表3　対象例の唾液腺線量

項目		中央値（幅）
耳下腺容積（cc）	左	27.7（12.4～59.3）
	右	28.2（14.6～50.1）
	全体	27.7（12.4～59.3）
平均線量（Gy）	左	29（11.7～44）
	右	29.1（5.8～53.4）
	全体	29.1（5.8～53.4）
中央値線量（Gy）	左	20.5（9.6～41.2）
	右	21.6（0.5～50.4）
	全体	21.5（0.5～50.4）
20Gy以下の容積（cc）		22.1（0.6～50.2）

表4　唾液腺シンチの駆出率による唾液腺機能評価

検査時期（患者数）	駆出率（%）
治療前（19）	左　56.9
	右　54.1
治療後3カ月（36）	左　26.5
	右　27.3
治療後1年（41）	左　42.6
	右　47

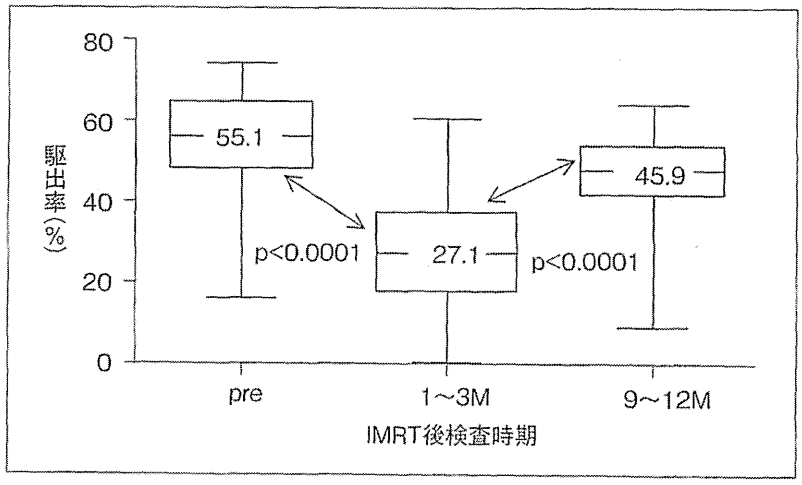

図2　唾液腺シンチ駆出率の治療後推移

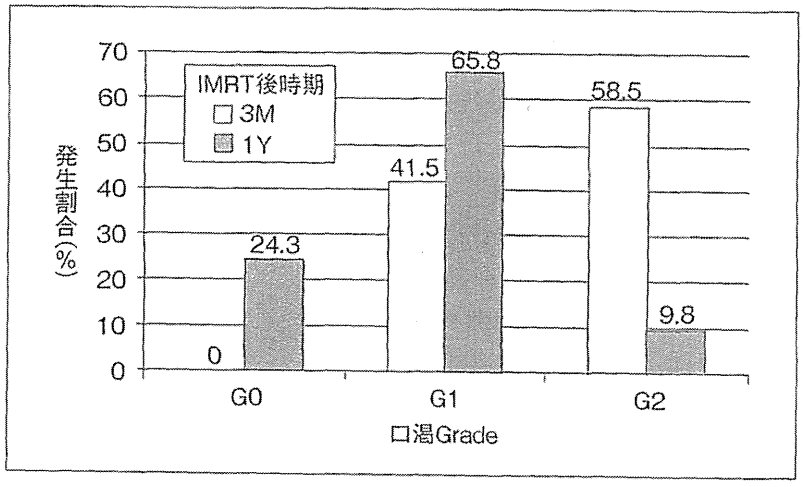

図3　IMRT治療後の口渇の発症頻度

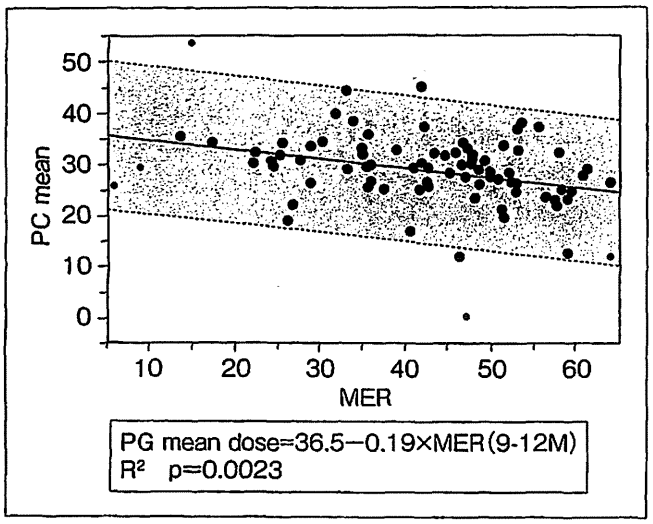

図4 治療後1年時の唾液腺平均線量と駆出率との相関関係

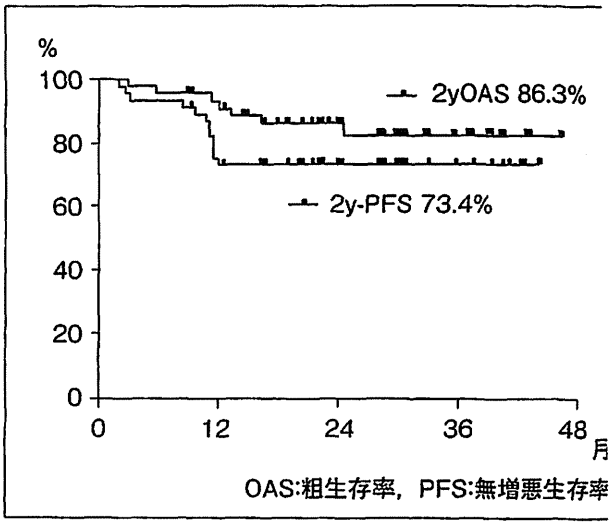

図5 上咽頭癌IMRT症例の治療成績

り（$p < 0.05$），1年時点の口渇症状がないG0の割合も全体の約4分の1を占めていた。1年時点でのCTCAEの口渇グレードがG0（n = 10），G1（n = 27），G2（n = 4）のグループにおける1年時のMER値（左/右）はそれぞれ，43.4/45.8，42/43.5，30/32という結果だった。G0とG2のMER値の差には有意傾向が観察された（$p = 0.08$）。またG0，G1，G2耳下腺容積はそれぞれ19cc，23cc，22ccだったが，各群の数値の平均には統計学的有意差は無かった。

次に耳下腺平均線量と治療後1年時点のMERの相関を検討したところ，相関係数−0.19で有意に負の相関（$p = 0.002$）を観察した（図4）。同様の関係は唾液腺中央値線量との関係でも認められ，相関計数−0.17で有意な負の相関関係を観察した（$p = 0.007$）。

3）上咽頭癌へのIMRTの治療成績

当院の頭頸部癌IMRTの治療成績の有効性を評価する目的で，当院の上咽頭癌へのIMRTの治療成績を検討した。2006年6月〜2009年4月に未治療の上咽頭癌に対して，根治治療目的でIMRTを行いかつ治療後1年以上経過観察が可能であった48例を解析した。併用化学療法のプロトコールは2008年12月までは5FUおよびNedaplatinによる交替療法3コースを併用し，2009年1月からはIntergroup 0099方式と同様にCisplatin 3コースの同時併用後，5FU + Cisplatinの2〜3コースのadjuvant chemotherapyを追加した。放射線投与法に関しては前述の方法により行った。

解析したグループの対象年齢は中央値55歳（1〜83），男性37例・女性11例で，臨床病期はII III：IV = 11：20：17という内訳だった。化学療法は45例に併用し，3例は放射線単独治療が行われた。WHOの病理組織分類のtype Iは12例（25%）type II-IIIは35例（73%），のこり1例は組織型判別不能であった。予後調査の解析時点で観察期間中央値は28.6カ月（9.4〜46.5カ月），無病生存は35例，担癌生存は5例，原病死が8例の内訳だった。図5に対象群の粗生存率および無増悪生存率曲線を示す。2年粗生存率は86.3%，無増悪生存率は73.4%という結果であった。単変量解析による予後因子解析では，T4はT1-3に対し有意に生存率が悪い結果であった（2y-OAS94.4% vs 55.6%；$p = 0.01$）。またWHO type Iのグループはtype II-IIIに比して有意に生存率が悪い結果を認めた（2y-OAS96.9% vs 57.1%；$p = 0.002$）。また，臨床病期毎の2年粗生存率はI-II期，III期，IV期で100%：89.7%，71.8%という結果だった。本グループにおける治療後1年時点のG2の口渇の発生割合は19.4%であった。

④ 考　察

頭頸部癌のNCCNガイドラインに基づく推奨によると，IMRT適応は上咽頭癌，中咽頭癌，鼻腔・副鼻腔癌とされている。これらの疾患では治療の対象領域（標的体積）が唾液腺，脳実質，脳幹部，脳神経，脊髄，下顎骨などの正常臓器に近接しているため通常法では線量制限を守りながら標的体積に十分と思われる線量を投与することが困難である。このような症例においてはIMRTの適応により十分な標的体積の線量集中性を保ちながら，正常臓器への線量低減を実現できるため，唾液腺機能温存に代表される治療後の有害事象軽減を実現可能な症例が増加する。そのため頭頸部癌へのIMRT適応は放射線治療後のQOL改善の点において極めて有益になると考えられる。実際に上咽頭，中咽頭癌に対し幾つかのランダム化試験の結果をもとにIMRTによる唾液腺機能改善が高いエビデンスを持って証明されている[5) 6)]。

当院ではIMRT専用機であるトモセラピーを治療装置として用いている。トモセラピーはヘリカル操作式のスライスビームを用いたユニークな方式のIMRT治療専用機である[7)]。また内蔵する同座標軸系を有する装置で効率よいIGRT運用が可能である[8)]。その他のトモセラピーの特徴として広い照射可能域を有しており，全骨髄照射による全身照射，つなぎ目のない全脳前脊髄照射などが行える利点がある。治療方式は51方向からのビームを用いバイナリーマルチリーフコリメータを介してビーム強度変調を行うというユニークな方式により複雑な形状のPTVにも高い線量集中性を達成でき，特に頭頸部癌ではリニアックIMRTに比較して線量分布の点で優るとの報告を複数認める[9) 10)]。またIMRTの実地臨床での運用に関し大きな制約になる物理検証も標準装備システムを用い省力化が可能となっている。

当院自験例では，前立腺，脳腫瘍にくらべ計画に時間を要する頭頸部癌の計画でも7～10日程度で準備を終え治療開始している。通常の施設では治療計画から治療開始までに2～3週程度を要する場合も少なくないため，より実用的な運用が行えている。

今回の我々の検討では多くの報告結果と同様にIMRT治療後の耳下腺機能の治療後経過に関し，主観的な口渇のグレードおよび唾液腺シンチグラフィによる定量的評価のいずれも1年時点の評価が治療後3カ月に比し顕著な改善を示していた。また治療後1年時点でのCTCAE G2の口渇頻度は9.8%で，臨床的に症状がほとんどないG0の割合も24.3%に観察された。この結果は通常の三次元治療で唾液腺温存が行えない場合の有害事象割合に比べ良好な結果であり，我々のIMRT初期経験では治療の特徴である唾液腺機能温存に関し目標レベルに到達していたと考える。また唾液腺シンチグラフィは自覚的な症状との関連を明確に認め，臨床的指標として有用と考えられた。

次に唾液腺シンチのMERと治療計画の耳下腺投与線量の解析を行ったが，唾液腺の平均および中央値線量は，治療後1年で測定したMER値との関係に有意な負の相関を認めた。耳下腺線量の増加は治療後1年時の，唾液腺機能と逆相関を示す結果で，得られた結果は臨床的に妥当と考えられた。またCTCAEのgrade毎のMER値の検討には，有意差は観察できなかったが中等度の口渇症状を示すG2では他のグループに比較しMERが低い傾向にあった。

代表的対象疾患である上咽頭癌に対するIMRTの治療成績でも高い有効性が示され従来法に遜色ない結果で，加えて有害事象の軽減効果も確認できIMRTの高い臨床的有用性が証明された。

今回我々は唾液腺シンチグラフィを用いて唾液腺機能の定量的な評価を試み，一定の成果を得たが，この検査法は唾液腺への被曝があること，費用的負担が大きい点などの欠点がある。現在我々はMRI撮影時にEquivalent cross-relaxation rate（ECR）imaging法を用いた耳下腺組織の評価法を調査中であり，初期経験では唾液腺シンチグラフィのMER値とECR値との良好な相関関係を確認している。本検査手技が確立すれば，通常の治療後の経過観察時に唾液腺機能の評価を低侵襲かつ簡易に実施でき，大変有望な手法となると考えている。

■ おわりに

当院におけるトモセラピーを用いた頭頸部癌のIMRTにおいて治療効果および治療後QOL改善の点で，その高い臨床的有用性が示された。今回評

価に用いた唾液腺シンチグラフィは唾液腺機能の評価に確立された有用な検査法の一つと考えられたが，今後より低侵襲で簡便な評価方法の開発が期待される。

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Summary

Clinical evaluation of parotid function of head and neck cancer patients treated with IMRT

We presented our preliminary results of initial experience by Helical TomoTherapy held at the 23rd annual meeting of JASTRO on October 2010. In this analysis, 82 parotid glands from 41 patients, who were treated with definitive IMRT combined with or without systemic chemotherapy, were assessed for the correlation of radiation dose with parotid function evaluated by salivary scintigraphy. Acquired results of salivary scintigraphy are well correlated with grade of xerostomia after IMRT. Initial experience of IMRT in our institute for head and neck cancer is thought to be promising at the viewpoint of both clinical efficacy and less toxicity.

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Regular Paper

Preliminary Results of Magnetic Resonance Imaging-aided High-dose-rate Interstitial Brachytherapy for Recurrent Uterine Carcinoma after Curative Surgery

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Recurrent uterine carcinoma/Magnetic resonance imaging (MRI)/Image-based brachytherapy/High-dose-rate brachytherapy.

This report presents initial experience with imaging-aided high-dose-rate interstitial brachytherapy (HDR-ISBT) for post-operative recurrence of uterine carcinoma. Fourteen patients presenting with post-operative recurrence of uterine carcinoma (nine cervix and five corpus) between July 2005 and October 2008 were enrolled in this study (median follow-up: 37 months, range: 6–59 months). We implanted magnetic resonance imaging (MRI)-compatible plastic applicators using our own ambulatory technique. HDR-ISBT treatment consisted of twice-a-day irradiation of 6 Gy each with at least a six-hour interval to provide the total prescribed dose. Treatment was based on treatment planning-computed tomography with MRI as a reference. Seven patients were treated with a combination of ISBT (median 30 Gy/5 fractions; range: 27–33 Gy) and external beam radiation therapy (EBRT), and the other seven with brachytherapy only (median 54 Gy/9 fractions; range: 48–54 Gy), one of whom had previously received pelvic EBRT. The three-year estimates of local control and overall survival rates were 77.9% (95% confidence interval (CI): 55.8–100%) and 77.1% (95% CI: 54.2–100%), respectively. Two patients, who had received combined treatment with EBRT showed untoward reactions, including a grade 3 subileus and grade 2 constipation. Another patient, who had been treated with ISBT alone, developed grade 2 urinary constriction. Our imaging-aided HDR-ISBT for post-operative recurrence of uterine carcinoma was found to be practical with promising preliminary results.

INTRODUCTION

Interstitial brachytherapy (ISBT) is a valuable treatment method for gynecological cancer. In cases of previously untreated uterine cervical carcinoma, the American Brachytherapy Society recommends that ISBT be used for problem situations such as bulky lesion, narrow vagina, inability to enter the cervical os, extension to the lateral parametrium or pelvic side wall, and lower vaginal extension.[1)] Moreover, several clinical studies have reported good local control results using low-dose-rate (LDR) or high-dose-rate (HDR) ISBT.[2–6)] Locally recurrent uterine carcinoma is also a good candidate for ISBT.[4,7)] Interstitial implantation is an effective approach for massive vaginal or parametrial tumor lesions when an intrauterine applicator for operative recurrence cannot be used, and several favorable results have been reported. Weitmann *et al.* reviewed the results from six institutes and found local control rates of 29–100% and overall survival rates of 56–63%.[8)]

Image guidance has potential to improve treatment results because the post-operative recurrent tumor is often large and its complex shape makes it difficult to achieve a satisfactory implant with non-image guidance. For applicator implantation, the applicability of ultrasonography (US),[9,10)] computed tomography (CT),[11–13)] and magnetic resonance imaging (MRI)[14)] has been investigated.

For our patients, we introduced our transrectal ultrasonography (TRUS) guided implantation and MRI-assisted CT treatment planning combined with our previously reported

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novel ambulatory implantation technique for prostate cancer.[15] We used flexible applicators with our own removable template so that patients could walk during the treatment. As a result, no metallic treatment items were used for our patients so that they could receive MRI examination. We have also suggested this method for previously untreated uterine cervical carcinoma.[16] Free-hand implantation without a template was used because it is easier to implant into a parametrial extension without pubic arch interference. Imaging modality guidance proved to be very useful for effective free-hand implantation. We report here preliminary results obtained with our imaging-aided ISBT technique for post-operative locally recurrent uterine carcinoma.

MATERIALS AND METHODS

Patient characteristics

All 14 patients enrolled in this trial underwent hysterectomy between January 2003 and September 2006 at the time of initial diagnosis of uterine carcinoma, and subsequently experienced vaginal recurrence. These patients (median age: 54.5 years; range: 27–82 years) were treated between July 2005 and October 2008. The primary site of nine patients was the uterine cervix, and that of the other five was the uterine corpus. Tumor size was determined by means of pelvic examination and transrectal ultrasonography (median: 2.7 cm; range: 1–8 cm). Superficial disease cases that could be cured with intracavitary brachytherapy were excluded from this study. In addition, patients with distant metastases were considered ineligible. Histologic findings showed three squamous cell carcinomas, nine adenocarcinomas (including all uterine corpus carcinomas), and two adenosquamous carcinomas. All patients underwent hysterectomy as initial treatment, 11 patients were treated with bilateral salpingo-oophorectomy (BSO) and 10 patients with pelvic lymph node dissection (PLND). One patient received postoperative pelvic irradiation (50 Gy). Table 1 summarizes patient characteristics in this study.

Table 1. Patient Characteristics

Age (y)		
Median (range)	54.5	(27–82)
Follow-up period (mo)		
Median (range)	37	(6–59)
Primary origin (no. of patients)		
Cervix	9	
Corpus	5	
Histology (no. of patients)		
SCC	3	
Ad	9	
AdSq	2	
Modality (no. of patients)		
ISBT+EBRT	7	
ISBT alone	6	
ISBT alone (previously irradiated)	1	
Tumor size (cm)		
Median (range)	2.7	(1–8)
Nodal metastasis (no. of patients)		
N0	13	
N1	1	
Whole pelvic EBRT (Gy)		
Median (range)	30	(20–30)
Center-shielded EBRT (Gy)		
	20	
ISBT (Gy)		
Median (range)	40.5	(27–54)

Abbreviations: EBRT, external beam radiotherapy; ISBT, interstitial brachytherapy; SCC, squamous cell carcinoma; Ad, adenocarcinoma; AdSq, adenosquamous carcinoma

EBRT

One patient had undergone postoperative pelvic EBRT, and she was treated with ISBT alone this time. Another patient 82 years of age was treated with ISBT alone due to advanced age (all 13 remaining patients in this study were 71 years of age or younger). Another patient with simultaneous local and nodal recurrence was treated with EBRT and ISBT. For the other 11 patients, indication of EBRT was determined according to whether the interval exceeded 12 months. Five patients with a longer interval (median: 31 months, range: 12–40 months) were treated with ISBT alone, while six with a shorter interval (median: seven months, range: 5–12 months) underwent combination therapy with EBRT and ISBT for pelvic control in view of the possibility of simultaneous subclinical nodal recurrence. The patients received EBRT to the whole pelvis with the median prescribed dose of 30 Gy (range, 20–30 Gy) or 2 Gy per fraction. In addition, they underwent center-shielded (CS) EBRT (20 Gy) with 2 Gy per fraction. Neither additional boost irradiation nor expansive irradiation of para-aortic lymph nodes was performed. ISBT was performed after whole pelvic EBRT and before CS EBRT. In principle, the midline block of CS EBRT was decided depending on the ISBT treatment volume. No patient received chemotherapy.

Applicator implantation

We performed multifractionated HDR irradiations with a single implant session for all patients. Implantation was per-

formed in the operating room with lumbar anesthesia and continuous epidural anesthesia. The implantation was monitored with the aid of TRUS (Aloka, Tokyo, Japan) and flexible needles (ProGuide Sharp Needle; Nucletron, Veenendaal, The Netherlands) were used for all patients. First, a single flexible needle applicator (anchor needle) was inserted through the center of the vaginal stump. A button stopper was then affixed to the anchor needle and placed in contact with the stump. After implantation of the anchor needle, a silicon cylinder was inserted into the vagina. This cylinder is custom-made from silicon rubber with the size depending on the patient's vaginal size and it has five implant holes, with the center hole used for the anchor needle. The concept of ambulatory technique has been described in detail elsewhere.[15] Briefly, the anchor needle and cylinder complex was sutured to the uterine cervix with silk thread. After inserting the cylinder, we attached a custom-made vinyl template to the patient's perineum. This template has holes for flexible needle applicators. The positions of the holes for freehand implantation are determined by consulting preimplantation TRUS, CT, and MRI images. We implanted four cylinder-guided needles into the holes of both the cylinder and the vinyl template. Next, we implanted the other applicators by free-hand implantation using the holes other than the cylinder's holes. The objective of the implantation was to cover the clinical target volume (CTV) with TRUS guidance. After implantation was complete, we fixed all needles to the vinyl template and the perineum with silk thread affixed to a color bead-button complex. The color beads, but not the anchor needles, were then affixed to the applicator with an adhesive before implantation. This fixation of the bead-button complex determined the needle length, and the beads were color coded for identification of the needle length. Finally, the protruding connector end of the applicator was cut off (Fig. 1).

Treatment planning and treatment

All patients underwent CT and MRI immediately after implantation was finished for the purpose of treatment planning. MRI examinations included T2-weighted and T1-weighted axial images and T2-weighted sagittal images using a pelvic surface coil. Both CT and MRI images were obtained with 3-mm thick sections (Fig. 2(a), 2(b)).

For CT-based planning, MRI was used as a reference to outline the CTV and organs at risk (OAR: rectum, bladder, sigmoid colon, small intestine). Clinical examination findings and information from the marker seed, which was implanted at the edge of the CTV, were also used for delineation. All contours were drawn on CT images (CT-MRI fusion was not used). Applicator positions were easily defined on both CT and MRI, and helped contouring as landmarks. For CTV-based dose prescription, the PLATO planning system (software version 14.2; Nucletron) was used with manual modification to cover CTV by the 100% isodose line on every slice after computer optimization using a geometrical optimization algorithm.[17] We did not use any single reference point for dose prescription. We kept the doses to the OAR below the 100% prescribed dose except in cases where the OAR were adhering to or invaded by the tumor.

HDR-ISBT treatment consisted of twice-daily irradiation of 6 Gy each time, with at least a six-hour interval to provide the total prescribed dose. Seven patients were treated with a

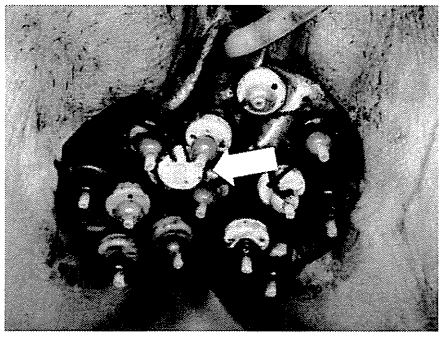

Fig. 1. The vinyl template-applicator was sutured to the perineum. The anchor needle was fixed with a button only (arrow), and the other needles were fixed with the button-bead complex.

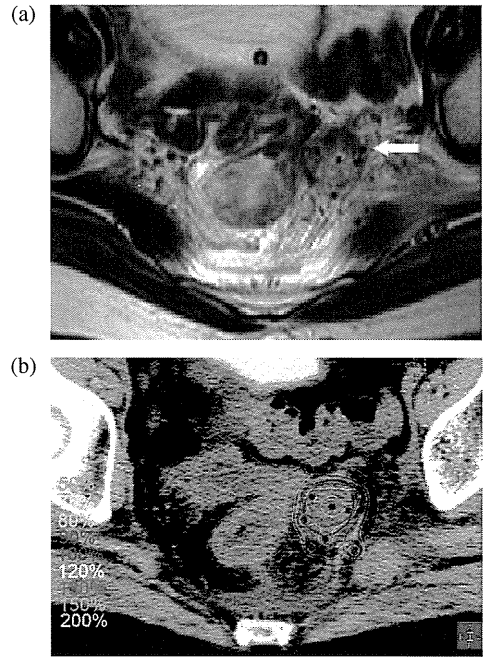

Fig. 2. (a) Magnetic resonance image of a patient obtained just after implantation. The flexible applicator is shown as a black dot (arrow). (b) Isodose curves on computed tomography image of the patient in Fig. 2(a). CTV is outlined with a thick red line based on the MRI image. CTV was almost covered by the 100% isodose line (thin red line).

combination of ISBT (median 30 Gy/5 fractions; range: 27–33 Gy) and external beam radiation therapy (EBRT). Brachytherapy only was used for six patients, five of whom received 54 Gy/9 fractions. The remaining patient was treated with 48 Gy/8 fractions because pelvic EBRT had previously been administered. We used the microSelectron-HDR (Nucletron) for treatment and 192Ir as the treatment source.

Follow-up and statistics

Toxicity was assessed according to the Common Terminology Criteria for Adverse Events version 3.0 (CTCAE-ver 3.0). As a rule, patients were monitored by means of monthly medical examinations both during and after treatment. All statistical calculations were performed with the aid of JMP8.0 statistical software (SAS Institute Japan Inc., Tokyo, Japan). We calculated local control, progression-free survival (PFS), and overall survival (OS) rates with the Kaplan-Meier method. Follow-up times for local control and survival were calculated from the start of radiotherapy (EBRT or BT).

RESULTS

The median follow-up for all patients was 37 months (range: 6–59 months). Three patients died of carcinoma and four cancer-bearing patients were alive at the time of writing. The three-year overall survival rate was 77.1% for all patients (95% confidence interval (CI): 54.2–100%) (Fig. 3).

Of the seven patients showing disease progression, three presented local failure (local only: one, local and distant: two), three developed distant metastasis only and one nodal and distant metastasis. The three-year progression-free survival rate was 50% (95% CI: 23.8–76.2%) for all patients, and the three-year local control rate was 77.9% (95% CI: 55.8–100%) (Fig. 4). The three patients who developed local recurrences had adenocarcinoma of the uterine cervix.

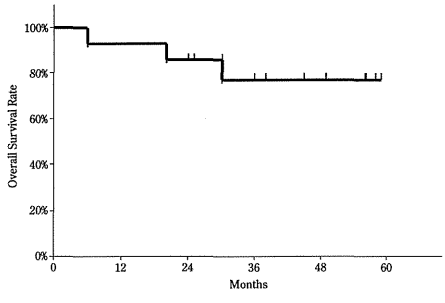

Fig. 3. Overall Survival.

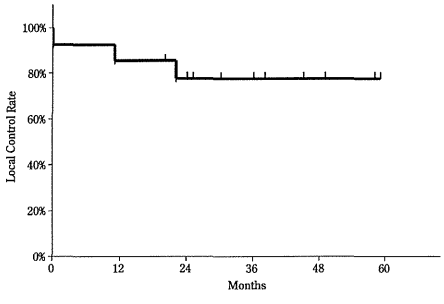

Fig. 4. Local Control.

One patient who developed local recurrence outside the initial CTV after one year of observation underwent another ISBT (48 Gy/8 fractions) as salvage therapy. However, local control could not be achieved.

Severe grade 3 adverse events developed in one patient treated with EBRT and ISBT. She experienced intestinal obstruction and needed total parenteral nutrition. Grade 2 adverse events were observed in two patients. One patient treated with a combination of EBRT and ISBT experienced neuroconstipation and neuralgia of the lower extremities. Another patient treated with ISBT alone developed urethral stricture and was treated with dilation.

DISCUSSION

Early-stage uterine carcinoma has a high cure rate for radical surgery. However, radical treatment becomes difficult if the tumor recurs locally because indication for salvage pelvic exenteration is limited.[18] EBRT with or without chemotherapy is a well-tolerated modality, but treatment outcome is not satisfactory.[19]

ISBT is an effective treatment option for locally-recurring uterine carcinoma after radical surgery. Charra *et al.* reported that 78 patients with upper-third vaginal recurrence attained five-year local control and overall survival rates of 70.4% and 56%, respectively.[7] In their study, LDR-ISBT with or without EBRT was used and eight of 78 patients (10.2%) showed grade 3 complication. Nag *et al.* reported their treatment results for 13 previously non-irradiated patients with isolated vaginal recurrences of endometrial carcinoma with a local control rate of 100%.[20] The cause-specific survival rate was 77% and two of the 13 patients (15%) showed grade 3–4 complications. Tewari *et al.* treated 30 vaginal recurrences of endometrial carcinoma and achieved a local control rate of 77%.[21] Five-year cause-specific survival rate was 65% and the severe complication rate was 17%. Jensen *et al.* treated 34 gynecological cancer patients (22 pelvic recurrences and 12 primary locally advanced diseases) for a local control rate of 53% and a 2-year survival rate of 63%.[22] Five of the 34 patients (15%) incurred acute major complications and 17 (50%) chronic complication. To summarize the above-mentioned reports, local control rates ranged from 53 to 100% and severe complication rates from 10.2 to 50% at 2–8 years. The authors emphasize that they used a template on implantation but they did not utilize an imaging modality. CT might have been used only for treatment planning but never for implantation

guidance.

On the other hand, image-guided implantation has been adopted in some other studies as follows. Eisbruch *et al.* visualized tumor and template by using preplanning CT to determine implant position and distance by "cylinder's eye view".[11] Twenty gynecological cancer patients including six recurrent cancer patients were treated in this manner. Local control rate was 55% and the slight to moderate late complication rate was 10%. Sharma *et al.* used implantation guided by TRUS monitoring, which enabled them to prevent accidental entry of the applicator into OAR.[23] The 25 uterine cervical cancer patients they treated included nine recurrent patients and the local control rate was 64% (56% for the recurrent patients), while 12% suffered severe late complications. Weitmann *et al.* also used TRUS-guided implantation and treated 23 recurrent uterine carcinoma patients.[8] The five-year cause-specific survival and local control rates were 43% and 47%, respectively. Grade 3 gastrointestinal and urinary late complications occurred in five of 23 patients (22%). Corn *et al.* introduced endorectal-coil MRI guidance.[24] Three of the first five patients they treated could be controlled locally even though the maximum diameter of the tumors was 4–7 cm. Popowski *et al.* developed a titanium-zirconium applicator for open MRI-guided implantation and reported their experience with six patients.[25] Finally, Viswanathan *et al.* reported their results for 10 recurrent endometrial carcinoma patients who underwent MR-guided interstitial brachytherapy and one (10%) showed grade 3 complication.[14] In summary, the rates of severe late complication, reported as 10–22% in the above-mentioned literature, seemed considerably lower than non-image guidance ISBT. However, it should be noted that the background of each report, such as the proportion of re-irradiated cases, differed.

The Image-Guided Brachytherapy Working Group recommended T2-weighted MRI with image-based intracavitary brachytherapy for cervical cancer.[26] The value of MRI in imaging gynecologic malignancies lies in its superior contrast resolution, which enables visualization of tumor size and volume, and discrimination of the tumor from normal tissue. Although these recommendations were originally aimed at intracavitary brachytherapy, the advantage of MRI seems apparently applicable to ISBT. That is why we have decided to utilize MRI on ISBT.

Just after the initial installation of the microSelectron-HDR at Osaka University Hospital in 1991, we tried several dose-fractionations for recurrent cancers in the pelvic area. A total dose of 24 to 50 Gy with a fraction dose of 5 to 7.5 Gy was administered for eleven patients from 1991 to 1994.[27] After the first experience, the fraction dose was fixed at 6 Gy. From 1995 to 1997 we treated 15 patients of recurrent carcinoma of the uterus with 42 Gy in seven fractions or 48 Gy in eight fractions. In this study we established the principle that non-irradiated cases receive 48 Gy while re-irradiated cases receive 42 Gy; this principle is still ongoing at Osaka University Hospital.[28]

We started using MRI-assisted treatment planning in 2005 at Osaka National Hospital. At the same time, we escalated the total dose to 54 Gy for non-irradiated cases and to 48 Gy for re-irradiated cases by adding one fraction of 6 Gy, to improve local control rate with the expectation that we can reduce the complication rate by MRI-assisted planning. On the other hand, for EBRT-combined cases, we used the same dose-fractionation as the one for fresh (previously untreated) cases of cervical cancer. We have reported a local control rate of 83% (15/18) even though all patients had advanced T3–4 stage tumors.[16]

In the current study, although we have treated only 14 patients, we achieved a three-year local control rate of 77.9% (95% CI: 55.8–100%), evidently an equivalent or better result than previously reported outcomes. The authors would like to emphasize that only 7.1% (one patient) experienced grade 3 complication, which seemed even lower than elsewhere in the literature. These results lead us to regard imaging-aided ISBT as useful for satisfactory delivery of prescribed doses to the CTV and, at the same time, for reducing the dose to the OAR. To determine the actual utility of our treatment, more patients and longer follow-up are necessary, and a comparison of outcomes for this novel treatment with those obtained with metal needles era will also be warranted. In conclusion, imaging-aided HDR-ISBT for the treatment of post-operative recurrence of uterine carcinoma was found to be practical, with promising preliminary results.

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がん放射線治療の現状と将来

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Radiation Therapy for Cancer: Current Status and Future Direction

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Radiotherapy has been one of the main options of the cancer treatment, and divided into three types of therapy; external beam radiotherapy, brachytherapy using sealed radiation source, and systemic radioisotope therapy using unsealed radiation source. Recent advances in the treatment planning system and radiotherapy equipment, three-dimensional conformal radiotherapy (3D-CRT) is becoming the standard treatment for a number of tumors. Stereotactic radiotherapy (SRT) is a special type of 3D-CRT targeting the well-defined tumors using narrow radiation beam. It is used for the treatment of small-sized tumors in the brain, spine and body trunk. Intensity-Modulated Radiation Therapy (IMRT) is an advanced type of 3D-CRT using intensity-modulation of external beams in order to optimize the isodose distribution. These high-precision radiation therapies allows better tumor targeting, and decrease the risk of side effects, and in the result, improved treatment outcomes.

Recently, particle-beam radiotherapy using ionizing particles (protons and heavy-ions) has been focused in the areas of cancer therapy. While ionizing particles penetrate the tissue, the radiation dose increases up to a maximum near the end of the particle's range (the Bragg peak), and thereafter drops to the almost zero. This feature in the energy deposition profile is very useful to concentrate the dose to the tumor and to decrease the dose to the important normal tissues adjacent to the tumors. Especially, heavy-ions represented by carbon ions have high biological effect to the tumor cells; the relative biological effectiveness (RBE) is considered 2.0-3.0 comparing to the photon (X-ray、γ-ray) and protons. Therefore, heavy-ions therapy is clinically very effective also in the treatment of radio-resistant tumor such as sarcomas, melanoma and adenocarcinoma, and large tumors including large number of hypoxic cells.

放射線療法は、身体の外から患部へ照射する外部照射治療と患部の中または近傍に直接放射線源を挿入し照射する密封小線源治療に大別される。近年のコンピュータ技術の進歩に伴い、CTシミュレーションをベースとした3次元放射線治療が標準的となるなど、特に、外部照射技術は著しい進歩をとげている。中でも、放射線をさまざまな方向から病巣にX線やガンマ線を集中的に照射する定位放射線照射（Stereotactic Radiotherapy: SRT）やコンピュータ制御で放射線強度を部分的に変化させて線量分布を最適なものとする強度変調放射線治療（Intensity Modulated Radiation Therapy: IMRT）などの高精度照射技術(High Precision Radiation Therapy)が開発され、治療効果の向上および副作用の低減に寄与している。

一方、従来用いられていたX線やガンマ線とは異なる性質をもつ陽子線や重粒子線を用いた粒子線治療の研究及び臨床応用が進み、その高い有用性が注目されている。粒子線には、飛程を持ち停止する直前で線量のピークを形成するという特徴があり、深部臓器の腫瘍に対して効率的に線量を集中させることができるため、副作用及び二次発がんリスクの低減が可能である。中でも、重粒子線（炭素線）は、①よりシャープな線量集中性、②高い生物学的効果（従来の放射線や陽子線に比較して約 2〜3 倍）を持つことにより、従来の放射線や陽子線では治療が困難であった重要リスク臓器に近接した腫瘍や放射線低感受性腫瘍（肉腫、黒色腫、腺癌など）に対しても高い治療効果が得られ、「がん放射線治療の切り札」と期待されている。

本稿では、がん治療における放射線治療の位置づけ、治療の種類、近年の高精度放射線治療、粒子線治療の進歩について紹介し、その現状と問題点、さらに今後の展望について概説したい。

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1. はじめに

現在、日本では2人に1人ががんに罹患し、3人に1人ががんで死亡する時代であり、がん対策は医療の中で最も重要視し取り組むべき事項である。放射線治療は、その言葉の通り「放射線を用いた治療」であるが、ほぼ全ての悪性腫瘍（がん）が対象とされ、外科療法、抗がん剤治療（化学療法）と並んで、がん治療の3本柱の1つとして重要な役割を担っている。放射線治療の利点は、非侵襲治療（観血的でない）で身体的負担が少ない、機能・形態の温存が可能、早期から進行期まで適応が広い（Fig. 1）、早期がんの治療成績は手術に匹敵するなどが挙げられる。逆に欠点としては、治療効果が腫瘍の放射線感受性にある程度依存する傾向にある、時に治療時に放射線の副作用が問題となるなどが挙げられる。高齢化社会を迎え、さらに、治療中及び治療後の生活の質（Quality of life: QOL）を重要視される時代となり、その役割は益々重要性を増してきている。現在、がん患者における放射線治療の適応率は日本では 25-30％程度と、欧米の適応率（50-60%）と比較しまだ低いが、年々増加傾向であり5-10 年後には欧米並みの数字になると予測されている。放射線治療に一般的に用いられている放射線としては、X 線、ガンマ線（いわゆる光子線）、電子線、ベータ線である。また、放射線治療は、外部照射と内部照射に大別でき、内部照射はさらに密封小線源治療と非密封小線源治療（アイソトープ内用療法）に分けられる（Fig. 2）。外部照射にはX線、ガンマ線及び電子線、密封小線源治療にはガンマ線放出核種、アイソトープ内用療法にはベータ線放出核種が用いられている。アイソトープ内用療法は主に核医学領域で扱われるものであり、本稿では、外部照射と密封小線源治療について述べる。

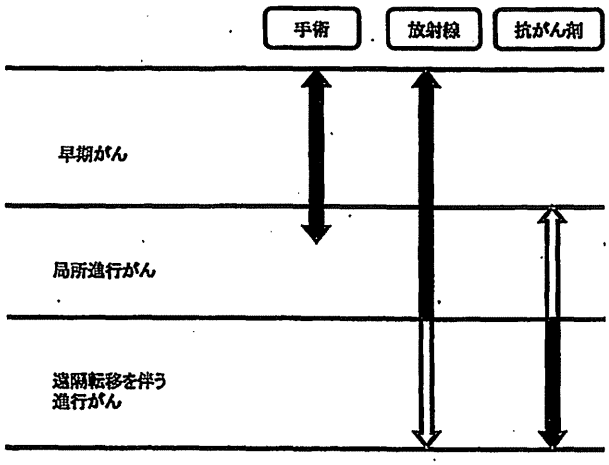

Fig. 1 Three pillars of cancer therapy and each therapeutic range

2. 密封小線源治療

密封小線源療法は、腫瘍の中または近傍に直接放射線源を挿入し照射する治療法であり、腫瘍内に挿入する組織内照射と管腔内に挿入する腔内照射とがある。歴史的には、226-Ra（ラジウム）や 137-Cs（セシウム）等の半減期が長いガンマ線放出核種がよく用いられたが、近年ンでは、60-Co（コバルト）、192-Ir（イリジウム）、125-I（ヨード）、198-Au（金）などのより半減期が短いものが用いられている。用いる線源には大きく分けて高線量率線源と低線量率線源があり、高線量率線源用いる場合は、実際の線源を遠隔操作で挿入する Remote After Loading System（RALS）が必要であり、現在は主に 192-Ir や 60-Co が線源として用いられている。1）医療者の被ばくがない、2）線量率が高いため治療が短時間で可能、3）隔離病室が不要などの利点がある。また、線源が小さいため、比較的細いチューブを介して線源挿入が可能なため、適応領域が広いのも特徴で、舌癌をはじめとする頭頸部腫瘍、前立腺癌に対する組織内照射、気管・気管支癌、食道癌、胆管癌、子宮癌に対する腔内照射などに用いられている。低線量率線源を用いる治療としては、198-Au、125-I、137-Cs を用いた舌癌、口腔底癌に対する組織内照射やを用いた組織内照射等がある。いずれにしても、密封小線源療法は、線源を腫瘍内または近傍に直接留置するため、腫瘍へ高い線量を集中的に照射することができ、高い局所効果が期待できるのが最大の特徴である[1]。但し、解剖学的に線源を挿入することが可能な部位しか適応とならないことや、適応範囲や治療成績が術者の技量に大きく依存することが欠点である。

3. 外部照射

一方、外から放射線を照射する外部照射は、非観血的（手術をせず）に体のどの部位でも自由に照射することが可能であるのが最大の利点である。外部照射の治療装置としては、数十年前まではコバルト照射装置

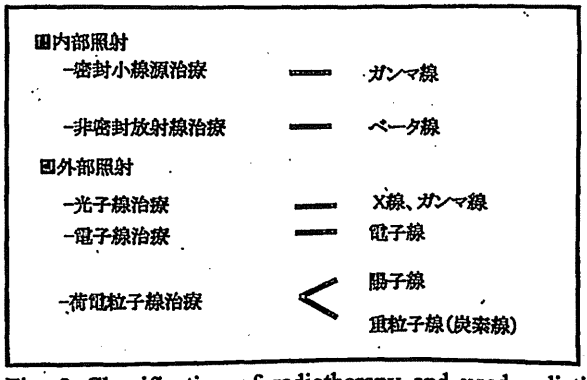

Fig. 2 Classification of radiotherapy and used radiation type

(60-Co) を用いたガンマ線治療が汎用されていたが、現在ではほとんど、医療用直線加速器（リニアック）をよる高エネルギーX 線及び電子線を用いた治療が行われている。それぞれの深部線量分布の特徴を考慮し、深部臓器の腫瘍には高エネルギーX 線、表在（皮膚・皮下）の腫瘍には電子線が主に用いられている。現在のリニアックには、照射野を形成するための装置であるマルチリーフコリメーターが内蔵されている。各リーフ幅も以前は 20 mm 程度と厚かったが、近年では 5 mm、3 mm と非常に細いコリメーターが開発され、より複雑な照射野を形成可能となってきており、副作用低減に寄与している。

現在の放射線治療の計画は治療計画用 CT をベースにした 3 次元治療計画が主流となっている。具体的には、1) 必要があれば治療時に用いる固定具を作製、2) 次に、解剖学的な基準点を設定し患部を含めた領域の CT を撮像、3) 3 次元治療計画用コンピュータを用いた治療計画、4) 治療計画データの検証、5) 治療装置へのデータ転送、6) 治療実施という流れである。3 次元治療計画用コンピュータを用いた治療計画には、各種標的体積、影響を受ける正常リスク臓器の体積、体輪郭入力、照射角度、照射方向数、各照射方向の照射野形状、照射線量、照射回数の決定、線量分布計算等の様々な項目が含まれる。治療計画上で、まず設定される標的体積は肉眼的標的体積（GTV）と言われるもので、画像（診察所見も加味）で明らかに腫瘍が存在する範囲として設定される。但し、CT では描出困難な標的腫瘍に関しては、MRI や FDG-PET などの様々な画像モダリテイーと治療計画用 CT との融合画像を作成し正確な標的体積の入力が行われる[2]。GTV に腫瘍の微視的浸潤程度やリンパ節への転移のリスクを考慮したマージンを付加したものを臨床的標的体積（CTV）、更に日々の照射位置の再現性の精度を考慮したマージンを付加したものを計画的標的体積（PTV）と呼ぶ。さらに呼吸性移動に代表される体内での標的の動きが問題となる部位では、その動きを考慮したマージンを付加したものを内的標的体積（ITV）として設定しなければならない[3-5]。最近では、正確な ITV の決定に 4 次元 CT が有用とされている。

4. 高精度放射線治療

放射線治療の治療効果を向上させる 1 つの方法として、これまでに、抗がん剤との同時併用療法（化学放射線療法）の有効性が証明され、多くの局所進行期のがんで化学放射線療法が標準療法となっている。また近年では、分子標的薬剤という腫瘍の増殖に関与する特定の分子を狙い撃ちにする新しいタイプの抗腫瘍薬剤との併用療法に関しても臨床試験が行われている。しかし、これらの薬剤との併用療法は治療効果が高まる反面、放射線治療の副作用も増強する傾向にあるのが大きな問題である。その為、放射線治療の空間的線量分布を改善するアプローチが必要とされる。つまり、標的体積への線量集中性を向上させ、腫瘍への線量増加による抗腫瘍効果の向上、正常組織への線量低減による副作用の軽減を目指したアプローチである。そのような目的で開発された照射技術が高精度放射線治療であり、3 次元原体照射（3D conformal radiotherapy: 3D-CRT）、定位放射線照射（Stereotactic radiotherapy: SRT）、強度変調放射線治療（Intensity Modulated Radiation Therapy: IMRT）などがそれに含まれる。

その中で、3D-CRT は最も基本的な照射技術であり、マルチリーフコリメーターにより標的体積の形状に一致させた照射野で多方向から照射する方法である。固定された複数角度から照射する方法を固定多門照射（static conformal radiotherapy）、装置を連続的に回転させながら照射する方法を運動原体照射（dynamic conformal radiotherapy）と呼ぶ。また、小さな腫瘍を対象に、非常に高い照射位置精度で 1 回に高い線量を集中的に照射する技術を特に定位放射線照射と呼び、頭部・頭頸部領域の治療では 2 mm 以下、体幹部領域では 5 mm 以下の精度で治療することが必要となっている。頭部・頭頸部領域の定位放射線照射に関しては専用治療装置も開発されている。臨床データとしても、脳腫瘍や早期肺癌等の小型腫瘍に対する定位放射線照射により手術に匹敵する良好な治療成績が示されている[6-9]。Fig.3 には早期肺癌に対する定位放射線照射の例を示す。

一方、IMRT は、3D-CRT の技術を更に進歩させたもので、各照射野内の線量強度を場所によって変化させ、近接する正常組織の線量を更に低減しつつ標的体積への線量集中性を向上させる照射技術である。頭頸部領域の腫瘍や前立腺癌等で特に臨床的な有用性が高い[10-11]。3D-CRT と IMRT の線量分布の違いを Fig.4 に示す。具体的には、各方向の照射において照射野内を多数のセグメント（サブフィールド）に分けて照射することによって場所による線量の強弱をつけ、更に、各照射方向の線量のウェートを調節することにより線量分布を最適なものとする方法である。非常に複雑で、もはや治療計画者が頭の中で考えて前向きに治療計画を行うことは不可能な治療法である。実際には、標的体積に照射したい線量や正常リスク臓器に照射される線量の制約などの様々な条件を設定し、治療計画コンピュータにその設定条件を満たす最適な治療計画を計算させるインバースプランニングという方法を用いる必要がある。

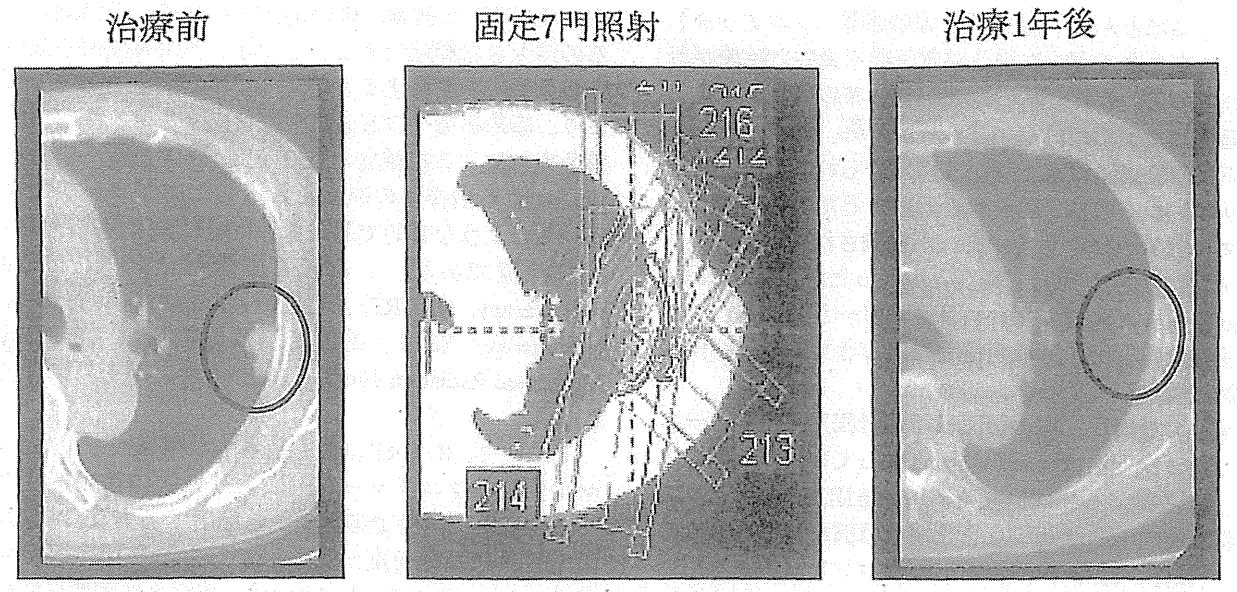

Fig.3 Stereotactic body radiotherapy (SBRT) for lung cancer

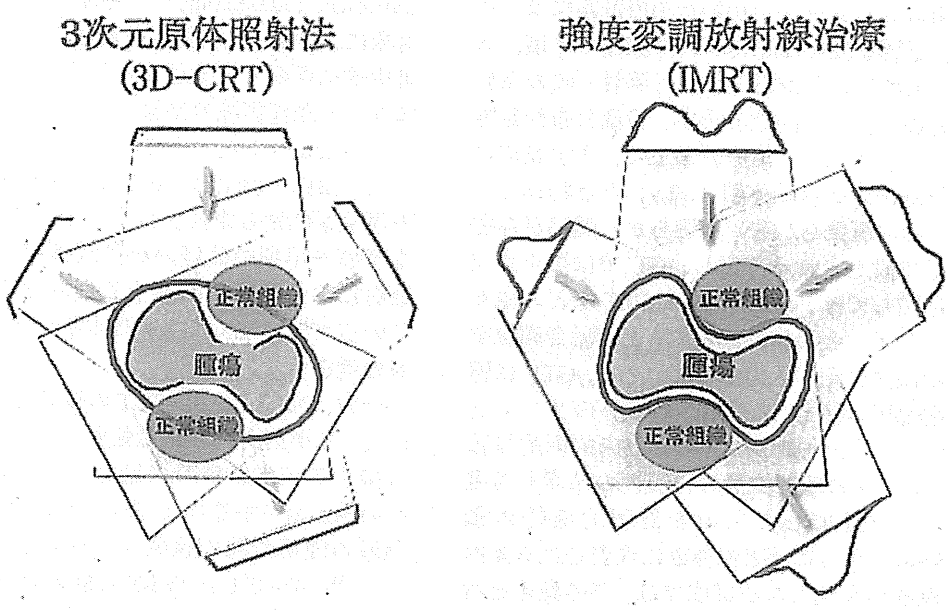

Fig. 4 3D-conformal radiotherapy (3D-CRT) and Intensity-modulated radiotherapy (IMRT). - The difference of dose distribution -

これら高精度放射線治療の精度管理上、最も重要な要素の１つが照射位置精度の担保であり、画像誘導放射線治療（image-guided radiotherapy: IGRT）という技術が開発された。CT 撮影装置や透視装置が搭載された治療装置を用いて、治療寝台上で治療直前あるいは治療中にリアルタイムで照射位置の照合や補正を行う方法であり、高精度放射線治療を支える技術として非常に大きな役割を持っており、IGRT 対応の様々な治療装置が開発されている。

5. 粒子線治療

上述のように、近年のＸ線やガンマ線を用いた高精度放射線治療技術の開発とその進歩は、放射線治療の治療成績向上及び副作用低減に大きく寄与しており、また、そのことが、がん治療における放射線治療の役割を更に重要なものとしているのは間違いない。しかし、Ｘ線やガンマ線を用いた治療の問題点や限界も考える必要性がある。副作用の面では、Ｘ線やガンマ線を用いる限り、その線量分布上の特性から、線量集中

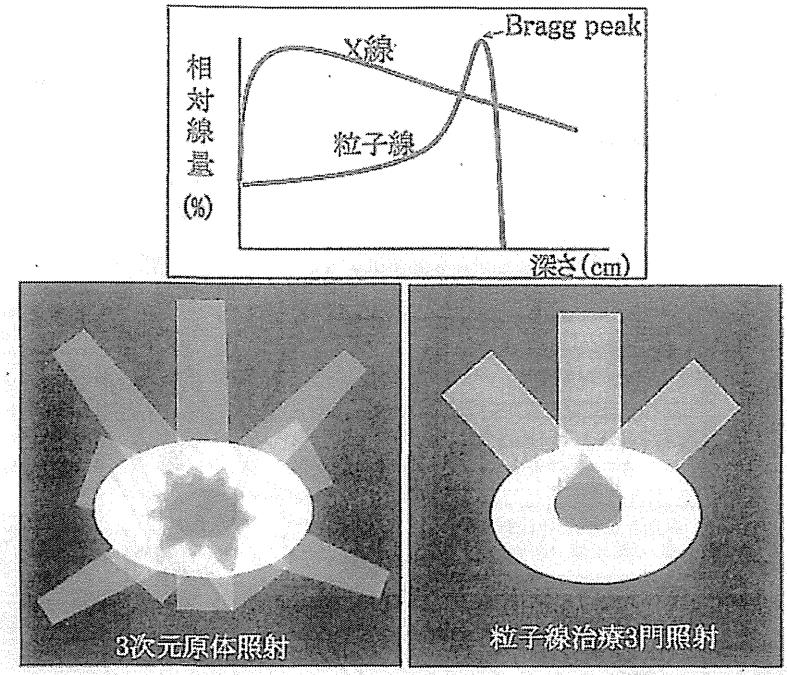

Fig. 5 Conformal radiotherapy using X-ray and Particle-beam radiotherapy. - The difference of dose distribution -

性を高めるにはどうしても多方向からの照射が必要となり、逆に、比較的低い線量ながら周囲正常臓器へ放射線を散らす結果となっていることである。標的体積が小さい場合であれば臨床上大きな問題となることは稀であるが、標的体積が大きな症例、放射線治療の副作用がでやすい内因性の要因を持つ症例、抗がん剤や分子標的薬剤を同時併用する場合等では、周囲への低線量照射領域の拡大による副作用が無視できなくなる可能性がある。また、全体での照射容積拡大による二次発がんのリスクを上昇の可能性も危惧されている。治療効果の面では、骨軟部腫瘍や悪性黒色腫に代表される放射線低感受性腫瘍に対する治療効果の限界も指摘されるところである。このような問題点や限界を克服するものとして期待されるのが、荷電粒子線治療と考えられる。荷電粒子線は重粒子線と陽子線に大別され、それぞれ重粒子イオン、陽子をサイクロトロンやシンクロトロンなどの円形加速器で光速の 60-80%にまで加速し照射する治療である。重粒子線では特に炭素線が臨床応用されており、陽子の 12 倍の質量を持つ。重粒子線、陽子線ともに飛程を持ち停止する直前で線量のピーク（ブラッグピーク）を形成するという特徴があり、深部臓器の腫瘍に対して効率的に線量を集中させることができ、副作用及び二次発がんリスクの低減が可能となる。この点が、X 線やガンマ線を用いた従来の放射線治療と比べて線量分布上の大きな利点であり（Fig.5）、臨床的なエビデンスも構築されつつある [12-15]。最近では、標的体積内を 3 次元的に小さなスポットに分割し、細いビームで高速でスキャンするように照射する技術（スポットスキャンニング技術）が実用化され、更に集中性の高い照射が可能となってきている。　以下、重粒子線（炭素線）と陽子線の比較について述べる。特に重粒子線（炭素線）は、陽子線に比べて更に線量のピークと平坦部分の比（ピーク/プラトー比）が高く、側方散乱も小さいため、更に線量集中性の高い治療が可能である。また、線量あたりの生物学的効果を X 線やガンマ線と比較すると、重粒子線（炭素線）では 2～3 倍、陽子線では 1.1 倍であり、重粒子線（炭素線）は X 線・ガンマ線、更には陽子線と比べ明らかに強力な生物学的効果を持ち、骨軟部腫瘍、悪性黒色腫、腺癌など放射線抵抗性と言われる組織系の腫瘍、それ以外にも大型の腫瘍（低酸素細胞成分が多い）、血流が不良な腫瘍、緩徐に増殖する腫瘍など放射線感受性が低い状態と考えられる腫瘍にも高い治療効果が期待できるのが特徴である [12),,6-18)]。また、重粒子線（炭素線）治療では、照射回数が X 線や陽子線治療と比べて非常に少なくて済むことも臨床上の大きな利点である。現在、国内では、放射線医学総合研究所、兵庫県粒子線医療センター（重粒子線＋陽子線）、群馬大学重粒子医学研究センターの 3 施設が稼働しており、平成 25 年に九州国際重粒子線がん治療センター（佐賀県鳥栖市）、平成 26 年に神奈川県立がんセンターにも開設が予定されている（Fig.6）。

陽子線治療は生物学的効果が X 線やガンマ線に近

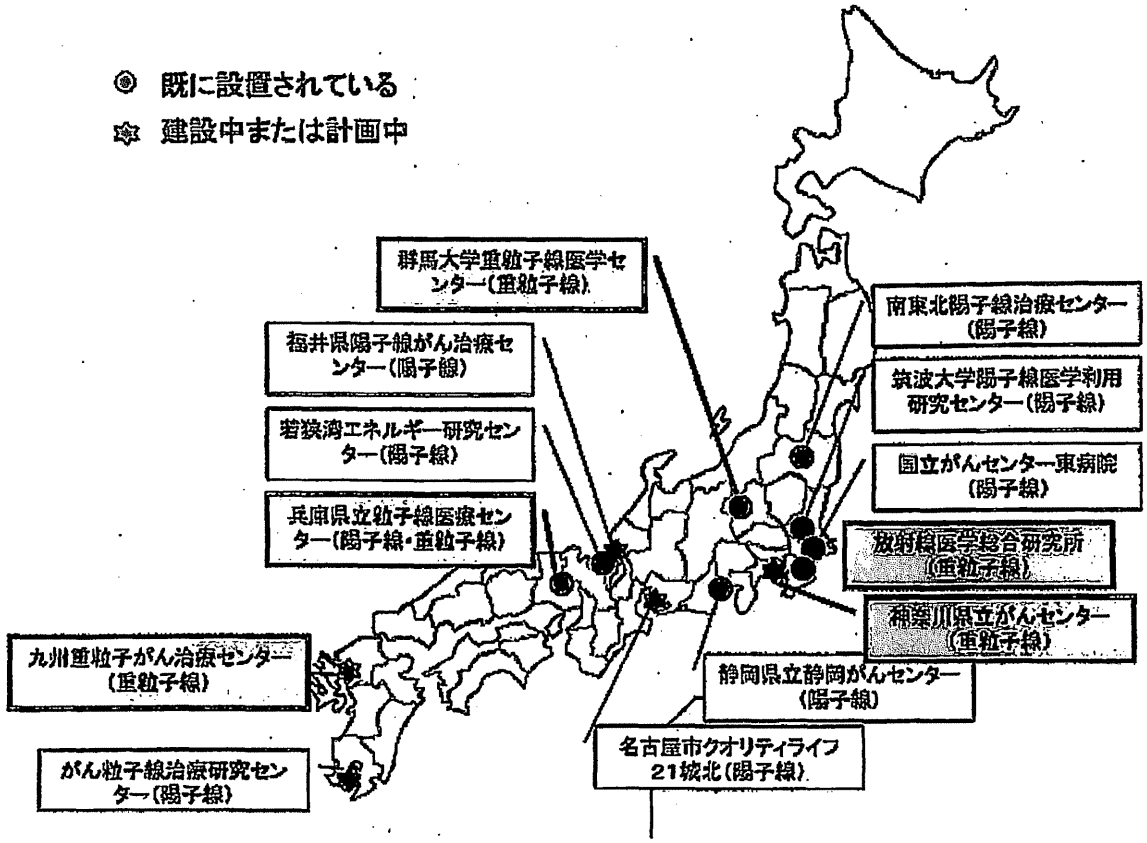

Fig. 6 Facilities of particle-beam radiotherapy in Japan

いため、線量効果関係や抗がん剤併用時の副作用などがX線やガンマ線を用いた過去のデータをもとに予測しやすく臨床上使いやすい、装置の小型化や低コスト化の面では重粒子線より有利などの特徴がある。現在、国内では、筑波大学、国立がんセンター東病院、静岡県立がんセンターなど5施設が陽子治療施設として稼働しており、新たに、鹿児島、名古屋、福井にも施設が開設予定である(Fig. 6)。上述のように、従来のX線やガンマ線を用いた治療と比べて線量分布上のメリットがあるのは事実であるが、近年のX線を用いた高精度放射線治療の進歩も著しいため、陽子線治療に関しては、高精度放射線治療と比較した場合に、明らかな臨床的な優越性を示せるかが今後の発展及び普及の鍵となるであろう。

6. 最後に

高精度放射線治療や粒子線治療に代表される放射線治療の進歩により、がん治療における放射線治療の役割と重要性が増してきている。しかし、これらの高精度放射線照射技術は、治療計画から実際の治療に至るまで高い水準の精度管理が担保されて初めて、有効かつ安全な治療となり得るものである。このような意味において、放射線治療に関連する医療機器の安全管理・保守、治療計画の立案・検証などの精度管理、関連する医用画像の扱いに精通した専門家の重要性と需要が益々増加している。中でも医学物理士には、これらの品質管理プロセスの責任者としての大きな役割が期待されていることは言うまでもない。もちろん、大学や研究機関においては、診療放射線技師や医学物理士等の人材育成のための教育、新しい照射技術、治療計画技術を開発するための研究も重要な業務である。現在、日本においては放射線腫瘍医が600名程度、医学物理士が500名程度であり、どちらも、まだ絶対的に不足しているのが実状であり、がん患者のための良質な放射線治療の提供と更なる放射線治療学の進歩には、我々放射線腫瘍医同様、医学物理士の人材育成と適正配置が急務である。

以上、非常に雑ぱくな内容で恐縮ではあるが、がん放射線治療の現状と将来について概説した。本稿を通じて、放射線がん治療に興味を持たれ、この分野で専門性を生かす道を目指して頂ける方がおられるとしたら望外の喜びである。

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Patterns of Practice in Intensity-modulated Radiation Therapy and Image-guided Radiation Therapy for Prostate Cancer in Japan

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Background: The purpose of this study was to compare the prevalence of treatment techniques including intensity-modulated radiation therapy and image-guided radiation therapy in external-beam radiation therapy for prostate cancer in Japan.
Methods: A national survey on the current status of external-beam radiation therapy for prostate cancer was performed in 2010. We sent questionnaires to 139 major radiotherapy facilities in Japan, of which 115 (82.7%) were returned.
Results: Intensity-modulated radiation therapy was conducted at 67 facilities (58.3%), while image-guided radiation therapy was conducted at 70 facilities (60.9%). Simulations and treatments were performed in the supine position at most facilities. In two-thirds of the facilities, a filling bladder was requested. Approximately 80% of the facilities inserted a tube or encouraged defecation when the rectum was dilated. Some kind of fixation method was used at 102 facilities (88.7%). Magnetic resonance imaging was routinely performed for treatment planning at 32 facilities (27.8%). The median total dose was 76 Gy with intensity-modulated radiation therapy and 70 Gy with three-dimensional radiation therapy. The doses were prescribed at the isocenter at the facilities that conducted three-dimensional radiation therapy. In contrast, the dose prescription varied at the facilities that conducted intensity-modulated radiation therapy. Of the 70 facilities that could perform image-guided radiation therapy, 33 (47.1%) conducted bone matching, 28 (40.0%) conducted prostate matching and 9 (12.9%) used metal markers. Prostate or metal marker matching tended to produce a smaller margin than bone matching.
Conclusions: The results of the survey identified current patterns in the treatment planning and delivery processes of external-beam radiation therapy for prostate cancer in Japan.

Key words: radiation therapy – urologic-radoncol – radiation oncology

INTRODUCTION

External beam radiation therapy (EBRT) has developed rapidly in recent years (1,2) and treatment equipment with which intensity-modulated radiation therapy (IMRT) and/or image-guided radiation therapy (IGRT) can be conducted are being introduced into Japan (3). IMRT and IGRT are particularly useful in EBRT for prostate cancer and are routinely used in the USA (4) and recommended in worldwide guidelines (5,6).

In Japan, IMRT and IGRT were listed as eligible for insurance reimbursement in 2008 and 2010, respectively. However, the present situation regarding the use of these techniques in EBRT for prostate cancer remains unclear (7,8). Therefore, we conducted a survey that would clarify the operational situation, treatment planning and treatment processes of IMRT and/or IGRT when used in EBRT for prostate cancer.

PATIENTS AND METHODS

In February 2010, we sent a questionnaire on EBRT for prostate cancer to 139 major facilities including university hospitals, cancer centers and designated prefectural cancer centers and hospitals. The questionnaire was also sent to the hospitals which had treatment machines with IGRT functions, including Novalis (BrainLAB, Heimstetten, Germany), Tomotherapy (Accuray Inc., Sunnyvale, USA) and MHI-TM2000 (Mitsubishi Heavy Industries, Ltd., Nagoya, Japan).

The survey was composed of categories regarding treatment planning, dose fractionation and methods of implementation of EBRT for prostate cancer. If methods differed according to the type of radiation techniques used such as three-dimensional radiation therapy (3DCRT) or IMRT, we required responses regarding the most precise radiation method presently used. Among the 139 facilities to which we sent the survey, 115 (82.7%) gave responses, which were then analyzed. The high response rate allowed an extensive and representative data analysis.

RESULTS

General Information

Figure 1 shows the distribution of the number of patients with prostate cancer treated with EBRT at facilities in 2009 over the course of 1 year. There were 30 facilities (26.1%) at which over 50 patients were treated in 1 year. Of the 115 total facilities, 67 (58.3%) conducted IMRT, 70 (60.9%) conducted IGRT and 58 (50.4%) conducted both.

Treatment Planning

Figure 2 shows the condition of the bladder at the treatment planning stage and during the treatment. In approximately

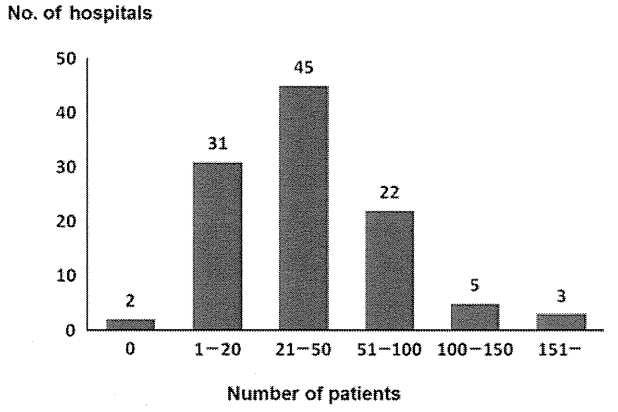

Figure 1. Total number of patients with prostate cancer treated with external-beam radiation therapy at facilities in 2009. Because some data were missing, the total numbers of patients were less than the actual number.

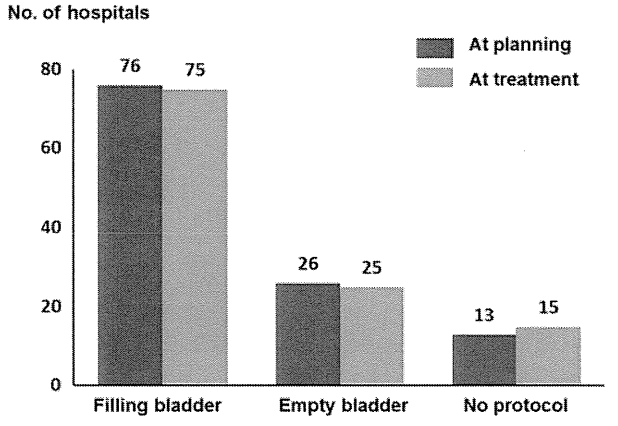

Figure 2. Condition of the bladder at the treatment planning stage and during treatment.

two-thirds of the facilities, a filling bladder was requested. The time spent pooling urine was 1 h at 56 facilities (48.7%), 1–2 h at 8 facilities (7.0%) and 30 min at 7 facilities (6.1%). Seven facilities (6.1%) also asked patients to drink water prior to treatment.

Figure 3 shows the condition of the rectum. Approximately 80% of the facilities inserted a tube or encouraged defecation when the rectum was dilated. Laxative medication was used at one-quarter of the facilities.

Simulations and treatments were performed in the supine position at 105 facilities (91.3%) and the prone position at 10 facilities (8.7%). Figure 4 shows methods of patient fixation. Some kind of fixation method was used at 102 facilities (88.7%). Although various methods were reported, a vacuum cushion, thermoplastic shell and foot support were used most frequently.

Magnetic resonance imaging (MRI) was routinely performed for treatment planning at 32 facilities (27.8%). Of these, 15 facilities (13.0%) performed computed tomography

(CT)-MRI image fusion with treatment planning software. MRI taken at the time of diagnosis was used as a reference at 66 facilities (57.4%), while 17 facilities (14.8%) did not use MRI for treatment planning.

Treatment

Radiation therapy was carried out with 2 Gy per fraction at 100 facilities (86.9%), 2.1–3 Gy at 14 facilities (12.2%) and 1.8 Gy at 1 facility (0.9%). Most facilities conducted treatment five times a week. Treatment was conducted three times a week at five facilities (4.3%) and four times a week at three facilities (2.6%).

Figure 5 shows the distributions of radiation doses delivered to the prostate at facilities using a fraction dose of 2 Gy. The median total dose was 76 Gy with IMRT and 70 Gy with 3DCRT. The doses were prescribed at the isocenter at the facilities that conducted 3DCRT. In contrast, the dose prescription varied greatly at the facilities that conducted IMRT. Of the 67 facilities that conducted IMRT, D95, which is the minimum absorbed dose that covers 95% of the planning target volume (PTV), was used as a dose prescription at 24 facilities (35.8%). A dose prescription requiring that 95% of the prescribed isodose line cover 95% of the PTV was used at 4 facilities (6.0%), the mean PTV dose was used at 13 facilities (19.4%) and other methods at 26 facilities (38.8%).

The most popular IGRT methods (54 facilities) involved 2D matching with X-ray fluoroscopy or 3D matching with a flat-panel cone-beam CT. Eight facilities used CT on rail and 4 facilities used ultrasonic devices. Of the 70 facilities that could perform IGRT, 33 (47.1%) conducted bone matching, 28 (40.0%) conducted prostate matching and 9 (12.9%) used metal markers. At the treatment of prostate cancer, 60 facilities (85.7%) always conducted IGRT, while 9 (12.9%) conducted IGRT at regular intervals.

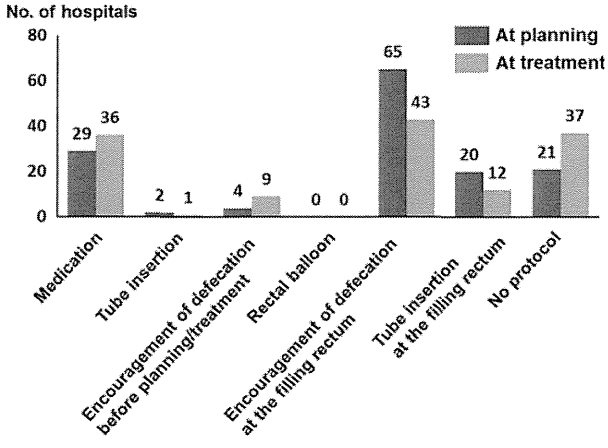

Figure 3. Condition of the rectum at the treatment planning stage and during treatment. Multiple answers allowed.

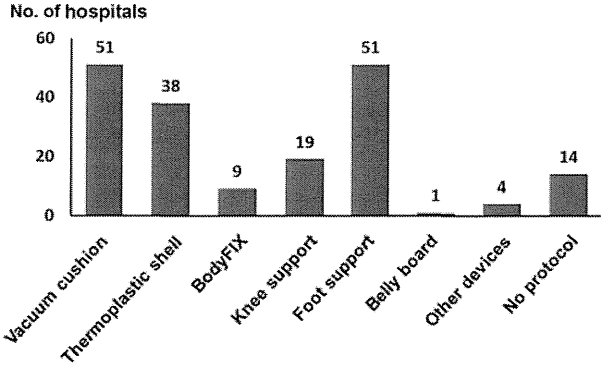

Figure 4. Fixation of the patients at the treatment planning stage and during treatment. Multiple answers allowed.

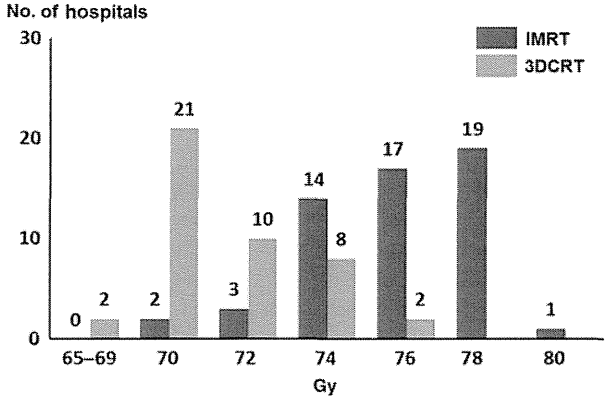

Figure 5. Total dose to the prostate.

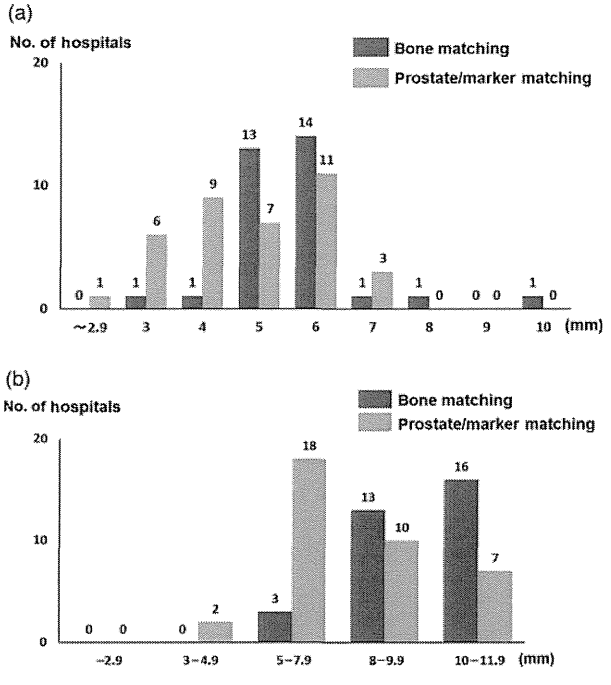

Figure 6. Margins from the prostate to planning target volume for patients with T1–2 tumors treated with IGRT: (a) rectal side and (b) other sides.