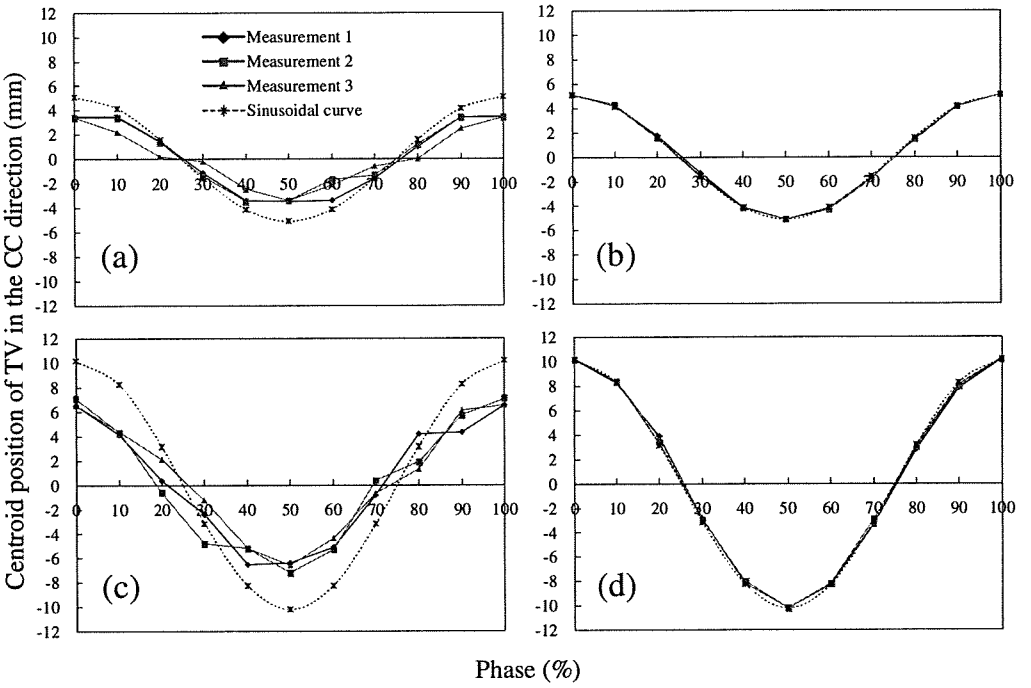

FIG. 6. Centroid position of TV in the CC direction. Broken curve shows the theoretical position as a function of phase: (a) (A,T)=(5.0 mm,2.0 s), (b) (A,T)=(5.0 mm,9.9 s), (c) (A,T)=(10.0 mm,2.0 s), and (d) (A,T)=(10.0 mm,10.0 s).

III.C. Comparison of TV_{4D} and TV_{MIV} to its theoretical volume

The ratios of mean TV_{4D} and TV_{MIV} size to V_{theory} are shown in Fig. 9. The volumetric error between TV_{4D} size and V_{theory} was within 5% except for T of 2.0 s. TV_{MIV} sizes were slightly larger than TV_{4D} sizes. Mean ± SD of TV_{MIV}/TV_{4D} was 102.79% ± 1.32%. An additional margin of up to 2.5 mm was required to encompass V_{theory} for TV_{4D} and TV_{MIV} in the CC direction. Centroid shifts between TV_{4D} and TV_{MIV} were within 0.6 and 0.2 mm in the CC and other directions, respectively.

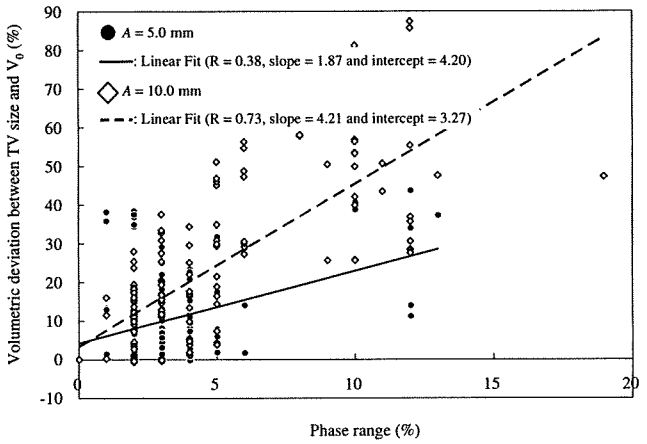

FIG. 7. Volumetric deviation between TV size and V_0 as a function of phase range. A positive value indicates that TV size is larger than V_0.

IV. DISCUSSION

We evaluated the impact of motion velocity on imaged objects by varying the amplitude and period of sinusoidal motion. Both misalignment and motion-blurring artifacts were caused by high motion velocity. A phase range of 2% was required even for T of 10.0 s. TV_{4D} sizes depended on the motion period and were smaller than V_{theory}. On the other hand, TV_{MIV} sizes were close to V_{theory} except for T of 2.0 s.

In the current study, projection data over a full gantry rotation of 1.0 s, which was the maximum rotational speed of our CT scanner, were used for image reconstruction. Reconstructed images were based on 1.0 s projection images. The large motion error with T of 2.0 s was because each reconstructed image included projection images that spanned 50% of all phase bins. The numerical results of the current study would be different if a different gantry rotational speed was used with a different CT scanner; for example, if a gantry rotational speed of 0.5 s was used with (A,T) =(10.0 mm,2.0 s), the results would be similar to that with (A,T)=(10.0 mm,4.0 s) in the current study.

The phantom moved along the longitudinal axis of the CT couch according to $\cos(t)$, not $\cos^4(t)$ modeled by some researchers,[20] because of the limitations of our phantom apparatus. Compared to $\cos(t)$, stationary time length near exhalation is longer and motion velocity is higher near midexhalation and midinhalation in $\cos^4(t)$. If the motion pattern of $\cos^4(t)$ was applied to phantom motion, volumetric variations would be smaller near exhalation and motion artifacts would be more pronounced near midexhalation and midinhalation.

Varying density distribution within the imaging plane

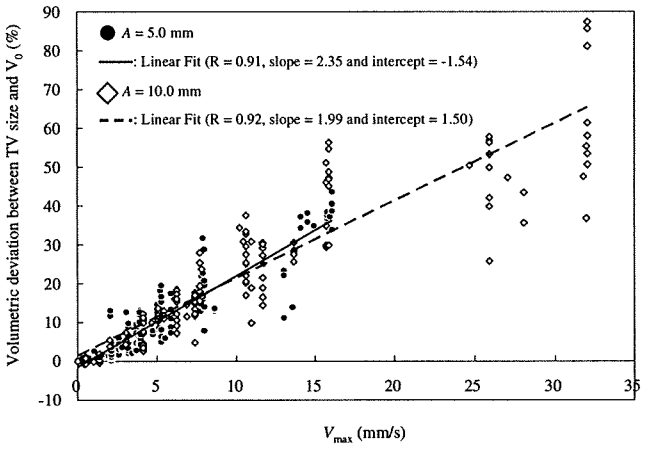

FIG. 8. Volumetric deviation between TV size and V_0 as a function of V_{max}. A positive value indicates that TV size is larger than V_0.

leads to in-slice artifacts. Rietzel *et al.*[11] performed a similar phantom study on 4D CT and indicated that spiral-like images of spherical objects in these axial images occurred due to the motion of the spherical object into or out of the imaging plane, which was particularly noticeable at the sphere pole. Materials around the spherical object in our QUASAR™ phantom were not styrofoam/air but acrylic, which had a CT number of around 130 HU. The effects of in-slice artifacts might have been less marked than in their study because of gradual density changes within the imaging plane.

Irregular respiration during 4D CT data acquisition results in the misidentification of respiration cycles. Mutaf *et al.*[15] concluded that temporal inaccuracies could lead to severe volumetric inaccuracies of up to 40% in the delineation of target volumes. Yamamoto *et al.*[16] reported that the root mean square respiratory irregularity was significantly related to the occurrence of motion artifacts. Thus, it is important to assign an accurate respiratory phase to generate temporally

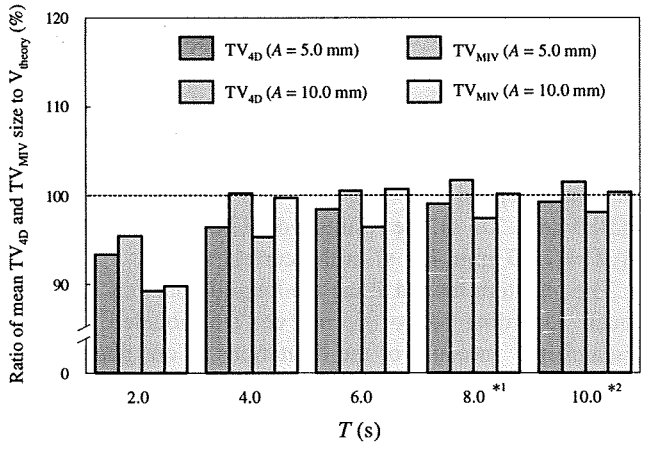

FIG. 9. Ratio of mean TV_{4D} and TV_{MIV} size to V_{theory}. TV_{4D} sizes show period dependency and are smaller than V_{theory}. On the other hand, TV_{MIV} sizes are slightly larger than TV_{4D} sizes and are close to V_{theory} except for T of 2.0 s. Actual averaged periods are 8.1 s*1 and 9.9 s*2 for A of 10.0 and 5.0 mm, respectively.

coherent 4D CT images.[17,18] To narrow the phase range with the current retrospective sorting method based on respiratory phase, the following two specific scan parameters for cine CT data acquisition are available on our CT scanner: (A) to shorten T_{images} and (B) to lengthen T_{cine}. The number of images per study will substantially increase when adjusting these parameters, which might exceed the maximum limit of 3000 slices per study on our CT scanner. Exposure dose to patients will also increase with (B) and thus these parameters have to be balanced. Furthermore, adjusting ISD will help reduce the phase range to some extent. Note, however, that in-slice and motion-blurring artifacts would remain even with a phase range of 0%. These artifacts are not attributed to retrospective sorting methods but can be reduced by a fast gantry rotational speed. CT images acquired with a fast gantry rotational speed can improve temporal resolution and will be closer to a perfect snapshot in time.

4D CT data are generally analyzed to determine the mean tumor position and tumor range of motion and allow us to design patient-specific internal margins;[11–13,21,22] however, data reliability is degraded under motion artifacts. Although Rietzel *et al.*[11] showed that trajectory differences between the center of mass calculation and rigid registration were within one voxel (2.5 mm in the CC direction in their study) for all motion phases, our maximum positional difference between TV and the theoretical centroid was 1.35 mm in the CC direction for $(A,T)=(10.0$ mm$,4.0$ s). As evidenced by the result of TV_{4D}/V_{theory}, TV_{4D} sizes were smaller than V_{theory} due to the centroid difference. Thus, motion artifacts yield volumetric errors, leading to potential geometric miss; therefore, geometrical errors should be recognized when determining TVs, especially with a fast period. Additional margins will be required to compensate for these uncertainties.

In order to improve 4D CT image quality, the American Association of Physicists in Medicine Task Group 76 recommends respiratory coaching at simulation.[23] Kini *et al.*[24] concluded that audio coaching could improve the stability of the respiration frequency of the patient. Based on the results of Kini *et al.*, we previously acquired 4D CT images for more than 20 patients with lung cancers under audio-coached conditions. While misalignment artifacts were substantially reduced by audio coaching, motion-blurring artifacts became more severe. Furthermore, the total tumor movement during the full respiratory cycle was visually greater on CT images by audio coaching, which has been introduced by Haasbeek *et al.*[25] On the basis of our results, volumetric deviation between TV size and V_0 was larger for A of 10.0 mm than that for A of 5.0 mm and had a strong correlation with motion velocity (Fig. 8). Motion-blurring artifacts are generally caused by interplay between the gantry rotational speed and respiratory motion.[1–3] Due to the promotion of interplay by audio coaching, motion-blurring artifacts might become more severe than under free breathing. The low variation in motion velocity could reduce motion artifacts on 4D CT images.[26]

TV_{MIV} sizes were slightly larger than TV_{4D} sizes. A possible cause of this difference is the method of generating

MIV. Riegel *et al.*[19] compared TVs on MIP_{cine} (MIV generated from all reconstructed CT data in our terminology) with those on $MIP_{4D\text{-}CT}$ (MIV reconstructed only from sorted 4D CT volumes in our terminology) and showed that the mean TVs on $MIP_{4D\text{-}CT}$ were significantly smaller than those on MIP_{cine}. While MIP_{cine} can capture the full extent of motion, $MIP_{4D\text{-}CT}$ would still underestimate the extent of motion if 0% and 50% phases did not represent the largest motion extent of the object. Thus, such phase assignment would cause a difference between TV_{MIV} and TV_{4D} sizes.

V. CONCLUSION

This phantom study demonstrated that motion artifacts were substantially reduced when the phantom moved longitudinally at low motion velocity during 4D CT image acquisition; therefore, geometrical uncertainties due to motion artifacts should be recognized when determining TVs, especially with a fast period.

ACKNOWLEDGMENTS

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京都大学におけるIMRT

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■ はじめに

当院では2000年より強度変調放射線治療（intensity modulated radiotherapy：IMRT）を実施している。毎年実施件数が増加し，2008年の1年間では132例を実施するに至った（図1）。その内訳は，前立腺癌105例，頭頸部癌19例，中枢神経5例，その他3例である。2008年4月より健保収載となり，今後も件数の増加が予想される。

本稿では当院におけるIMRTの実際，主として治療計画について述べる。

❶ 前立腺癌のIMRT

1）固定具

図2のように腹臥位で固定する。

1時間程度の蓄尿の後に治療計画CTを撮影する。直腸内ガスが著明な場合には排ガスを行ってから撮影を行う。日々の照射も同様の条件で行う。

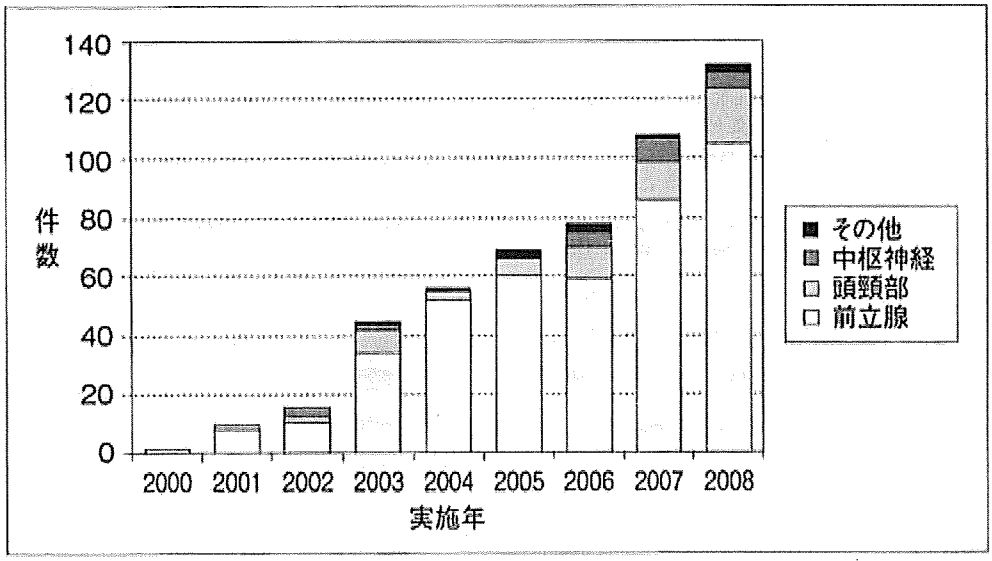

図1　京都大学におけるIMRT実施件数の推移

*1　Y. Matsuo, Y. Norihisa, M. Narabayashi, K. Takayama, N. Horii, N. Mizowaki, M. Hiraoka　京都大学大学院医学研究科　放射線腫瘍学・画像応用治療学　*2　S. Yano, M. Nakata　京都大学医学部附属病院　放射線部
〔索引用語：強度変調放射線治療，前立腺癌，頭頸部癌〕

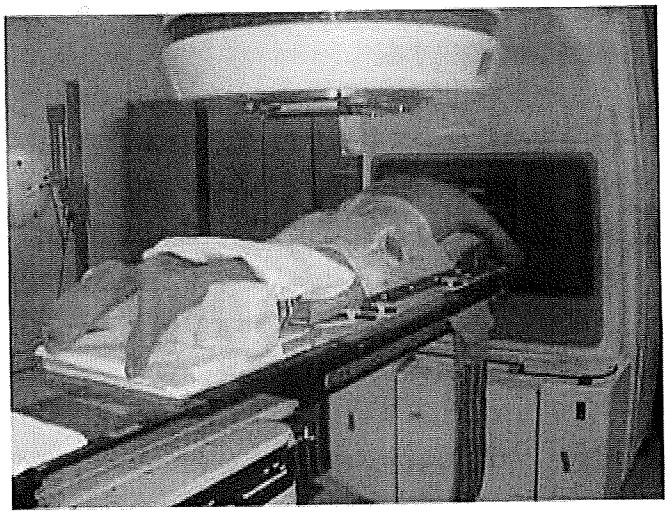

図2　前立腺癌における患者固定

表1　前立腺癌 IMRT における線量制約

structure		constraint (preferable)
PTV	D95	≥ 90% (≥ 95%)
	V90	≥ 96% (≥ 98%)
	Max	≤ 110%
	Mean	≥ 99%, ≥ 103%
RECT_W	V40Gy	≤ 65% (≤ 60%)
	V60Gy	≤ 35% (≤ 30%)
	V70Gy	≤ 25% (≤ 20%)
	V78Gy	< 1%
BLAD_W	V40Gy	≤ 65% (≤ 60%)
	V70Gy	≤ 35%
Bowel_L	V65Gy	≤ 1.0 ml (≤ 0.5ml)
Bowel_S	V60Gy	≤ 1.0 ml (≤ 0.5ml)

RECT_W：直腸の壁部分，BLAD_W：膀胱の壁部分，Bowel_L：大腸，Bowel_S：小腸

2）輪郭入力

CTV

臨床標的体積（clinical target volume：CTV）の設定に先立って，前立腺と精嚢の輪郭を治療計画用 CT 上に入力する。病期判定の際に撮像された MRI を参考にしながら，前立腺と膀胱の境界や前立腺尖部を注意深く入力する。また周囲の静脈叢や筋肉を前立腺に含めないようにする。

CTV は前立腺と精嚢の輪郭をもとにして設定する。低～中リスク症例では前立腺および精嚢基部，高リスク症例では前立腺および精嚢近位 2/3 で定義される。精嚢遠位 1/3 は Kestin らの報告[1]に基づき CTV から省くが，T3b 症例では精嚢全体を CTV に含める。

C 期高リスク症例の一部では，総腸骨・内腸骨動脈リンパ節を中心とした予防照射領域および腫大リンパ節にも CTV を設定し，それぞれ 58.5Gy（1.5Gy/Fr），66.3Gy（1.7Gy/Fr）を処方する標的体積内同時ブースト法（simultaneous integrated boost：SIB）を用いることがある。

PTV

計画標的体積（planning target volume：PTV）の設定は 3D マージンで CTV + 9mm（背側 6mm）を基本に微調整を行う。

OAR

リスク臓器（organ at risk：OAR）としては，膀胱，直腸およびターゲット近傍の大腸・小腸を設定する。膀胱は臓器全体を入力し，4mm 厚で生成した壁構造を線量評価対象とする。直腸は，前立腺または精嚢（CTV の方が大きい場合には CTV）から頭尾 15mm の範囲を入力する。線量評価には，4mm 厚で生成した壁構造のうち頭尾端それぞれ 5mm を除いた部分を用いる。

3）ビーム配置

照射に用いる X 線のエネルギーは 15MV もしくは 6MV である。強度変調は sliding window 法で行う。

ビーム配置は 15 MV X 線の場合で 5 門（0，75，145，215，285 度）を用いることが多い。

4）処方線量と線量制約

処方線量は低～中リスク症例に対して 74Gy（2Gy ×37 回），高リスク症例に対しては 78Gy（2Gy × 39 回）を原則としているが，年齢や併存疾患，既往治療を考慮して決定する。

治療計画装置上の線量分布を評価し，50%等線量曲線が直腸後壁をあまり越えないこと，PTV 背側が 90 ～ 95%等線量曲線にほぼ一致していることなどを視覚的に確認する。また，表 1 に示す線量制約の数値目標が満たされていることも確認する。なお，PTV と直腸または大腸・小腸とのオーバラップが大きい症例で平均線量が大幅に上昇することを避けるために，線量処方に関して PTV D95 での一律の正規化は行っていない[2]。

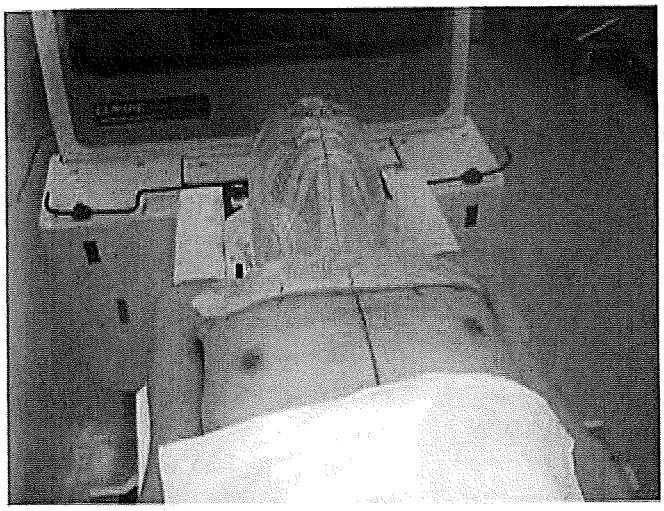

図3　頭頸部癌における患者固定

❷ 頭頸部癌のIMRT

1）対象疾患

頭頸部領域においては，根治照射症例を対象としてIMRTを実施しており，上・中・下咽頭癌，上顎洞癌などが対象となっている。本稿では上咽頭癌に対するIMRTについて述べる。

2）固定具

固定具として，頭部用ベースプレートにU字シェルを乗せ上胸部まで引き伸ばした物を用いる（図3）。シェルにはバイトプレートを接着する。

3）輪郭入力

GTV

肉眼的腫瘍体積（gross tumor volume：GTV）は，診察所見やMRI，CTおよびFDG-PET等の各種画像検査で明らかな原発腫瘍ならびに転移リンパ節とする。

CTV70

CTV70は，GTVとその周辺構造を入力する。GTV＋5mmを基本とし，原発巣においては上咽頭壁全体を含むように拡大する。転移リンパ節の節外浸潤範囲に関してApisarnthanaraxらが病理学的検討を行っている。節外浸潤の範囲は平均2.2mmであり，96％のリンパ節では5mm未満であったとされる[3]。この報告に基づき転移リンパ節におけるCTV70もGTV＋5mmを基本とした入力としている。

CTV63

CTV63は高リスクの予防照射域とし，原発巣の浸潤を来しやすい領域および高率に転移がみられるリンパ節領域を設定する。

上咽頭癌は広範に浸潤することが多々みられ[4]，CTV設定には慎重を要する。原発巣のCTV63に関してはEisbruchらの論文[5]を参考にして以下の範囲で定義する。前縁は上顎洞後壁や翼口蓋窩を含める。外側縁は卵円孔および棘孔を含み，また傍咽頭間隙（parapharyngeal space）を含める。後縁は斜台前部1/3～1/2を含める。

予防リンパ節領域のCTV63としては，両側の咽頭後リンパ節（retropharyngel node）およびレベルII，IIIリンパ節領域を設定する。転移リンパ節が含まれる領域とそれに隣接するリンパ節領域もCTV63とする。レベルII転移が高度な場合には同側のレベルIbもCTV63に含める。また，Gregoireらの論文[6]に基づき，節外浸潤の疑われるリンパ節が広範に筋肉と接している場合には，その筋肉を広くCTVに含めることとしている。なお，リンパ節領域の入力にあたってはDAHANCA，EORTC，GORTEC，NCIC，RTOGの共同ガイドラインを参照して行う[7]。ただし，上咽頭癌症例においてCTV 63のレベルIIは常に頭蓋底（＝retrostyloid space）まで含める。

CTV56

CTV56は低リスクの予防照射域とし，CTV63以外の両側レベルIV，Vおよび鎖骨上リンパ節としている。

PTV

PTVはCTV＋5mmを基本とするが，リスク臓器や皮膚との位置関係により適宜修正を施す。標的体積の入力例を図4に示す。

OAR

OARとしては，脊髄，脳幹，側頭葉，視神経・視交叉，耳下腺，喉頭などを設定する。

4）ビーム配置

照射に用いるX線のエネルギーは4～6MV。強度変調は前立腺と同じくsliding window法で行う。ビーム配置は，側方から後方の7門（80，120，150，180，210，240，280度）を用いることが多い。

5）処方線量と線量制約

線量処方は，CTV70，63，56それぞれに70Gy（2Gy/Fr），63Gy（1.8Gy/Fr），56Gy（1.6Gy/

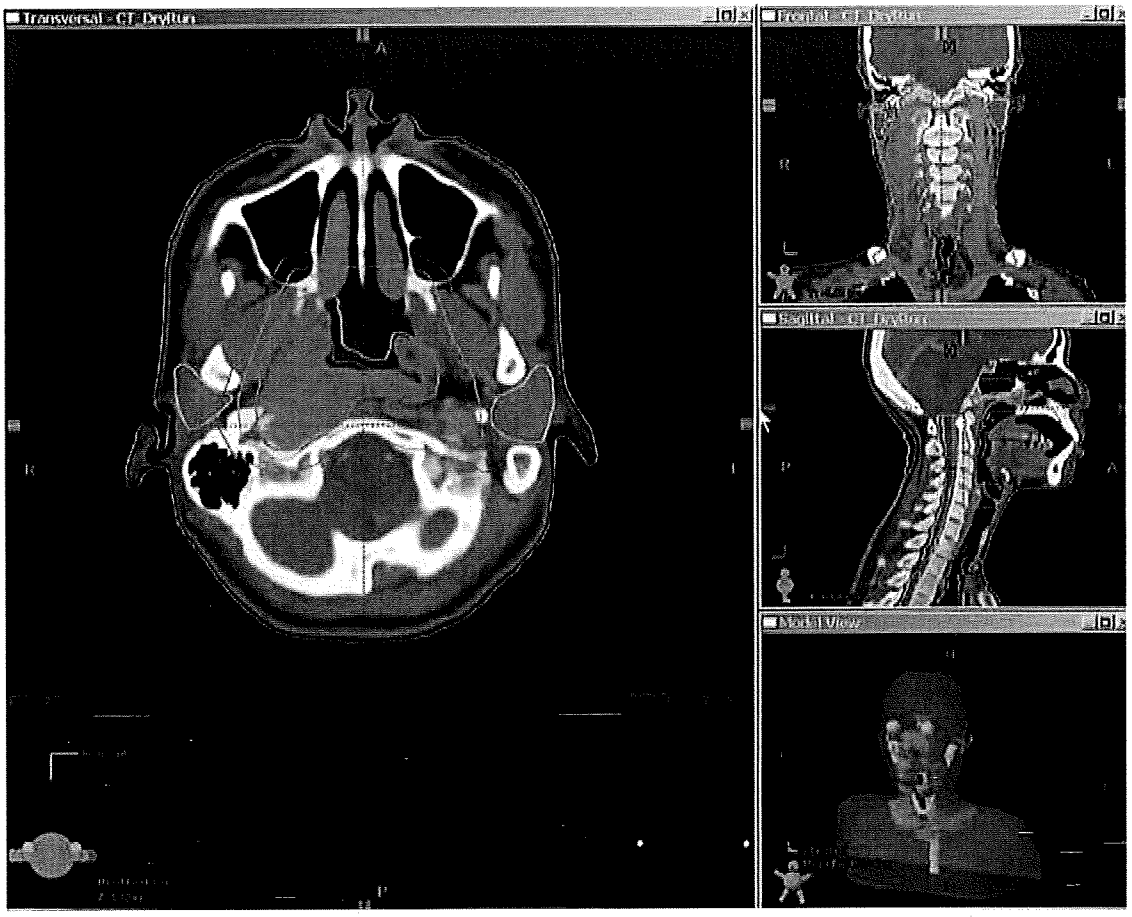

図4　頭頸部癌における標的体積入力例
紫色塗りつぶしがCTV70，橙色がCTV63である。CTV56は冠状断像における青色の領域である。

Fr）を処方するSIB法で行う。PTV D95での一律の正規化は行っていない。

線量制約目標を表2に示す。優先順位は，(1) 脊髄，脳幹などのcritical organ，(2) 標的体積（CTVおよびPTV），(3) その他の正常臓器（耳下腺など）としている。最終的に線量分布図で極端な高線量域や標的体積内の低線量域が生じていないかを確認し，治療計画を承認する。

頭頸部癌IMRTにおいては耳下腺機能温存が注目されがちであるが，耳下腺内再発の報告[8]もある。レベルIIリンパ節転移が高度な場合には同側の耳下腺温存を断念することが少なくない。

顎下腺機能温存[9]や咽頭括約筋の機能温存[10]が報告されつつあるが，我々の施設ではまだ検討段階であり，線量制約として明示はしていない。

表2　頭頸部癌IMRTにおける線量目標

structure		goal (acceptable)
GTV	Min	≧100%
CTV70, 63, 56	D95%	≧100% (95%)
	V93%	＞99%
PTV63, 56	D90%	＞95%
Spinal cord	Max	＜45Gy (50Gy)
Brainstem	Max	＜54Gy (60Gy)
Optic nerve	Max	＜54Gy (60Gy)
Parotid gland	V30Gy	＜50%
Larynx	Mean	＜45Gy
Inner ear	Mean	＜45Gy (50Gy)

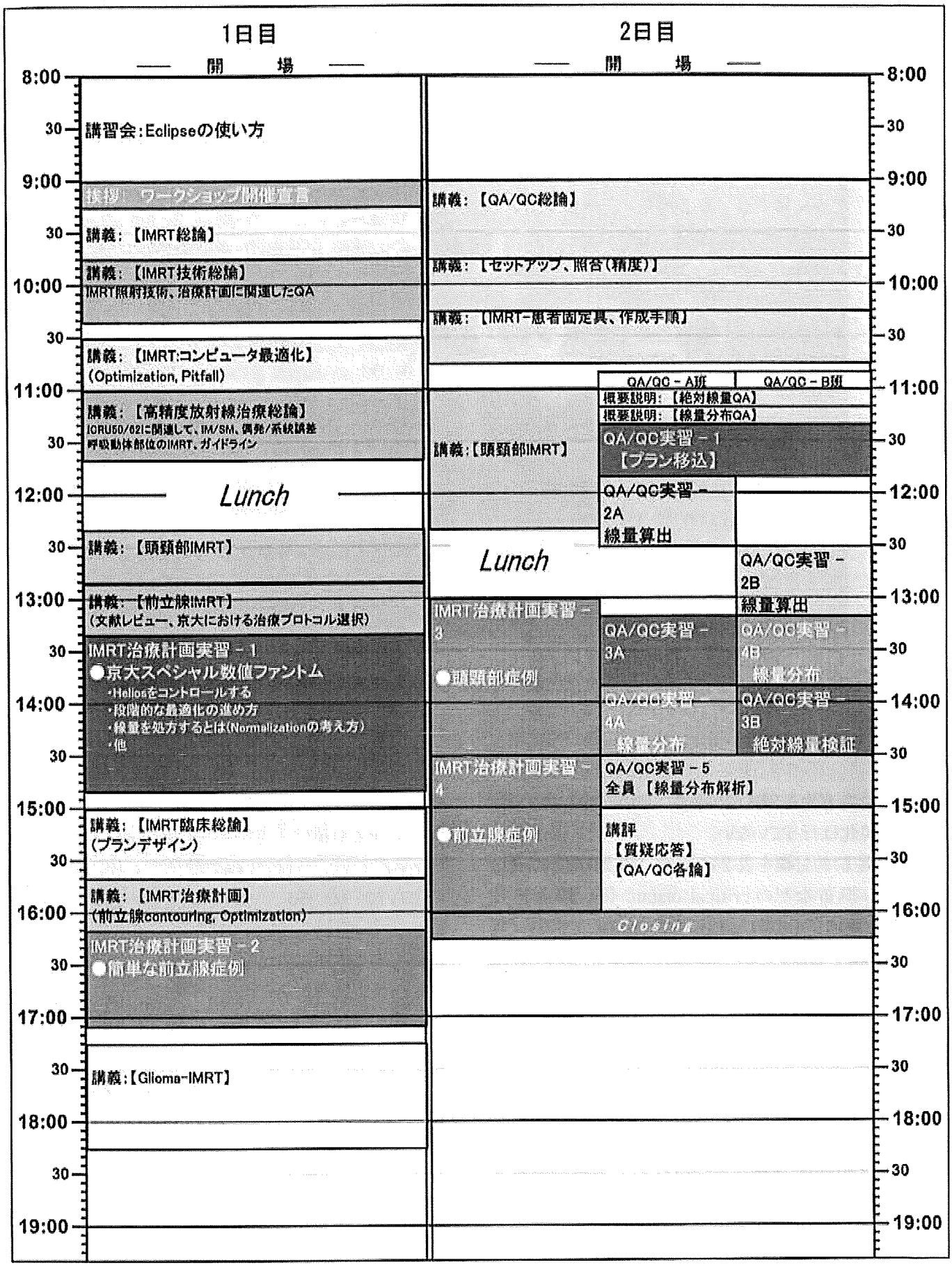

図5　京大病院高精度放射線治療ワークショップのプログラム例

❸ QA

治療計画の quality assurance（QA）は，絶対線量検証と線量分布検証からなる。許容値の目安として絶対線量で3%，線量分布で5%としている。これに達しない場合には，追加の検証を行う。

最終的にQA担当者と治療担当医との間で検討し，治療開始の可否を判断する。必要に応じて治療計画の修正を行い，まれではあるが治療中止の判断を行うこともある。

❹ 高精度放射線治療ワークショップ

IMRTの普及に向けた活動として，我々の施設では2005年より高精度放射線治療ワークショップを開催している。これまでに10回開催され約40施設から参加があった。

本ワークショップでは，講義に加えて治療計画やQAに関する実習を行い（図5），参加施設におけるIMRT導入の参考として頂いている。

■ おわりに

我々の施設におけるIMRTの実際について概説した。現在IMRTに関する標準的手法が確立したとは言えない状況であり，施設ごとに差異がみられる。今後，放射線腫瘍医や医学物理士，診療放射線技師等が建設的な議論を重ねていき，IMRTに関するコンセンサスを形成していくことが望まれる。

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Summary

Practice of IMRT in Kyoto University

Kyoto University started intensity modulated radiotherapy (IMRT) in 2000. During a year of 2008, we performed IMRT for 132 patients. For prostate cancer, prescription dose ranges from 74 Gy to 78 Gy based on its risk. Simultaneous integrated boost is used for head and neck cancer with 70 Gy for gross tumor, 63 Gy for high-risk area, and 56 Gy for low-risk area, respectively. In this article, practical aspects of our IMRT procedure are described.

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Review Article

Oligometastases and Oligo-recurrence: The New Era of Cancer Therapy

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Recurrence or metastasis of cancer has been considered to occur in the last stage of the patient's life. However, the new notions of oligometastases and oligo-recurrence have been proposed and the paradigm shift in the conceptualization of cancer metastasis or cancer recurrence. Oligometastases is the state in which the patient shows distant relapse in only a limited number of regions. Local therapy such as surgery, radiotherapy and radiofrequency ablation for the relapsed sites could thus improve patient's survival. On the other hand, oligo-recurrence is a notion similar to oligometastases. However, the conditions of oligo-recurrence has a primary site of the cancer controlled, meaning that all gross recurrent or metastatic sites could be treated using local therapy.

Key words: oligometastases – oligo-recurrence – local therapy – systemic therapy – paradigm shift

Recurrence or metastasis of cancer has usually been considered to occur in the last stage of the patient's life. From this perspective, even if only one site of recurrence or metastasis is present, the cancer can be seeded throughout the body hematogenously, meaning that local therapy cannot eradicate all cancer cells. Systemic chemotherapy can then only prolong life, rather than achieving cure. However, Hellman and Weichselbaum proposed an alternative notion in 1995, bringing about a paradigm shift in the conceptualization of cancer metastasis or cancer recurrence. This new notion is that of oligometastases (1).

OLIGOMETASTASES

Oligometastases is the state in which the patient shows distant relapse in only a limited number of regions. Local therapy such as surgery, radiotherapy and radiofrequency ablation for the relapsed sites could thus improve patient's survival. The state of oligometastases (Fig. 1) represents an important concept, but one important problem remains to be solved. Oligometastases did not eliminate the uncontrolled primary site with several distant metastases. Then, all metastatic sites were thoroughly treated with local therapy, which did not lead to disappearance of all gross tumors and not might have achieved cure. As the primary site was not or could not be treated with local therapy, the primary site would exacerbate sooner.

OLIGO-RECURRENCE

Niibe et al. (2–4) proposed the new notion of oligo-recurrence to overcome these problems. Oligo-recurrence is a notion similar to oligometastases. However, the conditions of oligo-recurrence are: (i) one to several distant metastases/recurrences (usually one) in one to several organs (usually one); (ii) primary site of the cancer controlled; (iii) one to several distant metastases/recurrences can be treated with local therapy; and (iv) no other distant metastases/recurrences other than those in (iii). This state of oligo-recurrence is shown in Fig. 2 and the differences

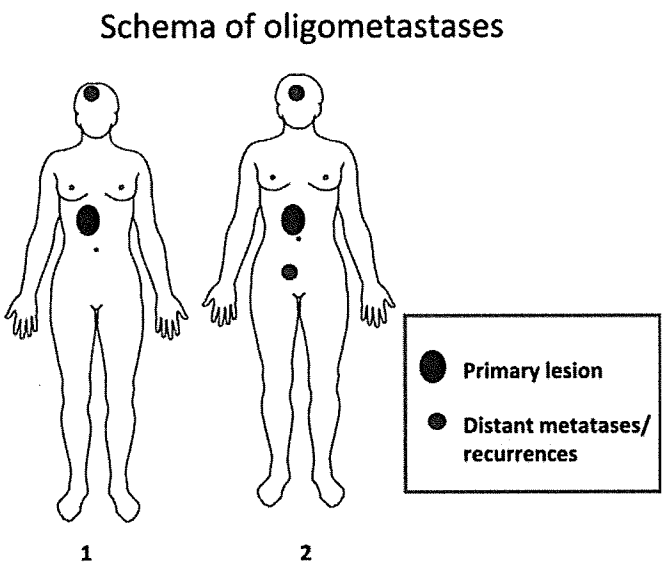

Figure 1. This is a schema of oligometastases. Schema 1 shows one distant metastasis/recurrence with a primary lesion. Schema 2 shows two distant metastases/recurrences with a primary lesion.

between oligometastasis and oligo-recurrence are listed in Table 1. In the state of oligo-recurrence, recurrent or metastatic sites with a controlled primary lesion were treated with local therapy, meaning that all gross recurrent or metastatic sites could be treated using local therapy.

SYSTEMIC THERAPY AND LOCAL THERAPY

Improvement of systemic chemotherapy including molecular-targeted therapy has allowed micrometastases

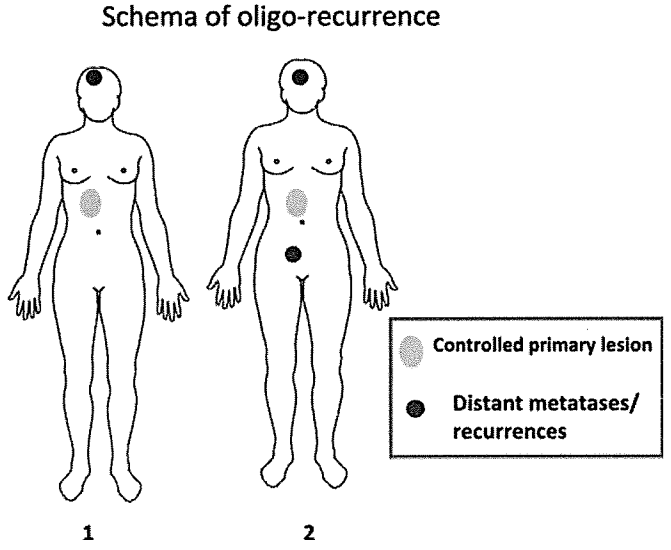

Figure 2. This is a schema of oligo-recurrence. Schema 1 shows one distant metastasis/recurrence with a controlled primary lesion. Schema 2 shows two distant metastases/recurrences with a controlled primary lesion. The biggest difference between oligometastases and oligo-recurrences lies in the uncontrolled or controlled primary lesion. Oligo-recurrence requires a controlled primary lesion.

Table 1. Oligometastases and oligo-recurrence

	Oligometastases	Oligo-recurrence
Reference	Hellman and Weichselbaum (1)	Niibe et al. (2,3,4)
Primary lesion	Uncontrolled/controlled	Controlled
No. of distant/metastases/ recurrences	One to several	One to several (one is better)

to be almost completely absent clinically. Theoretically, if several gross metastatic or recurrent sites could be eradiated by local therapy, these patients could be cured with concomitant systemic chemotherapy. Punglia et al. (5) reported that if systemic therapy improved, the role of local therapy would improve and proposed a figure for this correlation. Here, a new figure of the correlation between local therapy and systemic therapy is proposed (Fig. 3), showing that the role of local therapy is initially increasingly important as systemic therapy improves, depending on the sigmoid curve. The current status of cancer therapy lies in the range between 0 and A. However, in the future, extreme improvements in systemic therapy will decrease the importance of local therapy, because cancers will be diminished by systemic therapy alone such as intravenous anti-cancer drug infusion or oral anti-cancer drugs. All cancerous lesions including gross tumors and microinvasive tumors could be eradicated with systemic therapy alone. This desirable state is shown as B in Fig. 3. In the present status (range: 0–A in Fig. 3), systemic therapy is not yet powerful enough that local therapy is not required for eradication, particularly for gross tumor.

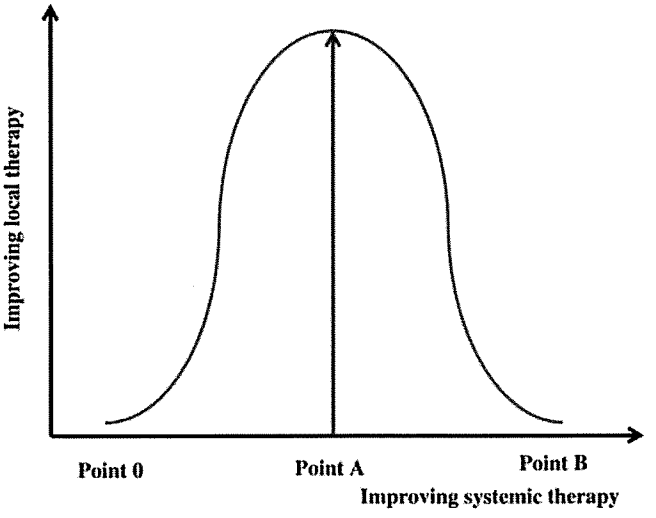

Figure 3. This shows correlations between systemic and local therapies. Until point A, the role of local therapy increases as systemic therapy improves. However, after point A, the role of local therapy decreases as systemic therapy improves, as all cancerous lesions can be cured by systemic therapy at point B.

BRAIN TUMOR

This section and the following four sections focus on organ-specific oligometastases and oligo-recurrence. First, oligometastases and oligo-recurrence of brain metastatic tumors are described.

Classification of metastatic brain tumors such as oligo-recurrence in recursive partitioning analysis (RPA) class I is widely recognized and accepted (6). This class I contains patients with: KPS $\geq$70; age $<$65 years; controlled primary; and no extracranial metastases. All RPA class I patients thus show oligo-recurrence. However, RPA class I requires age $<$65 years, so if age is $\geq$65 years and even KPS 100, the patient is classified as RPA class II. Rapid progress has recently been made in reducing the invasiveness of surgery and radiotherapy. The age of 65 years is thus no longer the limit of aggressive therapy. The RPA classification was developed in 1997, and more than a decade has passed since the proposal of this classification. Given recent advances in modern medicine, oligo-recurrence is considered to be more appropriate.

Kocher et al. (7) compared 117 patients with one to three previously untreated cerebral metastases who underwent stereotactic radiosurgery (SRS) between 1991 and 1998 with 138 patients with one to three lesions treated using whole-brain radiotherapy (WBRT) between 1978 and 1991. The first modality represents a more powerful treatment of metastatic brain tumors. Of these patients, 32 were classified as RPA class I (SRS, $n = 23$; WBRT, $n = 9$). Median survival was 25.4 months with SRS, compared with 4.7 months with WBRT ($P < 0.0001$). Furthermore, Andrews et al. (8) reported a Phase III trial comparing WBRT to WBRT plus SRS, in which multivariate analysis indicated that patients with WBRT plus SRS survived longer than those with WBRT alone in RPA class I ($P < 0.0001$). These findings suggest that more powerful local treatment was efficacious for RPA class I. As for oligo-recurrence involving the brain, Niibe et al. (9) reported 17 metastatic brain tumors in 10 patients treated with SRS and surgery achieved 3-year local control in 90% and 3-year overall survival in 51.9%.

LUNG TUMOR

Survival benefits were being reported for complete resection of metastatic lung tumors even in the 1990s. The International Registry of Lung Metastases (IRLM) reported that 5-year overall survival for patients with complete resection of metastatic lung tumors was 36%, compared with 13% for patients without (10). However, clinical outcomes with stereotactic body radiotherapy (SBRT) for Stage I primary lung tumors are reportedly almost the same as with surgery. Onihsi et al. (11) reported a 5-year overall survival of 70.8% for operable Stage I patients, equivalent to that with surgery. This indicates that oligo-recurrent patients, who have no extrathoracic lesions, could receive survival benefit from SBRT. In fact, Bloomgren et al. (12) first reported that 14 metastatic lung tumors in 10 patients treated with SBRT achieved 92% local control. Uematsu et al. (13) reported that 43 metastatic lung tumors in 22 patients treated with SBRT achieved 98% local control. Nagata et al. (14) using SBRT with 48 Gy in four fractions to the isocenter reported that nine metastatic lung tumors in nine patients achieved 67% local control. From the same institution as Nagata, Norihisa et al. (15) using SBRT at 48–60 Gy in four to five fractions to the isocenter reported that 43 metastatic lung tumors in 34 patients achieved a 2-year local control rate of 90% and a 2-year overall survival rate of 84.3%. These are excellent outcomes. However, all these analyses were retrospective. In 2009, Rusthoven et al. (16) reported a Phase I/II prospective study of SBRT for metastatic lung tumors. Thirty-eight metastatic lung tumors in 63 patients treated with SBRT achieved a 2-year local control rate of 96% and a 2-year overall survival of 39%. This result was inferior to that of surgery according to the IRLM. One of the important reasons of poor prognosis in SBRT is that the prospective study included patients with extrapulmonary lesions, meaning oligometastases and no oligo-recurrence. Limited to oligo-recurrence and the small numbers of lung metastases, overall survival may be better and might be almost equivalent to that of the IRLM (16).

LIVER TUMOR

SBRT has also been applied to metastatic liver tumors. In 1998, Blomgren et al. reported that a pilot study using 20–40 Gy in one or two fractions to the periphery of the planning target volume (PTV) achieved 95% local control (17). Several prospective studies have recently been reported. Herfarth et al. (18) reported 56 metastatic liver tumors in 33 patients treated with SBRT using 14–26 Gy per fraction (prescribed to 80%), achieving 78% local control. Kavanagh et al. (19) reported 28 metastatic liver tumors in 21 patients treated with SBRT using 12–20 Gy in three fractions to the periphery of the PTV, achieving 93% local control. Mendez Romero et al. (20) reported 34 metastatic liver tumors in 14 patients treated with SBRT using 37.5 Gy in three fractions (prescribed to 65%), achieving 94% local control. In 2009, Rusthoven et al. (21) reported 63 metastatic liver tumors in 57 patients treated with SBRT using 36–60 Gy in three fractions, achieving a 3-year local control rate of 92% and a 2-year overall survival rate of 30%.

BONE

Oligo-recurrence and oligometastases of bone have been reported in breast cancer. The summary is that high-dose radiotherapy relieves pain for a long time and can even improve overall survival.

Niibe et al. (4) reported on solitary bone metastases in seven patients treated with conventional radiotherapy. Six of

seven patients achieved complete remission of pain, which was prolonged at the last follow-up. Only one patient showed relapse of pain. This patient received 30 Gy in 10 fractions (BED_{10}, 39 Gy), representing the smallest dose in that series (other patients received 40–50 Gy in 20–25 fractions; $BED_{10} \geq 48$ Gy). In 2009, Milano et al. (22) reported 85 metastatic lesions in 40 breast cancer patients treated with SBRT, achieving a 2-year overall survival rate of 76% and a 4-year overall survival of 59%. Among these, the most favorable prognostic factor for breast oligometastatic patients was metastases only involving bone. This indicated high-dose radiotherapy using SBRT for bone metastases could contribute to patient survival.

LYMPH NODES

Oligometastases and oligo-recurrence of distant lymph node metastases have been reported for uterine cervical carcinoma. Uterine cervical carcinoma spreads through the lymphatic route rather than hematogenously (2,23). The first site of distant metastasis of uterine cervical carcinoma is the para-aortic lymph node. This has been confirmed in a large population-based study (2).

Hong et al. (24) reported 35 patients with isolated para-aortic lymph node recurrence treated with concurrent chemoradiotherapy achieving a 5-year overall survival rate of 34%. Kim et al. (25) reported 12 patients treated with hyperfractionated radiotherapy totaling 60 Gy combined with concurrent chemoradiotherapy, achieving a 3-year overall survival rate of 19%. To date, the largest study has been reported by Niibe et al. (3) in Japan. They reported 84 patients treated with conventional radiotherapy with or without chemotherapy achieved a 5-year overall survival rate of 31.3%, similar to the 38% for 5-year overall survival rate in a previous, small, population-based study in Japan (26). Recently, Choi et al. (27) reported that 30 uterine cervical and corpus cancer patients with isolated para-aortic lymph node recurrence treated by SBRT using a cyberknife achieved a 4-year overall survival of 50.1%.

CONCLUSIONS

Curative local therapy for oligometastases and oligo-recurrence represents a brilliant opening to the era of cancer therapy. Several decades ago, most metastatic and recurrent cancer patients died within a year. However, we cope with metastases or recurrences considering whether the state is oligometastases or oligo-recurrence. In the state of oligo-recurrence, all the gross tumors could be treated with local therapy, meaning curative treatment. However, in the state of oligometastases, clinicians should judge a primary site to be controlled or not before treatment. If the primary site is controlled, meaning oligo-recurrence, they should pursue to cure the patients. However, if the primary site is uncontrolled or extra-target metastases lesions exist, they intend to prolong survival not to pursue cure.

More appropriate target cancers, treatment modalities and schedules should be established for oligometastases and oligo-recurrence. Moreover, adjuvant chemotherapy will improve dramatically because of molecular-targeted drugs. Further clinical studies are required in this field.

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Conflict of interest statement

None declared.

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CLINICAL INVESTIGATION **Lung**

CLINICAL OUTCOMES OF STEREOTACTIC BODY RADIOTHERAPY FOR SMALL LUNG LESIONS CLINICALLY DIAGNOSED AS PRIMARY LUNG CANCER ON RADIOLOGIC EXAMINATION

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Purpose: Image-guided biopsy occasionally fails to diagnose small lung lesions, which are highly suggestive of primary lung cancer. The aim of the present study was to evaluate the outcome of stereotactic body radiotherapy (SBRT) for small lung lesions that were clinically diagnosed as primary lung cancer without pathologic confirmation.
Methods and Materials: A total of 115 patients were treated with SBRT in 12 institutions. Tumor size ranged from 5 to 45 mm in diameter, with a median of 20 mm.
Results: The 3-year and 5-year overall survival rates for patients with a tumor size ≤20 mm in diameter ($n = 58$) were both 89.8%, compared with 60.7% and 53.1% for patients with tumors >20 mm ($n = 57$) ($p < 0.0005$), respectively. Local progression occurred in 2 patients (3.4%) with a tumor size ≤20 mm and in 3 patients (5.3%) with tumors >20 mm. Among the patients with a tumor size ≤20 mm, Grade 2 pulmonary complications were observed in 2 (3.4%), but no Grade 3 to 5 toxicity was observed. In patients with a tumor size >20 mm, Grades 2, 3, and 5 toxicity were observed in 5 patients (8.8%), 3 patients (5.3%), and 1 patient (1.8%), respectively.
Conclusion: In patients with a tumor ≤20 mm in diameter, SBRT was reasonably safe in this retrospective study. The clinical implications of the high local control rate depend on the accuracy of clinical/radiologic diagnosis for small lung lesions and are to be carefully evaluated in a prospective study. © **2009 Elsevier Inc.**

Lung cancer, Stereotactic radiotherapy, Stereotactic body radiotherapy.

INTRODUCTION

Pathologic diagnosis is essential for the treatment of primary lung cancer. However, image-guided biopsy occasionally fails to diagnose small lung lesions, which are highly suggestive of primary lung cancer. When patients refuse re-biopsy or surgical resection, watchful waiting is usually indicated. There are other groups of patients in whom a pathologic diagnosis is very difficult to make, such as those with medical reasons for not being able to undergo biopsy and those with a history of surgical resection of non–small-cell lung cancer (NSCLC) and a small peripheral lung lesion on follow-up computed tomography (CT). The patients in the latter group often have difficulty undergoing a second surgical resection because of lowered respiratory function resulting from the previous surgery. Patients with cancer who are under watchful waiting are at risk for invasive growth of the primary tumor, lymphatic spread, and distant metastasis. Patients who choose to receive elective surgical resection of the small lung lesions to quantify the pathologic diagnosis may experience serious respiratory dysfunction. A proportion of the patients who do not have malignant tumors are inevitably overtreated and experience surgical complications.

Stereotactic body radiotherapy (SBRT) has been one of the treatments for Stage I NSCLC in medically inoperable patients. Recently, high local control and survival rates of SBRT were

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reported in several studies (1–7). Onishi *et al.* summarized the results of a Japanese series retrospectively and reported that a pulmonary complication rate of above Grade 2 arose in only 5.4% of patients (1). For the patients who received a dose compatible with the biologic effective dose (BED) of 100 Gy or more, the local control rate was 91.6%. For the patients who were judged to have been operable but who were treated with SBRT, the 5-year overall survival rate was 70.8%, which is equivalent to that achieved in the previously mentioned surgery series (1).

A serious question among radiation oncologists is whether it is ethically justifiable not to give SBRT to those patients who have peripheral lung lesions highly suggestive of lung cancer but who failed to have lung cancer diagnosed pathologically. If SBRT is as safe as image-guided re-biopsy and as effective as surgical resection, it may be ethical to give SBRT to these patients. However, we cannot answer this question, because the risk and benefit have not been compared between elective surgical resection, watchful waiting, and SBRT for small peripheral lung lesions without pathologic confirmation.

We have found in a national survey of SBRT that a small number of patients with the clinical diagnosis of NSCLC are actually treated with SBRT without pathologic confirmation in each institution. The aim of the present study was to evaluate the outcome of SBRT for peripheral small lung lesions that were clinically diagnosed as primary lung cancer without pathologic confirmation in 12 institutions during the past 10 years in Japan.

METHODS AND MATERIALS

Eligibility criteria

Twelve institutions were selected from the member institutions of the Japan Clinical Oncology Group trial, JCOG0403, for which the quality of clinical record and dosimetry accuracy of SBRT had already been evaluated by audit (8). This is a multi-institutional retrospective study using the same eligibility criteria, which were that (a) surgery was contraindicated or refused, (b) the tumor diameter was <50 mm, (c) tumors were highly suggestive of primary lung cancer and diagnosed as Stage I lung cancer clinically but the patients did not have a pathologic diagnosis, and (d) the performance status was 0 to 2 according to World Health Organization guidelines.

Patients

A total of 115 patients who were highly suspected of having lung cancer but who lacked pathologic confirmation of the disease were diagnosed with Stage I lung cancer clinically and treated with SBRT in 12 institutions during the last 10 years in Japan. The patient characteristics are given in Table 1. There were 93 cases of T1N0M0 and 22 cases of T2N0M0 disease. The number of medically operable and inoperable patients was 43 and 72, respectively. Tumor size was recorded at the maximum diameter on the CT scan taken at the start of radiotherapy. The median tumor size was 20 mm (range, 5–45 mm). The median follow-up period was 14 months (range, 1–142 months). There were 11 patients whose follow-up period was <4 months at the time of this analysis.

Diagnosis was based on CT findings and enlargement of the lesion on sequential examination with or without fluorodeoxyglucose (FDG)–positron emission tomography (PET) findings. The tumors were diagnosed as highly suggestive of primary lung cancer by diagnostic radiologists when there was definitive enlargement of the lesion on sequential CT examination and/or positive findings on FDG-PET without any metastatic lesion in the diagnostic evaluation. Several findings such as the configuration of the lung lesion were also used in the diagnosis. Of 72 patients who were examined with FDG-PET, 67 patients had positive findings on FDG-PET. Other clinical history and findings as well as laboratory findings were also used for diagnosis as much as possible to prevent inclusion of patients with metastatic lung tumors or inflammatory or granulomatous lesions in the study population.

Table 1. Characteristics of patients (115 patients)

Characteristic	Value
Age (y)	
Median	77
Range	50–92
Gender (*n*)	
Male	87
Female	28
Tumor size (mm)	
Median	20
Range	5–45
T stage (*n*)	
T1	93
T2	22
Medical condition (*n*)	
Operable	43
Inoperable	72

The reasons for the lack of pathologic confirmation were as follows: (a) bronchoscope- or CT-guided biopsy failed in 59 patients, and these patients refused re-biopsy or surgical resection; (b) 21 patients were not indicated for a biopsy procedure or surgery because of medical complications; (c) 14 patients refused a biopsy procedure as well as surgery even at the initial examination; (d) a biopsy was not indicated in 14 patients because their history of NSCLC was strongly suggestive of the new development of a second primary NSCLC, likely inoperable, and they refused surgery; and (e) a biopsy was not indicated in 7 patients because there was little possibility to confirm the pathology because of the tumor's small size, and these patients refused surgery.

Radiotherapy

All patients underwent irradiation using stereotactic techniques. Three-dimensional treatment planning was performed using non-coplanar static ports or dynamic arcs. Various techniques using breathing control or gating methods and immobilization devices such as a vacuum cushion with or without a stereotactic body frame were used to reduce respiratory internal margins. Appropriate margins were adopted for the clinical target volume and the planning target volume.

A total dose of 30 to 70 Gy at the isocenter was administered in two to 10 fractions. Using a linear-quadratic model, we defined the BED as $nd(1+d/\alpha/\beta)$, with Gray units, where n was the fractionation number, d was the daily dose, and the α/β ratio was assumed to be 10 for tumors. The BED was not corrected with values for tumor doubling time or treatment term. The median BED at the isocenter in this study was 106 Gy (range, 56–141 Gy).

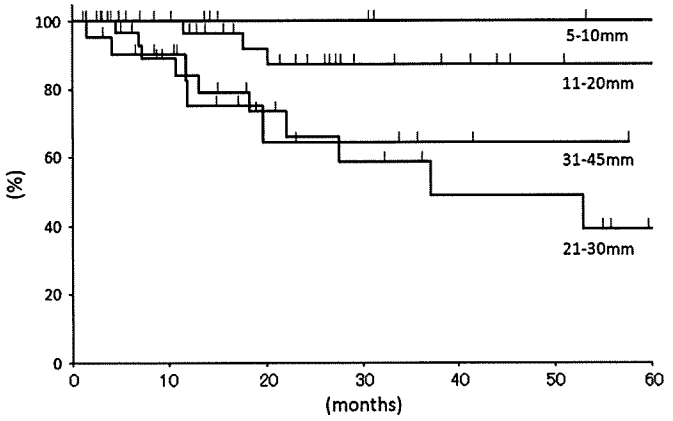

Fig. 1. Kaplan-Meier curve of overall survival rates for the patients with a tumor size (diameter) of 5 to 10 mm (n = 11), 11 to 20 mm (n = 47), 21 to 30 mm (n = 35), and 31 to 45 mm (n = 22).

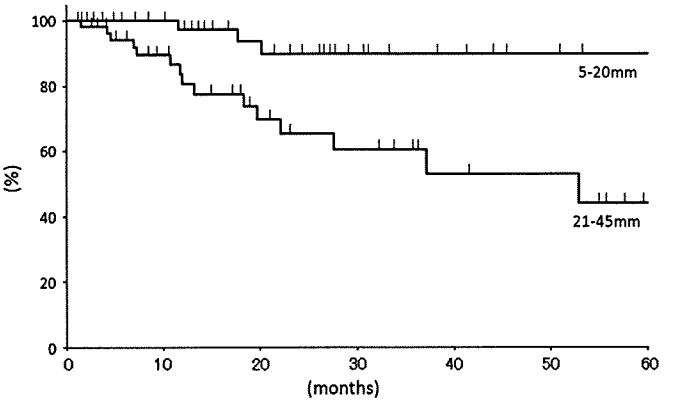

Fig. 2. Kaplan-Meier curve of overall survival rates for the patients with a tumor size (diameter) of 5 to 20 mm (n = 58) and 21 to 45 mm (n = 57). A statistically significant difference was found ($p < 0.0005$) between the two groups.

Ethical considerations

Use of SBRT was approved for Stage I lung cancer by the ethics committee in each institution. Clinically diagnosed Stage I lung cancer was not included in the ineligibility criteria at each institution. Written informed consent to receive SBRT was obtained from all patients. This retrospective study was approved by the ethics committee of each institution and was performed in accordance with the 1975 Declaration of Helsinki, as revised in 2000.

Statistical analysis

Overall survival rates were calculated from the first day of treatment using the Kaplan-Meier method. The log-rank test was used to calculate statistically significant differences. A value of $p < 0.05$ was considered to be statistically significant.

RESULTS

Survival

We separated the patients into four groups by tumor size at its maximum diameter, consisting of the 5 to 10 mm (Group A; n = 11), 11 to 20 mm (Group B; n = 47), 21 to 30 mm (Group C; n = 35), and 31 to 45 mm (Group D; n = 22) groups. The 3-year and 5-year overall survival rates were both 100% for Group A, both 87.2% for Group B, 58.7% and 48.9% for Group C, and both 64.5% for Group D (Fig. 1). When we excluded the 11 patients whose follow-up period was <4 months, there was no apparent difference in these results; 3-year and 5-year overall survival rates were both 100% for Group A, both 87.2% for Group B, and 58.7% and 39.2% for Group C, and both 67.7% for Group D.

The 3-year and 5-year overall survival rates were both 89.8% for patients with a tumor size ≤20 mm (n = 58) compared with 60.7% and 53.1% for patients with a tumor size >20 mm (n = 57) (p <0.0005; Fig. 2). According to medical operability, the 3-year and 5-year overall survival rates for operable patients (n = 43) were both 88.4%, compared with 67.0% and 60.9% for inoperable patients (n = 72) (Fig. 3). According to BED, the 3-year and 5-year overall survival rates for the patients with BED <100 Gy (n = 17) were both 71.8%, compared with 76.6% and 61.9% for the patients with BED ≥ 100 Gy (n = 98) (Fig. 4).

Local tumor response and distant metastases

Local progression occurred in 2 patients (3.4%) with a tumor size ≤20 mm and in 3 patients (5.3%) with a tumor size >20 mm. Lymphatic and distant metastasis were observed in 3 patients (5.2%) and 6 patients (10.3%) with a tumor size ≤20 mm and in 6 patients (10.5%) and 10 patients (17.5%) with a tumor size >20 mm, respectively. For the patients with BED <100 Gy, no local progression occurred.

Toxicities

Pulmonary adverse effects were graded according to the Common Toxicity Criteria for Adverse Events version 3.0. In brief, radiation pneumonitis was graded as follows: Grade 1, asymptomatic, radiologic findings only; Grade 2, symptomatic, not interfering with activities of daily life (ADL); Grade 3, interfering with ADL, O2 indicated; Grade 4, life-threatening, ventilatory support indicated; and Grade 5, death.

Of patients with a tumor size ≤20 mm in diameter, Grade 2 pulmonary complications were observed in 2 patients (3.4%), whereas no patients experienced Grade 3 to 5 toxicities. In patients with a tumor size >20 mm, Grades 2, 3, and 5 pulmonary toxicities were observed in 5 patients (8.8%), 3 patients (5.3%), and 1 patient (1.8%), respectively. A Grade 5 pulmonary complication occurred in 1 patient with interstitial pneumonia, which resulted in acute worsening from SBRT after 1.5 months. One case of radiation pleuritis, one case of intercostal neuralgia, and one case of rib fracture were observed, but these patients' symptoms were controlled easily by conservative treatment. Grade 2 pulmonary toxicity occurred in 3 cases (17.6%) in patients with BED <100 Gy and in 8 cases (8.2%) in patients with BED ≥100 Gy.

DISCUSSION

There is no doubt that pathologic diagnosis is the most accurate diagnosis for lung tumors. When possible, clinicians

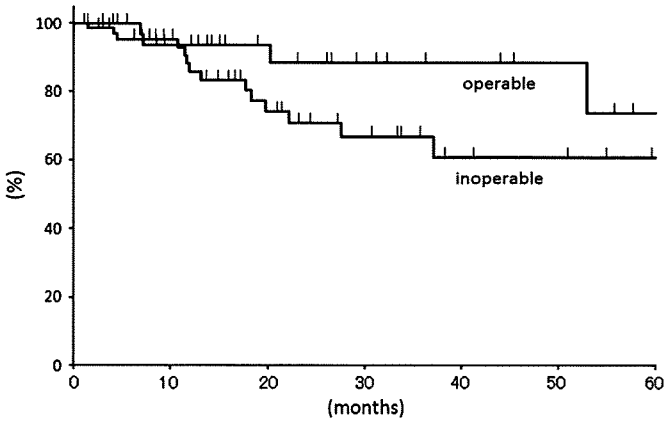

Fig. 3. Kaplan-Meier curve of overall survival rates for operable (n = 43) and inoperable (n = 72) patients. No statistically significant difference was found (p = 0.07) between two groups.

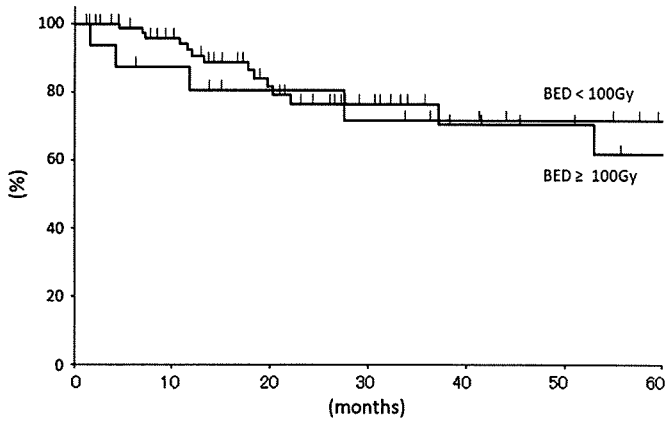

Fig. 4. Kaplan-Meier curve of overall survival rates for the patients with a biologic effective dose (BED) <100 (n = 17) and a BED ≥100 (n = 98). No statistically significant difference was found (p = 0.95) between the two groups.

should persuade patients to receive pathologic confirmation before SBRT and to receive surgical resection if they are operable. However, as we have observed in this retrospective study, for patients with poor respiratory function, pathologic confirmation of the small lung lesions is often difficult or life threatening and occasionally abandoned by pulmonologists and thoracic surgeons. Therefore, it is extremely important to find a subset of patients who would benefit from SBRT instead of the conventional strategy of watchful waiting or elective surgical resection.

In patients with clinically diagnosed lung cancer ≤20 mm in diameter, the 3-year survival rate was 89.8% in our series. Although the median follow-up is still short, the 5-year survival rate was projected to be 89.8% for these patients. Because of the very low complication rate for these patients, SBRT for inoperable patients highly likely to have Stage I lung cancer with tumors ≤20 mm in diameter may be justifiable. However, the excellent survival rates for those patients with tumors ≤20 mm may be partly caused by the inclusion of nonmalignant lesions in the radiation-treated patients. The clinical implications of the high local control rate depend on the accuracy of clinical/radiologic diagnosis for small lung lesions and are to be carefully evaluated in a prospective study.

Median follow-up period 14 months was relatively short, including 11 patients whose follow-up period was <4 months. However, 3- and 5-year survival data were not impacted so much by them because follow-up period of the other patients was much longer.

Onishi *et al.* reported that the patients treated with BED <100 Gy had a tendency to have worse clinical outcomes than those treated with larger dose in SBRT (1). In this study, there were only 17 patients who received BED <100 Gy. There was no significant difference in overall survival rates between those treated with BED <100 Gy and those treated with BED≥100Gy, probably because of the small number of the patients who received BED <100 Gy.

Improvement of clinical/radiologic diagnosis of small lung tumors is essential if SBRT is used for clinically diagnosed Stage I lung cancer. Before the introduction of FDG-PET, the percentage of benign diseases in the solitary lung nodules detected by plain chest X-ray or CT was reported to be 25% to 50%, which is obviously too high (9–12). However, improvement of imaging modalities has made it possible to diagnose small peripheral lung cancer much more precisely than before. There were recent reports that FDG-PET and PET/CT showed 88% to 96.8% sensitivity, 77% to 77.8% specificity, and 91.2% accuracy in diagnosis of primary lung cancer (13, 14). A combination of positive FDG-PET findings, enlargement of the nodule on CT image, and negative laboratory tests for worsening of inflammatory diseases would reduce the false-positive diagnosis of Stage I lung cancer. However, Nomori *et al.* reported that lung nodules that were <10 mm in size or that showed ground-glass opacity on CT image cannot be evaluated accurately by FDG-PET (15). Therefore, for solid round tumors ≤10 mm and those with ground-glass appearance, watchful waiting would be the preferable choice at present, and improvement in diagnostic imaging is warranted. In addition, even if small lung lesions are highly suggestive of primary lung cancer on clinical/radiologic examination, the possibility of small-cell lung cancer (SCLC), for which it is better to be given additional chemotherapy, cannot be excluded. Some tumor markers such as neuron-specific enolase or progastrin-releasing peptide are shown to have relatively high sensitivity and specificity for SCLC (16). Tumor marker screening has the potential to reduce the inclusion of SCLC, although the tumor size may be too small to detect marker elevation.

Recently video-assisted thoracoscopic surgery (VATS) for lung cancer has become a safe and common procedure. In comparison with open surgery, VATS is less invasive and is associated with less morbidity and mortality (17). However, a recent review showed that VATS still has a 3.3% to 13.4% complication rate for surgical biopsy and a 7.7% to 36.6% complications rate for lobectomy (17). In 567 patients with peripheral NSCLC ≤20 mm who were operable as evaluated by cardiopulmonary function tests and had no history of previously treated cancer, the complication rate was reported to be 6.6% for sublobar resection and 7.3% for lobar

resection with 1 operative death (18). In the present SBRT study, for patients with a peripheral lung tumor ≤20 mm who were often inoperable based on cardiopulmonary function tests and who could have a history of previously treated cancer, only 3.4% (2 of 58) experienced Grade 2 pulmonary complications and none experienced Grade 3 to 5 complications. Therefore, although the comparison of the complication between surgery and SBRT is difficult, SBRT can be regarded as a safer treatment than lobectomy using VATS and as safe as biopsy using VATS for patients with a tumor size ≤20 mm. On the contrary, for patients with a tumor size >20 mm, Grade 2, 3, and 5 pulmonary complications were observed in 8.8% (5 of 57), 5.3% (3 of 57), and 1.8% (1 of 57) of study patients, respectively. Because the risk of SBRT is not minimal for these patients, the indication of SBRT for clinically diagnosed Stage I lung cancer with a tumor >20 mm should be very carefully evaluated by members of the cancer board in each institution.

It is important to state that our study does not give any guidance for inoperable patients whose tumors are highly suggestive of benign lesions but that cannot be definitely determined not to be malignant, as this study looks only at those with tumors highly suggestive of malignant lesions. Patients with benign pulmonary lesion such as hamartoma, granulomatous inflammation, and focal fibrosis may require pathologic confirmation because these patients sometimes have tumors highly suggestive of benign lesions but that cannot be definitely determined not to be malignant. At present, it is obvious that VATS should be recommended for operable patients with tumors that are highly suggestive of benign lesions but that cannot be definitely determined not to be malignant, as VATS gives us pathologic confirmation.

CONCLUSION

In conclusion, in clinically diagnosed Stage I lung cancer patients with a tumor ≤20 mm in diameter, SBRT was reasonably safe in this retrospective study. The clinical implications of the high local control rate depend on the accuracy of clinical/radiologic diagnosis for small lung lesions and are to be carefully evaluated in a prospective study.

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