A Two-Year Experience of Implementing 3 Dimensional Radiation Therapy and Intensity-Modulated Radiation Therapy for 925 Patients in King Chulalongkorn Memorial Hospital

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Background and Objective: *Three dimensional conformal radiation therapy (3D CRT) and intensity-modulated radiation therapy (IMRT) have been implemented at Department of Therapeutic Radiation and Oncology, King Chulalongkorn Memorial Hospital (KCMH) since July 2005. This is the first study in Thailand to evaluate the pattern of care and utilization of 3D CRT and IMRT for treatment in each individual cancer.*
Material and Method: *Between July 2005 and July 2007, 925 newly diagnosed cancer patients underwent IMRT or 3D CRT at KCMH. The authors retrospectively reviewed the experience and utilization of 3D CRT and IMRT for each disease site and region.*
Results: *There were 471 males and 454 females. There were 332 patients (35.9%) treated with IMRT. Among the 332 IMRT patients, there were 100, 32 and 27 nasopharyngeal, lung and prostate cancers, respectively. On the contrary, 593 patients (64.1%) were treated with 3D CRT. Among these, breast, cervix and lung cancers were the most common diseases. Except for head and neck as well as genitourinary cancer, 3D CRT was still the main technique used in more than 60% of the patients at KCMH.*
Conclusion: *3D CRT and IMRT have been successfully implemented at KCMH for 2 years. Three dimensional conformal radiation therapy was still the main technique used in more than 60% of the patients at KCMH. Prospective studies evaluating tumor control and treatment sequelae are expected*

Keywords: *Intensity-modulated radiation therapy (IMRT), Thailand*

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Radiation therapy(RT) has a long history in the multidisciplinary treatment of malignancies. Traditional radiation treatment technique uses fluoroscopy-based images (or 2-dimensional images) for planning of radiation therapy portal, so-called 2-dimensional radiation therapy (2D RT). Radiation field aperture and angle are defined based on the correlation of tumors and bony structures seen on 2D radiograph. A typical 2D RT practice delivers tumoricidal radiation dose (60-70 Gy) to anatomical structures at risk of tumor invasion by two or more radiation therapy fields, with appropriate shielding for protecting the vital surrounding organs. Although effective, 2D RT has a number of limitations. Conventional 2D RT results in the treatment of large

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volumes of normal tissues, exposing patients to numerous treatment-related toxicities. Moreover, some patients remain at increased risk of recurrence and may benefit from a higher dose which is impossible for some regions surrounded by sensitive organs such as parotid gland, bladder or rectum.

Over the last 20 years, much progress has been made in improving the therapeutic index of radiation therapy by using computerized tomography (CT) images or magnetic resonance images (MRI) for planning of radiation portal, the so-called 3-dimensional conformal radiation therapy (3D CRT), to avoid radiation dose to non-targeted structures and minimize errors arising from poor visualization of tumor boundaries[1,2]. Based on 3D images, radiation oncologists decide the radiation beam configuration (beam energy, beam aperture, gantry angle, wedge and weighting factors) in the computer. This process is called "virtual simulation". The aims of the treatment were to maximize target coverage as well as minimize normal tissue dose. Furthermore, 3D CRT allows for spatial inaccuracies introduced by set-up errors and movement of the patient or internal organs, through the addition of safety margins to the tumor target and adjacent organs in accordance to the 'ICRU 50 & 62' recommendations[3,4]. Three-dimensional conformal radiation therapy also utilizes a more accurate dosimetric computing algorithm such as the Monte Carlo method, which caters for tissue heterogeneity better than 2D computing algorithm. There are some limitations of 3D CRT planning since it needs an experienced planner. The planners manually adjust beam directions, beam shapes and beam intensities on the basis of their planning experience and "trial and error" to meet the optimal dose distribution. This process is called "forward planning" which works well for tumors with simple shapes. For complex tumor geometries, such as concave tumors and tumors surrounded by sensitive structures, i.e. rectum or bladder which is adjacent to the cervix, the forward planning method may be limited by the experience of the individual planner and the restricted beam intensity variation inside each beam.

Intensity-modulated radiation therapy (IMRT), an advanced form of 3D CRT, does provide the ability to highly conform the prescription dose to the shape of the target tissues and may decrease the risk of RT-related sequelae by limiting the dose delivered to the surrounding normal tissues. Unlike 3D CRT, IMRT usually involves inverse planning, whereby dose volume constraints for targets and normal tissues are defined a priori, then optimized with the use of a computer algorithm, and this advantage is currently being exploited to escalate tumor dose[5]. Recently, increasing attention in the literatures has focused on IMRT. Numerous studies demonstrated the potential benefits of IMRT planning in many tumor sites, including head and neck cancer[6-10], brain tumors[11-15], breast cancer[16-22], lung carcinoma[23-28], gastrointestinal tumors[29-32], prostate carcinoma[33-37] and gynecologic tumors[38-41]. Although most studies had limited follow-up, many reports have suggested that IMRT results in less treatment sequelae[42-49] and improved tumor control[50-53].

Since KCMH is a medical school and there are post-graduate training programs for master degree students and residency training, it would be better to provide adequate examples and to ensure that our trainees will have considerable experience in this new standard of care. The objective of this review was to report the experience and utilization of these advanced techniques in the beginning period at Department of Therapeutic Radiation and Oncology, King Chulalongkorn Memorial hospital (KCMH).

Material and Method

Patient databases were used to retrospectively identify all patients underwent IMRT or 3D CRT at KCMH between July 2005 and July 2007. Diagnosis and disease site were reviewed, along with technique of radiation therapy for each patient.

Results

There were 471 males and 454 females. Breast, nasopharyngeal and lung cancers comprised the most common cancers in the present study. Of the 925 patients, 332 (35.9%) were treated with IMRT. Among these 332 IMRT patients, there were 100, 32 and 27 nasopharyngeal, lung and prostate cancers, respectively (Table 1). These were the top three cancers using IMRT. While the most common regions treated with IMRT were head and neck, central nervous system and lung (Table 1). The regions that have high proportion of using IMRT compared to 3D CRT were head and neck, genitourinary and lung (Fig. 1).

On the contrary, 593 patients (64.1%) were treated with 3D CRT. Among these, breast, cervix and lung cancers were the most common cancers. Breast, central nervous system and gastrointestinal tract were the most common regions treated with 3D CRT (Table 2). Except for head and neck as well as genitourinary cancers, 3D IMRT was still the main technique used in more than 60% of the patients.

Table 1. The top ten diseases treated with 3D conformal radiation therapy (3D CRT) and intensity-modulated radiation therapy (IMRT)

Disease	3D CRT n	IMRT n	Total n
Ca nasopharynx	20	100	120
Ca lung	47	32	79
Ca prostate	3	27	30
Ca breast	102	21	123
Ca esophagus	16	16	32
Glioblastoma	15	12	27
Ca tongue	5	10	15
Ca maxillary sinus	4	10	14
Meningioma	6	9	15
Astrocytoma	9	5	14
Total	227	242	469

Table 2. Number of patients treated with 3D CRT and IMRT classified by region of disease

Regions	3D CRT n	IMRT n	Total n
Head and neck	79	155	234
Central nervous system	96	37	133
Lung	47	32	79
Gastrointestinal	96	30	126
Genitourinary	16	29	45
Breast	102	21	123
Gynecology	79	6	85
Sarcoma	18	6	24
Hematology	36	5	41
Miscellaneous	24	11	35
Total	593	332	925

Physicians began using IMRT after the third quarter of the year 2005 (Fig. 2). The proportions of IMRT to 3D CRT usage varied between 33.3 and 44.2% over the 2-year period. No increasing trend of using IMRT was observed. However, the number of patients treated with either technique significantly increased in the first quarter of the year 2007 because of the opening of an evening clinic to cope with the increasing number of the patients in December, 2006. Numbers of nasopharyngeal, lung and prostate cancer patients treated with IMRT and 3D CRT over the treatment period are illustrated in Fig. 3, 4 and 5, respectively.

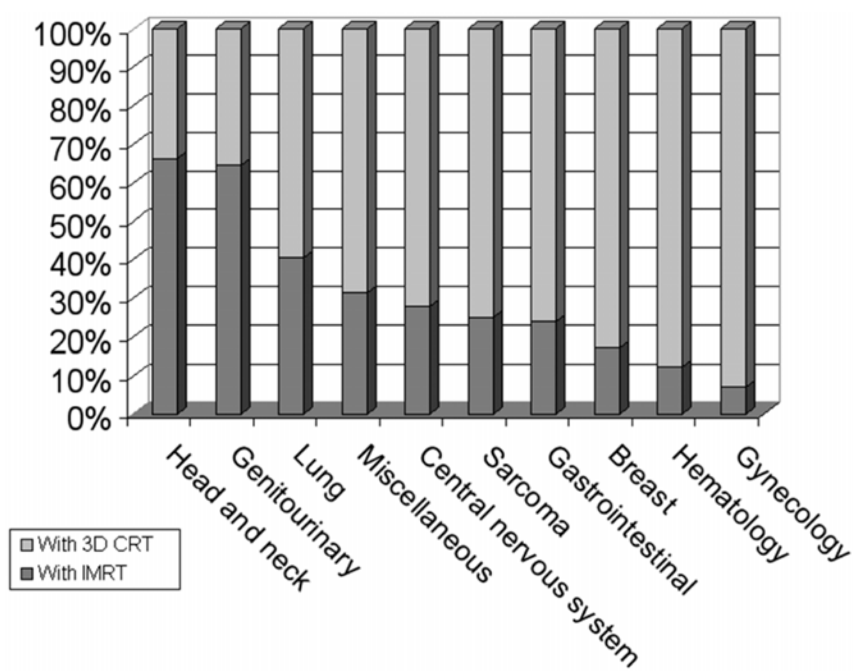

Fig. 1 Proportions of IMRT to 3DCRT usage in each region

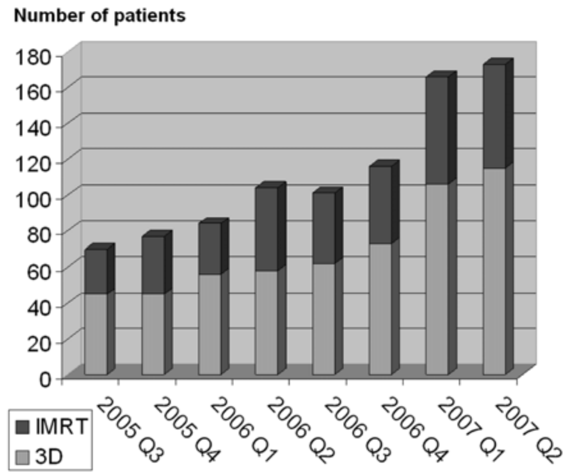

Fig. 2 Number of patients treated with IMRT and 3D CRT illustrated by period of time

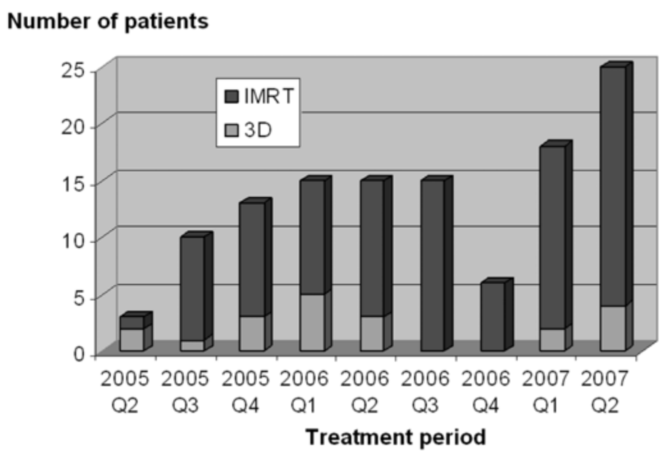

Fig. 3 Number of nasopharyngeal cancer patients treated with IMRT and 3D CRT illustrated by treatment period

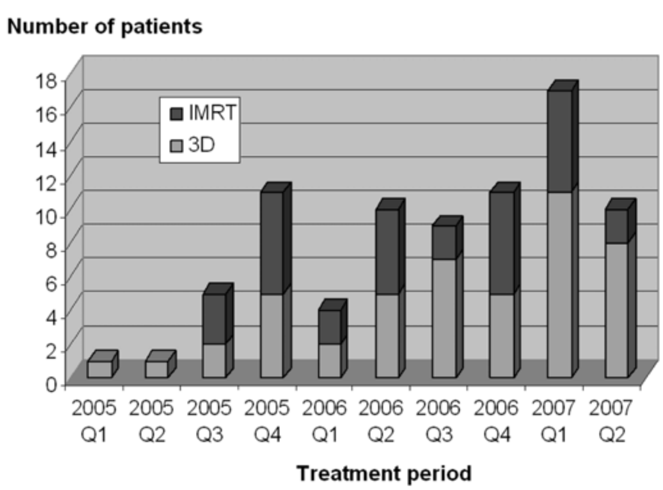

Fig. 4 Number of lung cancer patients treated with IMRT and 3D CRT illustrated by treatment period

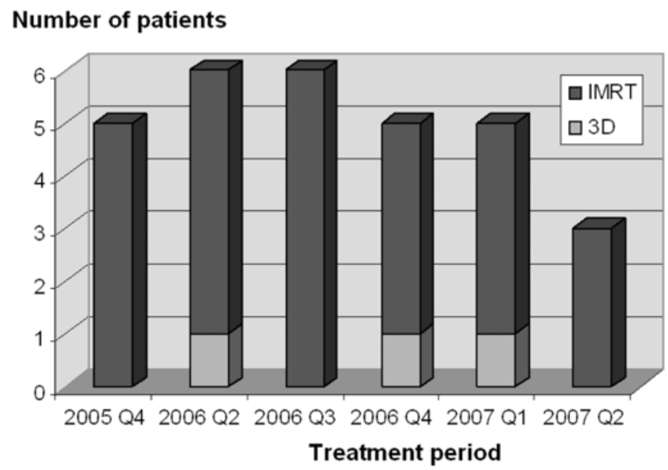

Fig. 5 Number of prostate cancer patients treated with IMRT and 3D CRT illustrated by treatment period

Discussion

IMRT is an advanced form of 3D CRT. It represents one of the most important technical advances in radiation therapy since the advent of the medical linear accelerator and is be coming increasingly common in both academic and private practices. Although there are only a few centers in Thailand implementing IMRT, nearly all centers not currently using IMRT have decided to adopt it in the near future depending on their budget and resources. To the authors' knowledge, the current study represents the first pattern of care study regarding IMRT use in Thailand and provides valuable insight into the changing field of radiation oncology.

IMRT has been implemented at KCMH since July 2005 following the USA for at least 5 years(54). The present results revealed approximately one-third of the patients treated with IMRT compared to 3DCRT. While IMRT users in the USA stated that they treated less than 25% of their current patients with IMRT(55).

The implementation of IMRT, at least initially, is a time-consuming endeavor, particularly with regard to commissioning and quality assurance procedures. Moreover, IMRT requires additional time demands on both physicians and physicists compared with conventional treatment. At KCMH, the authors decided to implement IMRT from the year 2002. We followed the multiple steps proposed by Galvin as demonstrated in Table 3(56). A junior attending physician was selected as a core leader to learn the principle and process of IMRT, together with gaining a clinical experience of IMRT abroad. Medical physicists and radiation therapists

Table 3. Intensity-modulated radiation therapy program implementation

Identify team leader and core team
Define program scope and goals
Evaluate staff needed
Identify space and necessary equipment
Develop a budget and purchase equipment
Perform acceptance testing and commissioning
Develop written policies and procedures
Train personnel
Develop and implement quality assurance program
Develop marketing and educational materials

Table 4. Personnel and equipments in our department

Radiation oncologists	5
Medical physicists	6
Radiation therapists	17
Nurses	5
Administrators	6
CT simulators	1
Conventional simulators	1
Linear accelerators	3
Cobalts machine	2
Treatment planning work stations	2
QA equipments	
Beam data scanner	2
Absolute dosimetry system	3
In vivo dosimetry system	1
IMRT film dosimetry	1
Diode array	1

were also appointed as a leading team to learn their individual responsibilities involving IMRT. Once the core team members had educated themselves, it was their responsibility to educate their colleagues. Table 4 summarizes the number of personnel and radiation therapy equipments at KCMH.

Given the large number of IMRT applications and studies, it is impossible for any individual person to stay abreast of the use of IMRT in every disease site. One of the first decisions is to define the scope of the IMRT program. The authors started IMRT in some common diseases such as head and neck cancer, especially nasopharyngeal and lung cancer (as noted in Fig. 3 and 4) and once experience was gained the authors moved forward to other diseases. It is not prudent to simply plan to switch to IMRT for all new patients at the first place. Initially, ten to fifteen patients were treated with IMRT per day per machine. After an IMRT learning curve exists for all members of the team, the authors gradually increased the number of patients in each machine as confirmed in Fig. 2. The percentage of IMRT and 3D CRT cases is a function of the diseases treated and the experience of the staff.

All of staff already have gained considerable clinical experiences with this technology. Moreover, their experiences span a wide spectrum of disease sites. Although most of staff currently use IMRT to treat a small percentage of patients, the number of patients treated with IMRT is likely to rise substantially in the near future as illustrated in Fig. 2. By far, the most common diseases treated with IMRT were nasopharyngeal, lung and prostate cancers, most likely reflecting the ample clinical experience in these diseases[6,7,23-28,37,44-45,49,50,53,57-59]. IMRT was more commonly used among head and neck, central nervous system and lung regions. The most common reasons for adopting IMRT in these regions are the improvements of the dose distribution as well as avoidance of toxicity to parotid glands, brainstem, spinal cord and contralateral lung. This is quite similar to the survey conducted in USA which showed the most common regions treated with IMRT were head and neck, genitourinary and central nervous system tumors[55]. Furthermore, Schomas evaluated the content and quality of information regarding intensity-modulated radiotherapy (IMRT) on the internet and found that prostate carcinoma and head and neck tumors were highlighted as diseases treated with IMRT, thus confirmed the public awareness of this novel treatment[60].

The authors have many dose-volume-constraint protocols for each disease site and most of the protocols still use conventional dose (i.e 70 Gy for gross tumor volume). This is in contrast to the majority of IMRT users in USA who used IMRT to deliver higher than conventional doses, predominantly in patients with genitourinary malignancies and head and neck tumors[55]. The preference to dose escalate is a cause for concern; because dose escalation, per se, remains experimental. However, promising results with higher than conventional doses have been reported recently in prostate carcinoma[53,61] and prompted staff to treat prostate cancer to at least 76 Gy.

IMRT was rarely used in gynecological and hematological cancer. One might have expected more adoption of IMRT among these types of cancer when there are growing evidences showing that IMRT yield better local control and less toxicity[38-41].

Since there were more than 900 cases treated with 3D CRT and IMRT at KCMH over 2 years, this ensured that radiation oncology residents and medical physics students were taught the principles of this technology and were trained to use 3D CRT and IMRT with adequate examples. Each resident has hands-on IMRT training and treated more than 30 patients. They have been involved in all aspects of the IMRT process, particularly target and tissue delineation as well as plan evaluation. While medical physics students are responsible for treatment planning and quality assurance.

The present study had several limitations. Aspects of IMRT use, such as the quality of plans, rational for selecting patient treated with IMRT, target delineation, treatment delivery, and quality assurance, were beyond the scope of the current study.

In conclusion, 3D CRT and IMRT have been successfully implemented at KCMH for 2 years. Prospective studies evaluating tumor control and treatment sequelae, with careful follow-up to monitor long-term risks and benefits, are expected as more patients are treated with IMRT.

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ประสบการณ์ 2 ปีของโรงพยาบาลจุฬาลงกรณ์ในการรักษาผู้ป่วย 925 รายด้วยการฉายรังสีแบบ 3 มิติ และแบบปรับความเข้ม

ชวลิต เลิศบุษยานุกูล, กาญจนา โชติเลอศักดิ์, ชลเกียรติ ขอประเสริฐ, ทวีป แสงแห่งธรรม, สรจรส อุณห์ศิริ, อิศรา อิศรางกูร ณ อยุธยา, โชติกา จำปาเงิน, ศิวลี สุริยาปี, ประยุทธ์ โรจน์พรประดิษฐ์

วัตถุประสงค์: *โรงพยาบาลจุฬาลงกรณ์เริ่มนำการฉายรังสีแบบ 3 มิติ และแบบปรับความเข้มมาใช้ตั้งแต่เดือน กรกฎาคม พ.ศ. 2548 รายงานนี้เป็นการศึกษาแรกในประเทศไทยที่ประเมินรูปแบบของการใช้เทคนิคการฉายรังสีแบบ 3 มิติ และแบบปรับความเข้มในมะเร็งแต่ละชนิด*

วัสดุและวิธีการ: *ทำการศึกษาผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็นโรคมะเร็งและได้รับการรักษาด้วยการฉายรังสีแบบ 3 มิติ และแบบปรับความเข้มที่โรงพยาบาลจุฬาลงกรณ์ระหว่างเดือน กรกฎาคม 2548-กรกฎาคม พ.ศ.2550 โดยศึกษาเทคนิคการรักษาในโรคมะเร็งบริเวณต่าง ๆ*

ผลการศึกษา: *มีผู้ป่วยชาย 471 ราย และ หญิง 454 ราย ผู้ป่วย 332 รายได้รับการฉายรังสีแบบปรับความเข้ม คิดเป็นสัดส่วนร้อยละ 35.9 ของผู้ป่วยทั้งหมดในการศึกษา ในจำนวนนี้มีผู้ป่วยมะเร็งหลังโพรงจมูก 100 ราย มะเร็งปอด 32 ราย และมะเร็งต่อมลูกหมาก 27 ราย นอกจากนี้ผู้ป่วย 593 รายได้รับการรักษาด้วยการฉายรังสีแบบ 3 มิติ คิดเป็นร้อยละ 64.1 โดยโรคที่พบบ่อยคือ มะเร็งเต้านม มะเร็งปากมดลูก และมะเร็งปอด โดยเฉลี่ยผู้ป่วยที่มารับการรักษาด้วยการฉายรังสีในโรงพยาบาลจุฬาลงกรณ์จะได้รับการฉายรังสีแบบ 3 มิติมากกว่าร้อยละ 60 ยกเว้นมะเร็งศีรษะและลำคอ และมะเร็งทางเดินปัสสาวะซึ่งได้รับการฉายรังสีแบบปรับความเข้มในสัดส่วนมากกว่าการฉายรังสีแบบ 3 มิติ*

สรุป: *ในระยะ 2 ปีที่ผ่านมาโรงพยาบาลจุฬาลงกรณ์ประสบความสำเร็จในการเริ่มใช้การฉายรังสีแบบ 3 มิติ และแบบปรับความเข้ม การฉายรังสีแบบ 3 มิติยังคงเป็นเทคนิคการฉายรังสีที่แพทย์รังสีรักษาในโรงพยาบาลเลือกใช้ในผู้ป่วยมากกว่าร้อยละ 60 และในอนาคตจะมีการรายงานผลการรักษาต่อไป*