

BrachyNext



Working Together to Shape the Future of
Brachytherapy

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Brachytherapy

Starting a Brachytherapy Program in Government-Controlled Healthcare Systems

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University Cooperation Platform

- **Design and Planning a Cooperation Platform**
 - Between Chiang Mai University/Thailand and Christian-Albrecht-University Kiel/Germany
 - Starting in 1999
 - **1/Aim to develop a University Center of Excellence in Thailand**



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 - 3/Aim to create a sustainable base for long-term development of image-guided brachytherapy in Chiang Mai
 - 4/Aim to ensure a long-term 2-Institution-cooperation programme – in other High-Tech fields as well !



Limited resources

- **How to manage limited resources in the context of a very high patient volume**
 - **Chemotherapy**
 - **High co-morbidity**

Limited resources

J. Radiat. Res., 52, 9-14 (2011)

Regular Paper

Impact of Incomplete Plan to Treatment Results of Concurrent Weekly Cisplatin and Radiotherapy in Locally Advanced Cervical Cancer

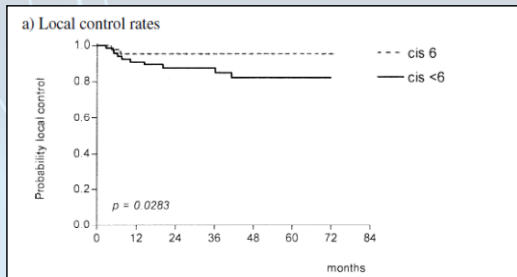
Ekkasit THARAVICHITKUL^{1*}, Attapol PINITPATCHARALERD², Vicharn LORVIDHAYA¹,
Pimkhuan KAMNERDSUPAPHON¹, Nantaka PUKANHAPHAN¹, Vimol SUKTHOMYA¹,
Imjai CHITAPANARAX¹ and Razvan GALALAE³

Cervical cancer/Concurrent chemoradiation/Compliance.

To evaluate the efficacy of incomplete treatment protocols of cisplatin in concurrent chemoradiation for locally advanced cervical carcinoma. This retrospective study was performed in 165 consecutively treated patients with locally advanced cervical cancer who received a weekly cisplatin regimen. The number of weekly cisplatin cycles of each patient was recorded and used to discriminate between patients. Local control, disease free survival, distant metastasis-free survival, and toxicities were calculated using the software package SPSS version 15.0. Ninety-two patients (55%) completed the planned protocol of six cycles of weekly cisplatin. With the median follow-up time of 38.2 months, the 3-year local control rate differed significantly in the two patient groups (95.4% of 6 cycles versus 84.8% of < 6 cycles; $p = 0.028$). No statistical significance was observed for disease-free survival (74.6% versus 74.5%; $p = 0.22$) and distant metastasis-free survival (76.5% vs. 75.7%; $p = 0.88$). In conclusion, the plan completion of concurrent cisplatin with radiotherapy was responsible for better local control. However, differences in disease-free survival and distant metastasis-free survival were not statistical significant.

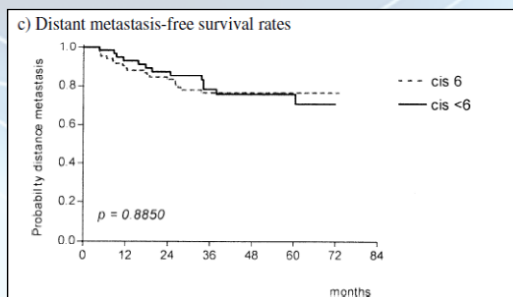


Limited resources



Local tumor control lower when Cis < 6 cycles

...but distant metastasis-free survival remains unchanged



Limited resources

[Eur J Cancer](#). 2007 Jun;43(9):1399-406. Epub 2007 Apr 27.

Chemoradiation comparing cisplatin versus carboplatin in locally advanced nasopharyngeal cancer: randomised, non-inferiority, open trial.

[Chitapanarux J](#), [Lorvidhaya V](#), [Kamnerdsupaphon P](#), et al. Division of Therapeutic Radiology and Oncology, Chiang Mai University, 50200, Chiang Mai, Thailand

Abstract

Purpose

This single centre, open labelled, randomised non-inferiority trial compared concurrent chemoradiotherapy with carboplatin versus standard concurrent chemoradiotherapy with cisplatin in patients with locoregionally advanced nasopharyngeal cancer (NPC).

Patients and methods

From August 1999 to December 2004, **206 patients with locally advanced NPC were randomised with 101 to cisplatin arm and 105 to carboplatin arm.** Planned radiotherapy was the same in both groups. All the patients were evaluated for toxicity and survival according to the as-treated principle.

Results

With a median follow-up of 26.3 months (range 3–74.6 months), **59% of patients in the cisplatin arm completed the planned concurrent chemoradiation treatment, compared to 73% in the carboplatin arm.** Forty-two percent of cisplatin patients completed the 3 cycles of adjuvant therapy compared to 70% in the carboplatin group. There were more renal toxicity, leucopenia, and anaemia in the cisplatin group, and more thrombocytopenia in the carboplatin arm. **The 3 year disease free survival rates were 63.4% for the cisplatin group and 60.9% for the carboplatin group (p = 0.9613)** (HR 0.70, 95% confidence interval (CI): 0.50–0.98). **The 3 year overall survival rates were 77.7% and 79.2% for cisplatin and carboplatin groups, respectively (p = 0.9884)** (HR 0.83, 95% CI: 0.63–1.010).

Conclusion

We concluded that the tolerability of carboplatin based regimen is better than that of the cisplatin regimen. Moreover, the treatment efficacy of carboplatin arm is not different from the standard regimen in the treatment of locoregional advanced stage NPC.



First project: image guided brachytherapy

- Projects aiming to develop and implement image guidance in brachytherapy
 - Computed tomography (CT) based BT in cervical cancer

First project: image guided brachytherapy

J. Radiat. Res., 52, 634-640 (2011)

Regular Paper

Preliminary Results of Conformal Computed Tomography (CT)-based Intracavitary Brachytherapy (ICBT) for Locally Advanced Cervical Cancer: A Single Institution's Experience

Ekkasit THARAVICHITKUL^{1*}, Somvilai MAYURASAKORN¹, Vicham LORVIDHAYA¹,
Vimol SUKTHOMYA¹, Somsak WANWILAIRAT¹, Sanchai LOOKAEW¹,
Nantaka PUKANHAPHAN¹, Imjai CHITAPANARUX¹
and Razvan GALALAE²

Cervical cancer/Intracavitary brachytherapy/Conformal CT-based planning.

Intracavitary brachytherapy using tandem and ovoids is an important component of definitive treatment for cervical cancer. In the present study, we analyzed the dose-volume histograms (DVHs) of the tumor volume and organs at risk including the sigmoid colon by CT-based treatment planning for high dose rate (HDR) intracavitary brachytherapy (ICBT) in cervical cancer. Seventeen patients with carcinoma of the cervix uteri were treated with external beam radiotherapy plus concurrent chemotherapy. For brachytherapy, the planning procedure started by performing a conventional plan which prescribed a dose of 6.5–7 Gy per fraction to point A, then optimized the dose based on CT imaging. Volumes and DVHs were calculated for the HR-CTV, bladder, rectum and sigmoid colon. The mean BED_{20y} total doses of post-optimized plans of HR-CTV, bladder, rectum and sigmoid colon were: 89.6, 94.1, 74.0 and 69.8 Gy, respectively. For conventional plans, the calculated mean BED_{20y} total doses of HR-CTV, bladder, rectum and sigmoid colon were 92.2, 120.1, 75.7 and 78.3 Gy, respectively. This study showed statistical significant higher BED_{20y} total doses for bladder and sigmoid colon ($p < 0.001$) using conventional plans versus post-optimized, CT-based plans, while no difference between HR-CTV and rectum BED_{20y} total doses could be detected. After a median follow-up of nineteen months, all seventeen patients had a clinical complete response. Two patients developed distant metastasis. Compared with conventional treatment, CT based brachytherapy planning was very effective in reducing doses to OARS, especially bladder and sigmoid colon whilst maintaining a high therapeutic dose for tumor target volumes in the treatment of cervical carcinoma.



First project: image guided brachytherapy

Results CT based IGBT

Table 1. Patient Characteristics.

Parameters	Numbers (N)
Median age (years)	50
Range in years	(36-60)
Karnofsky performance status	
80-100%	17
FIGO Stage	
IB2	1
IIB	12
IIIB	4
Size of tumor	
≤ 5 cm	12
> 5 cm	5
Pathological reports	
SCC	16
ACA	1

FIGO: Fédération Internationale de Gynécologie et d'Obstétrique – International Federation of Gynecology and Obstetrics.
SCC: Squamous cell carcinoma.
ACA: Adenocarcinoma.

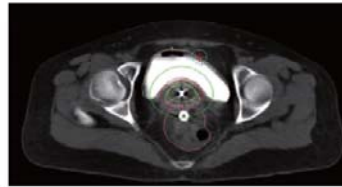


Fig. 1. CT imaging of patients with applicator, high-risk clinical target volume (HR-CTV: light blue line) and Organs at risk (bladder and rectum). The 150%-, 100%- and 50%-isodose lines were shown in yellow, red and green colors, respectively.

Table 2. Dose comparison in terms of BED_{2Gy} in Gy for HR-CTV (D90), bladder (D2cc), rectum (D2cc) and sigmoid (D2cc) of standard versus CT-based conformal plans.

Parameters	Pre-optimized dose (standard plan)	Optimized dose (CT based 3D conformal plan)	P-value
D90 HR-CTV	92.2+/-9.7	89.6+/-5.2	0.16
D2cc bladder	120.1+/-20.7	94.1+/-6.6	< 0.001
D2cc rectum	75.7+/-8.7	74.0+/-5.6	0.29
D2cc sigmoid	78.3+/-11.4	69.8+/-9.2	< 0.001

Second project: image guided brachytherapy

- **Projects aiming to develop and implement image guidance in brachytherapy**
 - Computed tomography (CT) based BT in cervical cancer
 - Magnetic resonance imaging (MRI) based BT in cervical cancer



Second project: image guided brachytherapy

J. Radiat. Res., 53, 313-318 (2012)

Preliminary Results of MRI-guided Brachytherapy in Cervical Carcinoma: The Chiangmai University Experience

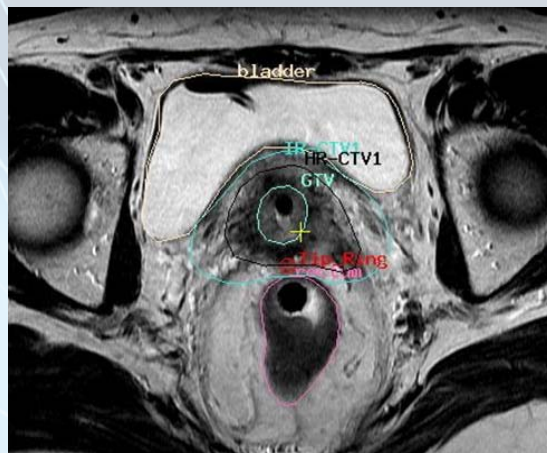
Ekkasit THARAVICHITKUL^{1*}, Chate SIVASOMBOON², Somsak WANWILAIRAT¹,
Vicharn LORVIDHAYA¹, Vimol SUKTHOMYA¹, Somvilai CHAKRABHANDU¹,
Sanchai LOOKKAEW¹, Imjai CHITAPANARUX¹ and Razvan GALALAE³

Advanced cervical cancer/Intracavitary/interstitial brachytherapy/Conformal MRI-based planning.

This study was performed to evaluate the feasibility of magnetic resonance imaging (MRI) in the treatment planning of image-guided brachytherapy for cervical carcinoma. Seventeen consecutive patients with locally advanced cervical cancer were enrolled in the study. Fifteen patients could be evaluated. When comparing the tumor at diagnosis (GTV-Dx) and the tumor at the first brachytherapy (GTV-BT), 11 of 15 patients showed a tumor regression of more than 80% while only four patients had less than 80% tumor regression. The mean D90 of HR-CTV and the calculated D2cc of the bladder, rectum, and sigmoid were 99.2 ± 11 Gy, 87.7 ± 5.7 Gy, 68.4 ± 5.4 Gy and 70.3 ± 6.8 Gy, respectively. No grade 3-4 acute toxicity was observed. The MRI can be a valuable tool for evaluating tumor response after external beam radiotherapy (EBRT) and is very helpful for prognosis prediction by residual GTV evaluation. Furthermore, MRI-guided brachytherapy allowed us to optimize the dose for both the target volumes and the OARs.

Second project: image guided brachytherapy

Why MRI in addition to CT?





Second project: image guided brachytherapy

Selection criteria – as in the CT trial but...

Parameters	Values
Age	53.6 years
FIGO Stage	
IIB	13
IIIB	2
Tumor size	
≤ 5 cm	6
> 5 cm	9
Histology	
Squamous cell carcinoma	9
Adenocarcinoma	6
Regression of disease at 1 st application	
More than 80%	11
Less than 80%	4

Second project: image guided brachytherapy

MRI – usefull in longitudinal TU monitoring as well

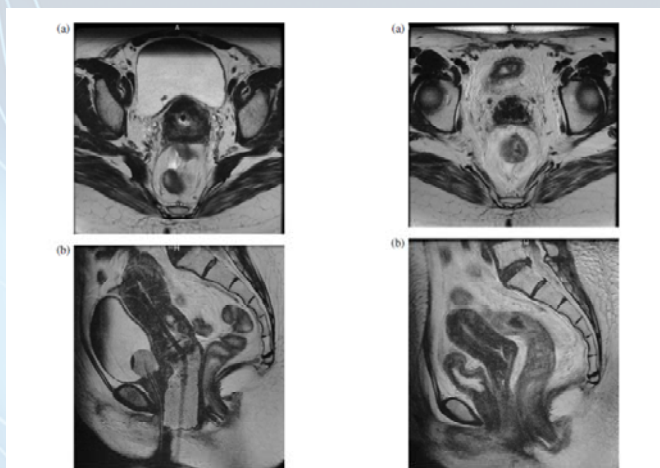


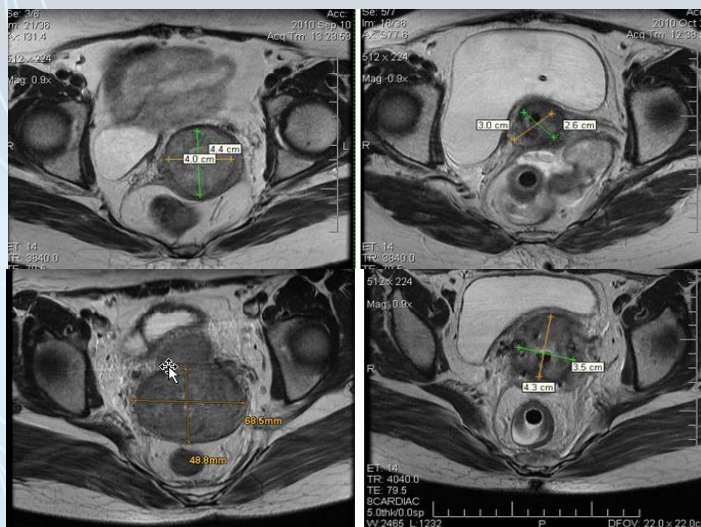
Fig. 3. Magnetic resonance imaging at 1st brachytherapy application in axial and sagittal views of the same patient depicting the correlations of Gross Tumor Volume (GTV).

Fig. 4. Magnetic resonance imaging at three months after treatment in axial and sagittal views of the same patient showing the correlations of Gross Tumor Volume (GTV) after treatment completion.



Second project: image guided brachytherapy

MRI – useful in longitudinal TU monitoring as well



Second project: image guided brachytherapy

Dose in critical organs significantly reduced while tumor doses > 95 Gy

Table 2. Comparison of dose parameters (mean D90 of HR-CTV, and D2cc of bladder, rectum, sigmoid) for the treatment of MRI-guided brachytherapy in locally advanced cervical cancer in term of BED_{2Gy} – standard versus optimized plans

Parameters	Standard-plan mean dose in Gy (dose range)	Optimized-plan mean dose in Gy (dose range)	P-value
D90 HR-CTV	115.2 (85.9–150.5)	99.2 (88.5–127)	0.005
D2cc bladder	127.7 (77.7–226.2)	87.7 (76.6–94)	0.003
D2cc rectum	79.5 (61.4–120.8)	68.4 (62.2–81.7)	0.015
D2cc sigmoid	85.2 (58.4–127.2)	70.3 (55.7–78.5)	0.012

Prescribed Dose- Limits:

Tumor EQD_{2Gy} min. 85 Gy High Risk CTV

Rectum / Sigmoid D2 cc ≤ 70 Gy_{α/β3}

Bladder D2 cc ≤ 90 Gy_{α/β3}

Table 3. Acute toxicity profile in 15 patients treated with MRI-guided brachytherapy

Side effects	Grade and number of patients with toxicity
Anemia	G1: 3 G2: 1
Leucopenia	G1: 3 G2: 1
Thrombocytopenia	G1: 1 G2: 0
Nephrotoxicity	G1: 1 G2: 0
GI	G1: 6 G2: 1
GU	G1: 2 G2: 0
Skin	G1: 0 G2: 0



Third project: image guided brachytherapy

- **Projects aiming to develop and implement image guidance in brachytherapy**
 - Computed tomography (CT) based BT in cervical cancer
 - Magnetic resonance imaging (MRI) based BT in cervical cancer
 - **Combination of High-Tech external beam radiotherapy with IGBT**

Third project: image guided brachytherapy

Clinical Investigations

Original paper

Image-guided brachytherapy (IGBT) combined with whole pelvic intensity-modulated radiotherapy (WP-IMRT) for locally advanced cervical cancer: a prospective study from Chiang Mai University Hospital, Thailand

Ekkrasit Thasavichitkul, MD, Samsak Wanwilairat, PhD, Samwela Chakrabandhu, MD, Pithayapornne Klunklin, MD, Witsak Chohan, MD, Damwongsak Tippangso, BSc, Wannapa Naprap, MSc, Ratan Galalae, MD, PhD, Ingjai Chitayapornwut, MD

The Division of Therapeutic Radiology and Oncology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; Faculty of Medicine, Christian-Albrechts-University, Kiel, Germany

Abstract

Purpose: A report of preliminary results and toxicity profiles using image-guided brachytherapy (IGBT) combined with whole pelvic intensity-modulated radiation therapy (WP-IMRT) for locally advanced cervical cancer.

Material and methods: Fifteen patients with locally advanced cervical cancer were enrolled into the study. WP-IMRT was used to treat the Clinical Target Volume (CTV) with a dose of 45 Gy in 25 fractions. Concurrent cisplatin (40 mg/m²) was prescribed during radiotherapy (RT) on weekly basis. IGBT using computed tomography was performed at the dose of 7 Gy × 4 fractions to the High-Risk Clinical Target Volume (HR-CTV).

Results: The mean cumulative doses – in terms of equivalent dose of 2 Gy (EQD2) – of IGBT plus WP-IMRT to HR-CTV, bladder, rectum, and sigmoid colon were 88.3, 85.0, 68.2 and 73.6 Gy, respectively. In comparison with standard (point A prescription) dose-volume histograms, volume-based image-guided brachytherapy improved the cumulative doses for bladder of 67%, rectum of 47% and sigmoid of 46%. At the median follow-up time of 14 months, the local control, metastasis-free survival and overall survival rates were 95%, 100% and 93%, respectively. No grade 3–4 acute and late toxicities were observed.

Conclusion: The combination of image-guided brachytherapy and intensity-modulated radiotherapy improved the dose distribution to tumor volumes and avoided overdose in OARs which could be converted in excellent local control and toxicity profiles.

J Contemp Brachytherapy 2003, 5: 1-10-16
DOI: 10.584/jcb-2003-34338

Key words: brachytherapy, cervical cancer, IGBT, IMRT.



Third project: image guided brachytherapy Combination of two "worlds" - but at very high level of technology

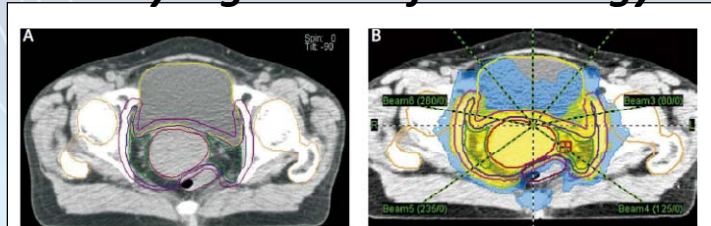


Fig. 1. Seven-beam whole pelvic intensity-modulated radiation therapy (WP-IMRT) in patient with stage IIB cervical cancer; A) target (CTV) and OARs contouring, B) dose distribution with 45 Gy in 25 fractions

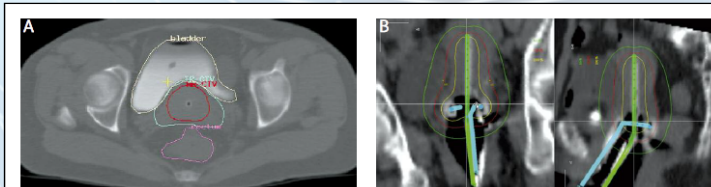


Fig. 2. Image-guided brachytherapy in patient with stage IIB cervical cancer; A) target and OARs contouring, B) dose distribution

Third project: image guided brachytherapy

Results at median FU of 14 months

Table 1. Characteristic data of patients in the study

Parameters	Data (mean; range)
Age	53 years (range: 47-61 years)
Pathology:	
SCCA	13
ACA	2
FIGO stages:	
IIB	12
IIIB	3
Total treatment time	54 days (range: 42-74 days)

SCCA – squamous cell carcinoma, ACA – adenocarcinoma, FIGO – the International Federation of Gynecology and Obstetrics

Table 2. Cumulative dose in EQD2 of point-based plan versus volume-based plan

Parameters	Point-based plan: Gy (mean ± SD)	Optimized plan: Gy (mean ± SD)	P-value (2-tailed)
HR-CTV	109.8 ± 16.3	88.3 ± 3.8	< 0.001
Bladder	113.9 ± 28.8	85.0 ± 9.3	< 0.001
Rectum	79.8 ± 16.2	68.2 ± 6.5	0.001
Sigmoid	90.8 ± 15	73.6 ± 6.3	< 0.001

WP-IMRT – whole-pelvic intensity modulated radiation therapy, IGBT – image-guided brachytherapy, EQD2 – equivalent dose of 2 Gy, HR-CTV – high-risk clinical target volume

Table 3. Acute toxicities of cervical cancer of combination of WP-IMRT plus IGBT

Parameters	Numbers of patients
Skin G1-2	1
Skin G3-4	0
Gastro intestinal toxicity (proctitis) G1-2	9
Gastro intestinal toxicity (proctitis) G3-4	0
Genitourinary toxicity (cystitis) G1-2	8
Genitourinary toxicity (cystitis) G3-4	0

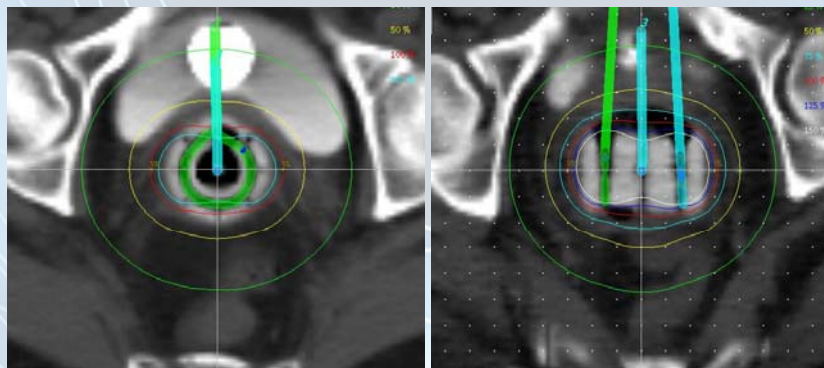
Chiang Mai Schedule:

IMRT Pelvis 45 Gy (25 fractions) + Cis 40 mg/m² weekly and 4 Fractions x 7 Gy HDR IGBT (HR-CTV) – D90



Fourth project: image guided brachytherapy

CT-images showing the vaginal point doses right (VR) and left (VL) according to ABS guidelines in tandem ring applicator, and tandem ovoid applicator



Fourth project: image guided brachytherapy

The dose at vaginal dose points per fraction, in EQD2 and in cumulative dose

Parameter	Point-based planning (pointA) (Gy)	Volume-based planning (Gy)	P-value
VR dose per fraction	8.2±1.5	7±1.7	<0.001
VL dose per fraction	8.1±1.5	6.8±1.7	<0.001
VR dose per fraction in EQD2	19±5.6	15.6±6.1	<0.001
VL dose per fraction in EQD2	18.6±5.5	13.7±5.8	<0.001
VR cumulative dose in EQD2	119.4±19.3	101.5±18.4	<0.001
VL cumulative dose in EQD2	117.5±18.8	98.2±18	<0.001
Means VR+VL cumulative dose in EQD2	118.4±18.6	99.8±17.2	<0.001

However, work in progress – not published yet



Fourth project: image guided brachytherapy

image-guided brachytherapy in combination with WP-IMRT protected as a by-product from overdoses to the vagina

Parameters	Grade 1 vaginal toxicity	Grade 2 vaginal toxicity
Whole group (N=26)	14	2
WP-3DCRT group (N=12)	9	2
WP-IMRT group (N=14)	5	0

However, work in progress – not published yet

Ongoing project: image guided brachytherapy

- **Projects aiming to develop and implement image guidance in brachytherapy**
 - Computed tomography (CT) based BT in cervical cancer
 - Magnetic resonance imaging (MRI) based BT in cervical cancer
 - Combination of High-Tech external beam radiotherapy with IGBT
 - Use of ultrasound for guidance and possibly planning of IGBT in gynaecological malignancies



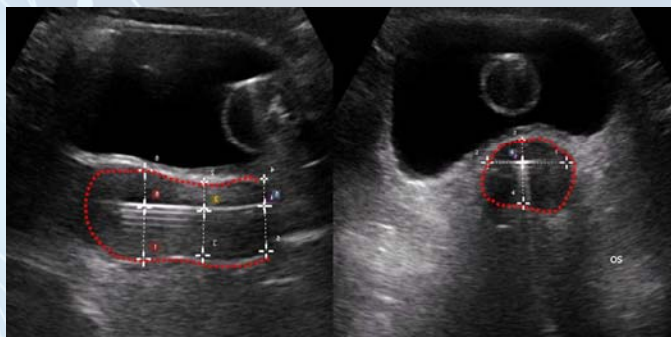
Ongoing project: image guided brachytherapy

Why US? Image guidance takes nearly double time in a context of > new 200 pts. per year!

Procedure	Equipment		Duration (min)	
	2D	3D	2D	3D
App. Insertion	Fletcher App. Mould	Fletcher App. Mould	10-15	10-15
Imaging	X ray radiography	Computed tomography	10-30	15-25
Dose calculation	Nucletron PLATO	Nucletron PLATO	5-20	30-50
Plan evaluation	Point dose	DVH	5-10	10-30
Tx delivery	mHDR	mHDR	15	15
		Total	45-90	80-135

Ongoing project: image guided brachytherapy

Trans-abdominal ultrasound (TAUS) images with applicator showing the structures (tandem, uterus and bladder) and measurement of cervix in sagittal and axial directions (red-dotted lines representing outlines of uterus and cervix)





Future projects: planning

- **Planned future projects**
 - Implementation of breast brachytherapy (multicatheter technique and APBI) in the context of a “Visiting Professor Programme” in Chiang Mai (planned duration 4-6 weeks end of 2014/beginn 2015)
 - Implementation of real-time prostate HDR brachytherapy (IGBT)
 - Implementation of breast stereotactic radiotherapy
 - Implementation of lung stereotactic radiotherapy and gated radiosurgery

Conclusions and Acknowledgments

- **Conclusions**
 - Intermediate-term analyses of high-dose-rate IGBT in patients with advanced gynecological cancer revealed excellent results
 - Magnetic resonance imaging (MRI) based adaptive BT is the golden standard in terms of HR-CTV definition
 - However, the combination of High-Tech external beam radiotherapy (IMRT/Tomo) with CT-based IGBT is easier to manage in a very high volume institution as Chiang Mai University
 - **Patient selection and productivity remain a (unsolved) problem**



Conclusions and Acknowledgments

- Acknowledgments are expressed to the entire Chiang Mai team and especially to [Dr. Ekkasit Tharavichitkul](#), [Prof. Vicharn Lorvidhaya](#), and [Dr. Somsak Wanwilairat](#) for the excellent and sustainable cooperation

Conclusions and Acknowledgments

