accuracy

Well type ionization chamber at Siriraj Hospital

Sandwich method at Chulalongkorn University Hospital

FNCA Cervix-I trial (RT alone)

Radiotherapy and Oncology 84:314-319, 2007

Original article

A regional cooperative clinical study of radiotherapy for cervical cancer in east and south-east Asian countries ☆,☆☆

FNCA Cervix-II trial (AHF-RT)

Int. J. Radiat. Oncol. Biol. Phys. 70: 1522-1529, 2008.

CLINICAL INVESTIGATION Cervix

ACCELERATED HYPERFRACTIONATED RADIOTHERAPY FOR CERVICAL CANCER: MULTI-INSTITUTIONAL PROSPECTIVE STUDY OF FORUM FOR NUCLEAR COOPERATION IN ASIA AMONG EIGHT ASIAN COUNTRIES

TATSUYA OHNO, M.D., PH.D.,* TAKASHI NAKANO, M.D., PH.D.,† SHINGO KATO, M.D., PH.D.,*

FNCA Cervix-III trial (CCRT)

Int .J. Radiat. Oncol.Biol. Phys. 77: 751-757, 2010.

ELSEVIER

CLINICAL INVESTIGATION

MULTI-INSTITUTIONAL PHASE II CLINICAL STUDY OF CONCURRENT CHEMORADIOTHERAPY FOR LOCALLY ADVANCED CERVICAL CANCER IN EAST AND SOUTHEAST ASIA

SHINGO KATO, M.D.,* TATSUYA OHNO, M.D.,† KULLATHORN THEPHAMONGKHOL, M.D.,† YAOWALAK CHANSILPA, M.D.,‡ YANG YUXING, M.D.,§ C. R. BEENA DEVI, M.D.,¶ ANITA Z. BUSTAM, FRCR.,‖ MIRIAM J. C. CALAGUAS, M.D.,# REY H. DE LOS REYES, M.D.,** CHUL-KOO CHO, M.D.,†† TO ANH DUNG, M.D.,‡‡ NANA SUPRIANA, M.D.,§§ HIDEYUKI MIZUNO, PH.D.,* TAKASHI NAKANO, M.D.,¶¶ AND HIROHIKO TSUJII, M.D.*

*Research Center for Charged Particle Therapy, National Institute of Radiological Sciences, Chiba, Japan; †Gunma University Heavy Ion Medical Center, Gunma University, Gunma, Japan; ‡Division of Radiation Oncology, Department of Radiology, Siriraj Hospital, Mahidol University Faculty of Medicine, Bangkok, Thailand; §Department of Gynecologic Oncology, Changzhou Tumor Hospital, Changzhou, China; ¶Department of Radiotherapy and Oncology, Sarawak General Hospital, Kuching, Malaysia; ‖Clinical Oncology Unit, University of Malaya Faculty of Medicine, Kuala Lumpur, Malaysia; #Department of Radiation Oncology, St. Luke's Medical Center, Quezon City, Philippines; **Department of Obstetrics and Gynecology, Dr. Jose R. Reyes Memorial Medical Center, Manila, Philippines; ††Department of Radiation Oncology, Korea Cancer Center Hospital, Seoul, Republic of Korea; ‡‡Department of Breast and Gynecology Radiotherapy, National Cancer Institute, Hanoi, Viet Nam; §§Department of Radiation Therapy, University of Indonesia Faculty of Medicine, Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia; ¶¶Department of Radiation Oncology, Gunma

FNCA NPC-I trial (CCRT)

J. Radiat. Res. 54: 467-473, 2013.

Radiotherapy concurrently with weekly cisplatin, followed by adjuvant chemotherapy, for N2–3 nasopharyngeal cancer: a multicenter trial of the Forum for Nuclear Cooperation in Asia

Tatsuya OHNO[1,*], Dang Huy Quoc THINH[2], Shingo KATO[3], C.R. Beena DEVI[4], Ngo Thanh TUNG[5], Kullathorn THEPHAMONGKHOL[6], Miriam Joy C. CALAGUAS[7], Juying ZHOU[8], Yaowalak CHANSILPA[6], Nana SUPRIANA[9], Dyah ERAWATI[10], Parvin Akhter BANU[11], Cho Chul KOO[12], Kunihiko KOBAYASHI[13], Takashi NAKANO[14] and Hirohiko TSUJII[15]

[1]Gunma University Heavy Ion Medical Center, Gunma University, Gunma, Japan
[2]Department of Radiation Oncology No. 3, Ho Chi Minh City Cancer Center, Ho Chi Minh City, Vietnam
[3]Department of Radiation Oncology, Saitama Medical University, Saitama, Japan
[4]Department of Radiation Oncology, Sarawak General Hospital, Malaysia
[5]Head and Neck Radiation Department, National Cancer Hospital, Hanoi, Vietnam
[6]Department of Radiology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand
[7]Department of Radiation Oncology, St. Luke's Medical Center, Quezon City, Philippines

FNCA Cervix-III trial (CCRT)

Int .J. Radiat. Oncol.Biol. Phys. 87: 100-105, 2013.

Clinical Investigation: Gynecologic Cancer

Long-term Follow-up Results of a Multi-institutional Phase 2 Study of Concurrent Chemoradiation Therapy for Locally Advanced Cervical Cancer in East and Southeast Asia

Shingo Kato, MD,*,† Tatsuya Ohno, MD,† Kullathorn Thephamongkhol, MD,‡ Yaowalak Chansilpa, MD,‡ Jianping Cao, MD,§ Xiaoting Xu, MD,¶ C. R. Beena Devi, MD,‖ Tang Tieng Swee, PhD,‖ Miriam J.C. Calaguas, MD,** Rey H. de los Reyes, MD,†† Chul-Koo Cho, MD,‡‡ To Anh Dung, MD,§§ Nana Supriana, MD,‖‖ Dyah Erawati, MD,¶¶ Hideyuki Mizuno, PhD,† Takashi Nakano, MD,## and Hirohiko Tsujii, MD†

*Department of Radiation Oncology, International Medical Center, Saitama Medical University, Saitama, Japan; †National Institute of Radiological Sciences of Japan, Chiba, Japan; ‡Gunma University Heavy Ion Medical Center, Gunma University, Gunma, Japan; §Division of Radiation Oncology, Department of Radiology, Siriraj Hospital, Faculty of Medicine, Mahidol University, Bangkok, Thailand; ‖School of Radiation Medicine and Public Health, Soochow University; ¶Department of Radiation Oncology, The First Affiliated Hospital of Soochow University, Soochow, China; #Department of Radiotherapy and Oncology, Hospital Umum Sarawak, Kuching, Malaysia; **Department of Radiation Oncology, St. Luke's Medical Center, Quezon City, the Philippines; ††Department of Obstetrics and Gynecology, Dr Jose R. Reyes Memorial Medical Center, Manila, the Philippines; ‡‡Department of Radiation Oncology, Korea Cancer Center Hospital, Seoul, Republic of Korea; §§Department of Breast and Gynecology Radiotherapy, National Cancer Institute, Hanoi, Vietnam; ‖‖Department of Radiation Therapy, Faculty of Medicine, University of Indonesia, Dr Cipto Mangunkusumo General Hospital, Jakarta, Indonesia; ¶¶Division of Radiotherapy, Dr Soetomo General Hospital, Surabaya, Indonesia;

Cooperation with IAEA/RCA

Duration	Project No. Lead Country Coordinator	Project Title
2005-2008	RAS 6040 T. Nakano (Japan)	Improvement in Quality of Radiotherapy for Frequent Cancers in the Region
2010-2014	RAS 6053 T. Nakano (Japan)	Improving Image Based Radiotherapy for Common Cancers in the RCA Region
2012-2016	RAS 6062 S. Kato (Japan)	Supporting 3D Image Guided Brachytherapy Services in the RCA Region
2012-2016	RAS 6065 C-K. Cho (Korea)	Strengthening in the Application of Stereotactic body Radiation Therapy to Improve Cancer Treatment

Treatment information obtained through FNCA clinical trials were lectured at IAEA/RCA RTCs. Three RCA experts (IND, PAK, SRL) attended FNCA workshops and shared relevant information.

FNCA WS, Suzhou China, 2012

FNCA WS FY2008 Indonesia

FNCA WS FY2009 Malaysia

Summary of FNCA clinical study

Although there are wide differences in culture and socio-economic status among countries, FNCA RO project has been conducting international clinical studies for more than 20 years in Asia.
This is a very unique activity.

We have improved the quality of clinical study step by step.
- diagnostic imaging
- RT techniques
- treatment compliance
- follow-up rate


Thank you very much.