is an effective and safe treatment for patients with newly diagnosed, localized nasal NKTCL. The results of this study should serve as a basis for future clinical trials for this disease.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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JASTRO NEWSLETTER

一般社団法人
日本放射線腫瘍学会

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JRRS/JASTRO合同学術雑誌発行に向けて

JASTRO編集委員長
中野隆史

6 月から日本放射線影響学会(JRRS)／日本放射線腫瘍学会(JASTRO)の合同学術誌として新Journal of Radiation Research(JRR)誌の編集を開始しました。現JASTRO誌への投稿は2009年 5 月31日で終了し，新JRR誌への投稿受付を2009年 6 月 1 日から開始しました。新JRR誌は2010年 1 月号51号から発行を開始する予定です。

新JRR誌が実現に至った背景には，JASTRO誌をさらに国際的な学術情報の発信の場に発展させることがあります。最も早くこの目的を達成するための方法として，JASTRO誌を廃刊し，JRR誌をJRRS/JASTROの合同学術誌として再スタートすることを編集委員会ならびにJASTRO理事会の総意として決定しました。運営はJRRS(主幹事)とJASTRO(副幹事)を幹事学会として，今後はその他の放射線関連学会も参画して行う予定です。

JASTRO准会員も正会員と同じ条件で扱われます。勿論，非会員も新JRR誌への投稿が可能です。JASTRO会員にはJRRS会員と同様に，学会加盟年数により頁チャージ料を最大50％割引という特典がありますので，投稿規定を一度お読みください。

論文審査については，投稿論文の著者名等はブラインドにしないで審査を行い，JASTRO会員の投稿論文は原則JASTRO側のVice Editor in Chiefが対応致しますので，医学博士予定論文の投稿などに積極的に活用していただければ幸いです。JRR誌としては基本的には原著論文を重視致します。症例報告については，相当なインパクトのある内容でないと受理することは困難ですので，投稿に際して留意してください。JASTRO会員の投稿が増えますと，それだけJASTROのJRR誌に対する貢献が評価されますし，JASTROの国際的な学術評価も上がりますので，積極的にご投稿をお願い致します。JASTRO編集委員会としても新JRR誌を盛り立て，より評価の高い国際学術誌となるよう努力致しますので，ご協力を宜しくお願い致します。

と，このがん診療連携拠点病院の整備は，がん診療の均てん化が目的であったはずだが，東京都内においても拠点病院は都心部に集中している傾向はあり，一部の地域では放射線治療認定医の不在など，必ずしも十分な体制が整備されていない部分も残されている。今後の取り組みを期待したい。

がん拠点病院の実態—島根県の場合—

島根大学放射線治療科　内田伸恵

島根県のがん対策の現状

島根県は全国で最も高齢化率が高い県であり，がんは島根県における死亡原因の第 1 位となっています。島根県のがん患者さんが東京に抗がん剤治療に通いながら，新規抗がん剤の早期承認やがん医療水準の地域格差の是正を社会や行政に訴えました。これが，がん医療の均てん化の促進を大きな柱とする『がん対策基本法』の制定のきっかけとなったことは記憶に新しいことです。当時の島根大学病院長とがん患者さんの団体の会談での「今すぐ島根県にがん治療医を増やしてください」との訴えに，病院長が「専門医の育成には10年かかります」と答え，「われわれにはそんな時間はないのだ」と患者さんが憤慨された光景が放映されたことを覚えています。病院長の言うことも真実なのですが，事態はもっと切迫していました。

こうした経緯から2007年 9 月，島根県は全国自治体で最初に『島根県がん対策推進条例』を制定しました。さらに患者代表，医療関係者，学識経験者等による『島根県がん対策推進協議会』を設置し，2008年 3 月に『島根県がん対策推進計画』を策定するなど，全国に先んじたがん対策を進めています。がん患者団体の動きも活発で，県内の主な病院には「がん患者サロン」があり，自主的な運営や病院との連携を行っています。がん拠点病院長とがん患者団体との意見交換会，がんの診断や治療のための医療機器整備等を目的とした「がん対策募金」なども行われています。このように，島根県はがん医療をめぐる患者，自治体のアクションは近年大変活発となり，全国的にも注目されているものと思います。医療政策に関するシンクタンク日本医療政策機構(本部・東京都)が昨年行った都道府県のがん対策推進計画の比較調査では，島根県の計画が全国 1 位でした。これは国の目標値を上回るがん死亡率の引き下げ，がん薬物療法や放射線治療の専門医の倍増計画など，積極的な数値目標が評価されたものと思われます。今後，計画の実現が大きな課題です。

島根県内のがん診療連携拠点病院は，島根大学病院が都道府県がん拠点病院，がん拠点病院が 5 カ所の合計 6 施設です(図 1)。その概要を表 1 にお示しします。

がん薬物療法専門医やがん薬物療法認定薬剤師，専門看護師等も全く不足している状態です。県西部のE病院は放射線治療装置を有していません。内科・外科の医師不足が深刻となっており，放射線治療の開始は困難ということで，今年の更新において，がん拠点病院の指定を外れる見通しです。これにより，県中西部のがん拠点病院は 2 カ所から 1 カ所に減り，県内のがん医療格差が進むことが懸念されています。病院長とも何度か意見交換をしたことがありますが，胃がん等の症例は比較的多く治療されており，緩和医療やがん患者支援にも熱心に取り組まれています。今後がん拠点病院から外れても，県民にとって重要な病院であることには相違ないと思います。がん拠点病院の認定要件に放射線治療の項目があることは，がん医療にとっても，放射線治療の推進にとっても大変重要なことです。しかしながら，地域のがん医療の現状は，このようにまだまだ厳しい状況です。

がん医療に限定される話ではありませんが，卒後臨床研修制度の必修化に伴う研修医の県外流出，地域医療機関から大学への医師の引き上げ，地域の医療崩壊という構図も非常に厳しい現実となっています。2008年度の文部科学省調査では，島根県

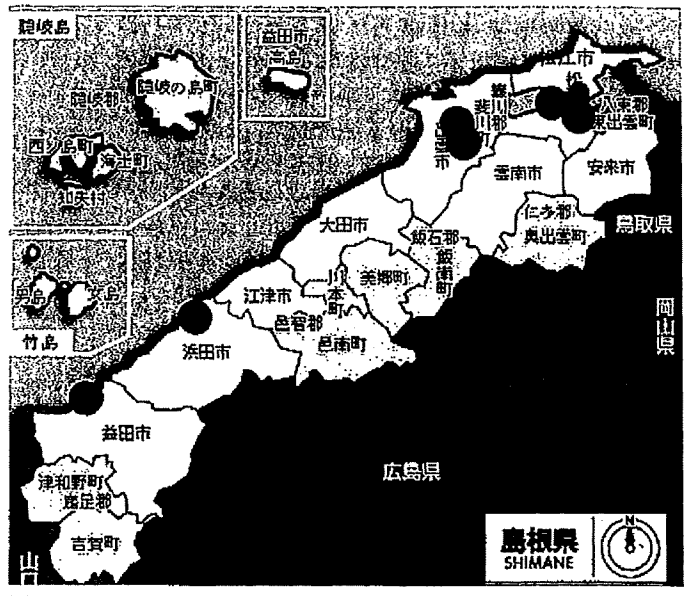

図 1

表 1

	A	B	C	島根大学病院	D	E
病床数	710	470	687	616	354	327
医師数	113	79	149	264	42	45
がん薬物療法専門医(暫定指導医)	(1)	-	(1)	1+(2)	(1)	-
JASTRO認定医	-	2	1	4	-	-
がん薬物療法認定薬剤師	1	1	1	1	1	-
放射線治療装置	○	○	○	○	○	×
密封小線源放射線治療装置	×	×	×	○	×	×
外来化学療法室	○	○	○	○	○	○
緩和ケア病棟	×	○	×	×	×	×
院内緩和ケアチーム	○	○	○	○	×	○
年間がん登録数	970	715	1,184	805	483	377

島根県HP，島根県がん登録集計等より抜粋改変
主たるデータは2007年度分

の研修医定着率は20％台で，全国最低レベルでした。地域での医療教育の充実，地域入学枠の拡大など医師不足・偏在の是正が大きな課題です。島根大学も自治体と協力して，県内出身者への奨学金，地域医療教育学講座の設置など，さまざまな対策を講じていますが，医療の現場で成果が出るのにはまだ時間がかかります。

島根県の放射線治療の現状

島根県内の放射線治療の現状については，2006年のJASTRO NEWSLETTERの「認定医が少ない県の放射線治療の現状と今後」で紹介させていただきました。それから 3 年経過しましたが，当時 2 名であった県内の認定医は現在 7 名，JASTRO認定施設が当院，認定協力施設が 2 施設と，3 倍(!)に増えています。

上述の日本医療政策機構による都道府県別の放射線腫瘍医数の人口比のデータでは，島根県は群馬県に続いて 2 位であり，全国第46位の県人口が影響している結果です。現実には放射線治療も県内の地域格差があります。東西に細長く，離島も有するなか，県東部には 5 カ所 6 台の放射線治療装置があるのに比べ，中西部には 1 カ所 1 台であることが 1 例です。通常なら外来で十分治療可能な前立腺がんの局所照射を，病院への通院時間や交通事情の問題で 7 週間以上の入院が必要となってしまう患者さんが多数おります。限られた医療資源を有効活用し，より多くの患者さんに良質な放射線治療を提供するためには，県内の放射線治療機能の役割分担と連携強化が必要です。放射線腫瘍医の育成とともに大きな課題であると考えています。

がん拠点病院の実態―神戸大学編―

神戸大学医学部附属病院放射線腫瘍科　佐々木良平

神戸大学医学部附属病院は2008年にがん診療連携拠点病院の指定を受けました。また，特定機能病院としての指定も併せて受けております。同病院が期待されている役割と実態を内部に働く一人の医師の視点で紹介させていただきます。

兵庫県は瀬戸内海と日本海に挟まれた縦長の県ですが，神戸市を中心とした阪神地域に人口が集中しているためか，県内に14指定されている「がん診療連携拠点病院」も実に10病院が阪神地域に所在しています。その中でも，われわれの施設の近隣には，兵庫県立がんセンター，兵庫医科大学病院，神戸市立医療センター中央市民病院等の実績があり，有名な大病院群が約 1 時間以内の移動距離の間にひしめき合っている実情があります。

個人的な見解を述べさせていただくと，そのような環境の中でも，神戸大学医学部附属病院は『がん対策基本法』の恩恵を受け，「がん診療連携拠点病院」の指定も含めてドラマチックに整備が進んだと思われます。それまでは，一部のがん診療に関して実績の高い診療科が，大学病院としての周囲関連病院との関係の中でがん診療の中心として活躍しておりましたが，「がん診療連携拠点病院」の指定に併

総説

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非小細胞肺癌の放射線治療

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■ はじめに

非小細胞肺癌治療における放射線治療の役割は多岐にわたるが，大別して，① 医学的に手術不能なI・II期，② 局所進行切除不能III期，③ 術前・術後照射，④ 骨転移・脳転移・上大静脈症候群・再発癌などに対する対症・緩和照射の4つが代表的である。

本稿ではこれらのうち，根治的治療の一環としての①～ ③について，現在までのエビデンスに基づく標準的治療と今後の展望について概説し，さらに三次元治療計画・近年進歩著しい治療技術についても述べる。

❶ 医学的手術不能I・II期

1）従来型放射線単独治療

早期肺癌の標準的治療は手術であるが，高齢や低肺機能・合併症など医学的理由で手術が不可能な患者には，放射線単独治療が適応となる事が多い。放射線単独治療についての成績をまとめたsystematic reviewを表1[1-3]に示す。通常分割60Gy前後の従来型放射線単独治療では，5年生存率15～20%前後，5年原病生存率25～30%前後と，症例選択のバイアスは大きいと考えられるものの，手術と比較して明らかに不良である。また，これらのreviewにより，再発形式としては局所再発が多いこと，高線量ほど治療成績が良好な傾向にあること，I期肺癌においては縦隔予防照射の利益は低いことが示された。

2）体幹部定位放射線治療

近年の著しい照射技術の発展により，肺原発腫瘍のみに多方向から高精度に集中して短期間に大線量を照射する体幹部定位放射線治療（stereotactic body radiotherapy：SBRT）が可能になった。方法の詳細については他を参照されたい[4]。日本の先行する14施設257症例の治療結果をまとめた報告によると，肺野型のI期非小細胞肺癌のうち，BED（biological effective dose）100Gy$_{10}$以上照射された215例では5年局所制御率84%と良好であった。さらに手術可能だが拒否され，BED100Gy$_{10}$以上照射された86例では，5年生存率70.8%と手術に匹敵する成績であった[5]。現在日本においてはJCOGで，IA期手術不能例・拒否例を対象にした48Gy/4fr/4daysのレジメンでの第2相試験（JCOG0403）の登録がほぼ終了し，IB期に対する線量増加第1相試験（JCOG0702）が開始された。他にもRTOGなど国外においても第1，2相臨床試験が進行中で，さらに手術と比較する第3相試験も計画されており，それらの結果が期待される。

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表1　医学的手術不能 I・II 期に対する従来型照射単独治療の systematic review

報告者・年	文献数	症例数	病期	線量（Gy）	5年生存率（%）	5年原病生存率（%）	備考
Rowell 2001[1]	26	2,003	I, II	BED 59～76	0～42	13～39	局所再発：6～70% IFRT*後の LN 再発：0～3%
Sibley 1998[2]	10	848	I	≈60	≈15	≈30	高線量で成績良好 予防照射意義少ない
Qiao 2003[3]	18	1,532	I	BED 62～76	21±8	25±9	局所再発中央値：40% 領域 LN 再発：0～3%

* IFRT：involved field radiotherapy

表2　照射単独 vs. 順次化学放射線療法についての第3相試験

報告者・年	導入化学療法	放射線療法（Gy）	症例数	MST**（M）	3年生存率（%）
Dillman	—	60	77	9.7	11
CALGB 1996[6]	CDDP/VBL	60	78	13.8	23
Le Chevalier 1991[7]	—	65	177	10.0	4
	VCPL*	65	176	12.0	12
Sause	—	60	152	11.4	11
RTOG/ECOG/SWOG 2000[8]	—	69.6HF	154	12.0	14
	CDDP/VBL	60	152	13.8	17

* VCPL：VDS, CPA, CDDP, lomustin, ** MST：median survival time

❷ 局所進行切除不能 III 期

1）照射単独治療から化学放射線治療へ

切除不能の定義は定まったものはなく議論のあるところであるが，一般に bulkyN2 または複数ステーション転移を有する IIIA 期以上は切除不能とされ，悪性胸水例を除く，IIIA・B 期が局所進行切除不能癌として根治的放射線治療の対象となる。1980 年代までは，60Gy 程度の胸部照射単独治療が標準治療であったが，80 年代後半以降，胸部放射線治療に導入化学療法を追加することで治療成績の向上（MST 約 10 カ月から約 13 カ月へ）が得られるようになった（表2）[6-8]。用いられた化学療法はシスプラチン（CDDP）+ビンブラスチン（VBL）などの旧薬（第2世代）レジメンであった。さらに大規模な NSCLC collaborative group による meta-analysis によっても，CDDP を含む導入化学療法の追加によって有意な生存期間の延長を認めることが証明され（HR0.87，p = 0.005，死亡リスク 13%減少，5 年生存率 2%上昇）[9]，順次化学放射線治療が標準治療となった。

2）順次化学放射線治療から同時化学放射線治療へ

続いて 90 年代後半～2000 年代にかけて化学療法の併用時期について順次併用と同時併用の比較試験が行われ，同時併用によりさらなる生存期間の延長が証明された（MST 約 13 カ月から約 16 カ月へ）。日本の West Japan Thoracic Oncology Group（WJTOG）の試験を含む代表的な 3 つの第 3 相比較試験の結果を示す（表3）[10-12]。Rowell らによる meta-analysis によると，同時化学放射線療法は放射線単独療法に対して 2 年で 7%，順次化学放射線療法に対して 2 年で 14%の死亡リスクの減少を認めたが，いずれも食道炎の発症の増加を認めた[13]。また Rolland らによる 7 つの試験，1,307 症例の meta-analysis では，CDDP を含む化学療法を同時に行うことにより，順次併用に比べて，3 年生存率が 5.7%改善した[14]。しかし有害事象の増加も認

表3　順次 vs. 同時化学放射線療法についての第3相試験

報告者・年	化学療法	放射線療法 (Gy)	症例数	MST (M)	4年生存率 (%)
Furuse WJTOG, 1997[10]	MVP (seq)	56	158	13.3	10.1
	MVP (conc)	56split	156	16.5	17.9
Curran RTOG 2003[11]	VP (conc)	60	205	14.6	12.0
	VP (seq)	60	203	17.0	21.0
	PVP (conc)	69.6HF	203	15.2	17.0
Fournel France 2005[12]	VinoP (seq)	66	101	14.5	14.2
	PVP (conc)	66	100	16.3	20.7

MVP：mtomycin/vindesine/cisplatin, VP：VBL/cisplatin, PVP：etoposide/cisplatin, VinoP：vinorelbine/cicplatin, HF：hyperfraction, Seq：順次, conc：同時

め，grade 3以上の食道炎の発症は4%から18%に増加した。化学療法の併用，特に同時併用は有効性も高いが，有害事象も有意に増加するため，適応症例の選択が重要である。年齢に関して高齢者のみを対象とした比較試験はないが，年齢別のsubset analysisによると，化学療法併用は70歳以上ではかえって治療成績が不良であったという報告[8]がある。しかし一方PSの良い高齢者（fit elderly）では生存率に差がないという報告[15]もあり，特にPSを考慮して適応を選択する必要があると考える。

3）併用化学療法：第2世代 vs. 第3世代

現時点における標準的併用化学療法は前述のようにCDDP＋第2世代full doseのレジメンであるが，根治照射の対象とならない進行肺癌において有用性の示されたプラチナ製剤＋第3世代新薬〔パクリタキセル（PTX），ドセタキセル（DTX），イリノテカン（CPT11），ビノレルビン（VNR）など〕を組み入れる試みが積極的に行われている。しかしfull doseの第3世代レジメンは放射線と同時併用した場合毒性が増強するため実施困難とされ，減量するか分割投与する方法が試みられている。しかしカルボプラチン（CBDCA）とPTXを分割しweeklyに投与する同時化学療法の比較試験（LAMP trial[16]，CBDCA39801[17]）の結果などは第2世代レジメンを上回る成績ではなかった。

日本において第2世代レジメンと第3世代レジメンの比較第3相試験が2つ施行された。Okayama Lung Cancer Study Group（OLCSG）ではCDDP＋DTX（DP）をMVPと比較した優越性試験が行われ，その最終報告が2008年ASCOにて発表された[18]。primary endpointである2年生存率はMVP群48.1%に対し，DP群が60.3%と有意に良好な結果であったが，5年生存率には有意差を認めなかった。血液毒性はMVP群で強く，食道炎・肺炎はDP群で多く認められた。また，WJTOGでは，CBDCA＋CPT11，CBDCA＋PTXをMVPと比較した非劣性試験（WJTOG0105）が行われた。すでに奏効率には差がなかったことが報告されており[19]，2009年ASCOでの最終報告が待たれる。

今後放射線との併用で期待されるその他のレジメンとしては，CDDP＋VNR，CDDP＋TS1などがある。前者は国立がんセンター単施設での第1相試験ではあるが，CDDP 80mg/m^2＋VNR 20mg/m^{2}とfull doseに近い用量が推奨用量と報告され[20]，短期成績も良好で今後のさらなる検討が期待される。

4）分子標的薬剤の併用

非小細胞肺癌への有効性が期待され，進行・再発肺癌において有用性が示されている分子標的薬剤としては，①EGFR-TKI（tyrosine kinase inhibitor）の中のgefitinib（Iressa®），erlotinib（Tarceva®），②抗EGFR抗体であるcetuximab（Erbitux®），③抗VEGF抗体であるbevacizumab（Avastin®）などがある。これらは，生物学的に放射線との併用効果も期待されており，化学放射線治療への上乗せ効果についても検討されつつある。

頭頸部腫瘍において化学放射線治療への上乗せ効果が証明されたcetuximabについては，局所進

表4　3D-CRT＋化学療法同時併用による線量増加の第1，2相試験

試験	試験デザイン	症例数	線量（Gy）	MTD (Gy/fr)	ENI	化学療法	MST (M)
North Carolina [25]	I/II	62	60～74	74/37	＋45Gy	導入＋同時 CBDCA/PTX	24
NCCTG N0028[26]	I	15	70～78	74/37	－	同時 CBDCA/PTX	(37)
CALGB 30105[27]	Randomized	43	74	－	－	導入＋同時 CBDCA/PTX	24.2
	II	26	74	－	－	導入＋同時 GEM	17.0
RTOG0117[24]	I/II	63	74～75.25	74/37	－	同時 CBDCA/PTX	(21.6)

ENI：elective nodal irradiation

行非小細胞肺癌においても化学放射線同時併用への同時併用の第2相試験（RTOG0324）が行われ，MST22.7カ月と良好な成績であり[21]，さらに第3相試験が予定されている。一方，gefitinibの同時併用についての第2相試験（CALGB30106）ではPS 2の症例ではMST 19カ月と比較的良好な成績であったが，PS 0～1症例では12カ月とむしろ不良であった[22]。今後は遺伝子変異の有無など感受性を考慮した個別化治療，費用対効果比も含めて，検討していくべき重要な分野である。

5）胸部放射線治療の進展：限局照射野による線量増加の試み

放射線治療についての現在の標準治療は1回2Gyの通常分割照射法で60Gy/30frを最低合計線量とするよう推奨されている。しかし，局所制御率はいまだ良好とはいえず，近年のコンピュータ治療計画の進歩も寄与して，3D治療計画を用いた線量増加の試みが行われている。RTOGではまず，化学療法を同時には行わずに予防的縦郭リンパ節照射（elective nodal irradiation：ENI）を省いた限局照射野（involved field radiotherapy：IFRT）で三次元原体照射法（three dimensional conformal radiotherapy：3D-CRT）を用いた線量増加第1，2相試験（RTOG9311）が行われた。肺のV20が25%未満では許容線量は83.8Gy/39fr，25～36%では77.4Gy/36frであった[23]。ついで化学療法同時併用（CBDCA＋PTX weekly）による線量増加第1,2相試験（RTOG0117）が同じく3D-CRTを用いたIFRTで行われ，V20を30%以下として許容線量は74Gy/34frとなった[24]。現在までに報告されている化学放射線同時併用時の線量増加第1，2相試験について代表的なものを表4[24-27]に示す。

このような線量増加の意義について，RTOGではCBDCA/PTX weekly同時併用，3D-CRT,IFRTを用いた60Gy/30frと74Gy/34frの比較第3相試験（RTOG0617）が2007年末より進行中である。日本においても，いくつかの第1，2相線量増加試験が進行・計画中でそれらの結果が期待される。

線量増加にあたっては，IFRTが用いられることが多いが，その根拠は主にretrospectiveなデータに基づいている。前述のIFRTを用いたRTOG9311では，中央経過観察期間16カ月で照射野外の縦郭リンパ節再発は9%と，局所制御率を考慮すれば低値であったと述べている[23]。中国においてIFRTでの線量増加とENIを含む通常線量の比較試験が行われ，IFI群において5年局所制御率（51% vs. 36%，p＝0.032）と2年生存率（39.4% vs. 25.6%，p＝0.048）の延長を認め，放射線肺炎の発症は低かった（17% vs. 29%，p＝0.044）と報告されている[28]が，症例数が少ないためかP値もぎりぎりであり，さらなる検討が望まれる。

❸ 術前・術後照射

1) IIIA/N2 症例の術前化学放射線治療

前述したように，IIIA/（non-bulky）N2 症例は切除可能と不能の境界領域であり，治療法の選択に議論が多い。この領域では，術前化学放射線療法を行った上で外科治療を追加する意義があるかについて，米国で intergroup trial（INT0139/RTOG9309）が行われた。病理学的に確認された 396 例の IIIAN2 例で，CDDP + VP16 +同時 RT45Gy 後に手術を加える群と 61Gy まで照射する群が比較された[29]。無再発生存期間中央値では手術群が有意に良好（14.0Mvs. 11.7M, p = 0.017）であったが，5 年生存率では同等（27.2% vs. 20.3%, p = 0.10）であり，治療関連死亡は手術群で有意に高く（7.9% vs. 2.1%），特に肺全摘群における手術死亡率は 26%と高率であった。これらの結果から IIIA/N2 期症例に対し，化学放射線治療後に手術を加える trimodality therapy は現在のところ標準的治療とはいい難いが，症例を選択すれば有用である可能性はあり，今後の研究がさらに必要な領域である。

2) 術後照射

術後放射線療法（postoperative radiotherapy：PORT）の有用性については，PORT Meta-analysis Trialists Group により 1998 年に 9 つの第 3 相試験 2,128 症例の meta-analysis の結果が報告された[30]。術後照射の追加により全生存期間はむしろ短縮し，術後 2 年生存率は PORT 群 48%，無治療群 55%であった。その傾向は I, II 期および N0, 1 例で顕著であったが，III 期，N2 症例では差は明らかではなかった。同グループにより再検討された追加報告でも同様の結果であった[31]。以上より I, II 期，N0, 1 症例に対しては，術後照射を行うべきではないとされている。N2 症例に対しては予後を悪化することはないが有用性も明らかではないとされた。その後，米国の SEER database からの大規模な報告[32]や，ANITA（Adjuvant Navelbine International Trialist Association）trial の subset analysis[33]では pN2 症例に限ると術後照射により生存期間が延長したという報告がなされた。これらのことから，pN2 症例に対する術後照射の有用性は再検討の余地があると考えられ，EORTC において pN2 症例に対する PORT の意義についての第 3 相試験が進行中である（Lung-Art trial）。

❹ 三次元治療計画・治療技術

1) 呼吸移動対策

肺癌の放射線治療における種々の物理的問題点の中でも，呼吸性移動への対応は非常に重要である。X 線シミュレーターで呼吸性移動を観察・評価する事も簡便で有用な方法であるが，CT 治療計画装置の導入に伴い X 線シミュレーターを持たない施設もある。そのような場合や，さらに高精度な呼吸移動対策を要する場合には近年の機械工学・コンピュータ技術の進歩によって種々の対策法が開発されており，施設の状況に応じて適切に取り入れていく必要がある。対策法の詳細は他を参照されたい[34]が，① 呼吸性移動による internal margin（IM）を正確に評価し，移動範囲を包容する方法と，② IM を減少させる方法に大別される。①としては slow scan CT，吸気呼気融合 CT，4D-CT などがあり，②には，呼吸ゲート法，息止め法，呼吸抑制法，動体追跡法などがある。両者を組み合わせることにより，より正確にかつ照射範囲を限局する照射が可能になる。SBRT においてはもちろん必須であるが，今後は進行肺癌における線量増加試験などでも肺など周囲正常臓器への線量を減少させつつ腫瘍への線量を増加させていくために必要になると思われる。前述の RTOG0617 ではいずれかの呼吸移動対策を必要条件としている。

2) 不均質補正の導入

CT を用いた三次元治療計画を行う意義のひとつに，不均質補正を用いて線量計算を行うことにより，より実際に近い線量分布が得られることがある。特に肺などの電子密度の低い臓器を含む肺癌放射線治療においてはその意義は大きく，JASTRO ガイドラインにおいても superposition 法相当以上のアルゴリズムを用い，不均質補正を行うことを推奨している[35]。しかしこの際に，2 次元治療計画や不均質補正を用いない三次元治療計画での治療経験との違いを認識し，各施設での品質管理・品質保証を十分に行う必要がある。例えば肺野を含む照射野では線量分布が不均一となり，同じ線量を処方する場合，不均質補正なしと比較して線量（MU 値）が低くなる可能

表5　NCCN v.1.2009によるリスク臓器の線量制約

リスク臓器	放射線単独治療		化学放射線治療	
	パラメータ	制限値	パラメータ	制限値
脊髄	Dmax	＜50Gy	Dmax	＜45Gy
肺	V20	＜40%	V20	＜35%
心臓	V40	＜100%	V40	＜50%
	V50	＜50%		
食道	V60	＜50%	V55	＜50%
腕神経叢*	Dmax	＜66Gy	Dmax	＜66Gy

* 腕神経叢の値はNCCNでは記載されていないため，RTOG0617の線量制約より引用

性がある事や，リスク臓器への線量制約の値も異なってくることなどに注意が必要である。

3) DVHによる正常組織の線量制約

三次元治療計画の意義のもうひとつにdose volume histogram（DVH）から導かれたパラメータを用いて正常組織の有害事象の発症を予測することがある程度可能になったことがあげられる。特に肺癌放射線治療における放射線肺炎に関しては研究が多く，実臨床に取り入れられている。Washington大学のGrahamらは非小細胞肺癌99例（照射単独58%）においてV20（20Gy以上照射される肺の全肺容積に対する割合）が32%を超えると重症な放射線肺炎の発症例を認め，40%を超えると発症率が高くなり17例中3例の死亡例を認めたと報告している[36]。当院の症例で検討した化学放射線同時併用71例ではさらに発症率が高く，V20が31%を超えた7例中2例に放射線肺炎による死亡を認めたため，化学放射線同時併用時にはV20が30%以下になるようにしている[37]。その他食道や心臓などでもDVHパラメータと有害事象の関連性の検討が行われ，それらを用いた正常組織の線量制約を行うことにより，より安全に放射線治療が行えるようになっている。線量制約の制限値についてはDVHの計算法（たとえば肺の場合の全肺容積は全肺－GTVや全肺－PTVの報告がある），放射線総線量，分割法，併用化学療法などによっても異なると考えられるため，一定したものがまだないが，一例として，2009年度版NCCNガイドライン[38]のものを表5に示す。各施設の治療法に合わせて，DVHによる線量制約を用いていくことが望まれる。

■ おわりに

非小細胞肺癌の放射線治療の中で，根治目的の治療にかかわる部分について，現在の標準治療と今後の展望について概説した。I期肺癌については，SBRTの初期成績は良好で，さらなる追跡と前向き臨床試験の結果が待たれる。III期局所進行肺癌については，80～90年代にかけて化学放射線併用療法による治療成績の向上が得られたが，まだ治療成績は良好とはいえない。併用する新規抗がん剤・分子標的薬剤の有用性の検討と共に，放射線治療としては，近年の著しい治療技術の発展によって安全に行うことが可能となった線量増加などに期待が寄せられている。

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Summary

Radiotherapy for non-small cell lung cancer

We reviewed the role of radiotherapy in the management of non-small cell lung cancer (NSCLC) . For stage I NSCLC, the initial results of stereotactic body radiotherapy (SBRT) have been promising and larger prospective trials are ongoing. For locally advanced NSCLC, concurrent chemoradiotherapy (CCRT) is the current standard of care for patients with good performance status. However, the prognosis of those patients is still poor. Radiotherapy combined with new third generation chemotherapy regimens and molecular target agents, and radiation dose escalation using novel IGRT techniques are under investigation.

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CLINICAL INVESTIGATION

VARIATIONS IN TARGET VOLUME DEFINITION FOR POSTOPERATIVE RADIOTHERAPY IN STAGE III NON–SMALL-CELL LUNG CANCER: ANALYSIS OF AN INTERNATIONAL CONTOURING STUDY

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Purpose: **Postoperative radiotherapy (PORT) in patients with completely resected non–small-cell lung cancer with mediastinal involvement is controversial because of the failure of earlier trials to demonstrate a survival benefit. Improved techniques may reduce toxicity, but the treatment fields used in routine practice have not been well studied. We studied routine target volumes used by international experts and evaluated the impact of a contouring protocol developed for a new prospective study, the Lung Adjuvant Radiotherapy Trial (Lung ART).**

Methods and Materials: **Seventeen thoracic radiation oncologists were invited to contour their routine clinical target volumes (CTV) for 2 representative patients using a validated CD-ROM–based contouring program. Subsequently, the Lung ART study protocol was provided, and both cases were contoured again. Variations in target volumes and their dosimetric impact were analyzed.**

Results: **Routine CTVs were received for each case from 10 clinicians, whereas six provided both routine and protocol CTVs for each case. Routine CTVs varied up to threefold between clinicians, but use of the Lung ART protocol significantly decreased variations. Routine CTVs in a postlobectomy patient resulted in V_{20} values ranging from 12.7% to 54.0%, and Lung ART protocol CTVs resulted in values of 20.6% to 29.2%. Similar results were seen for other toxicity parameters and in the postpneumectomy patient. With the exception of upper paratracheal nodes, protocol contouring improved coverage of the required nodal stations.**

Conclusion: **Even among experts, significant interclinician variations are observed in PORT fields. Inasmuch as contouring variations can confound the interpretation of PORT results, mandatory quality assurance procedures have been incorporated into the current Lung ART study.** © 2009 Elsevier Inc.

Non–small-cell lung cancer, Resection, Postoperative radiotherapy, Target volumes, Interobserver variability.

INTRODUCTION

The role of postoperative radiotherapy (PORT) in patients with completely resected non–small-cell lung cancer is still controversial. Despite increasing local control rates (1–3), a large meta-analysis has shown a detrimental impact of PORT on overall survival, particularly in patients with no mediastinal involvement (4). However, the meta-analysis has been criticized because the studies included may have led to higher morbidity and mortality rates resulting from the use of two-dimensional radiotherapy techniques, high doses and fraction sizes, and large-field radiotherapy that incorporated the entire mediastinum using suboptimal radiotherapy techniques and lacking modern verification procedures or trial quality assurance (QA) (5–7).

Recently, data from the Surveillance, Epidemiology, and End Results (SEER) database and an unplanned subgroup analysis of a Phase III trial suggested that PORT using more recent techniques may improve survival in patients with resected N2 disease (8, 9). This has renewed interest in evaluating PORT in this patient category. A new international Phase

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III trial, the Lung Adjuvant Radiotherapy Trial (Lung ART), has been activated to compare PORT with no PORT in patients with completely resected N2 disease, irrespective of the use of chemotherapy (10). However, the cornerstone of radiotherapy is the use of consistent and reproducible target definitions, and current literature suggested that many groups were using target volumes defined in the era of two-dimensional radiotherapy (7, 11). In addition, large interobserver variations in target volumes have been observed in patients presenting with lung tumors that were visible on CT or positron emission tomography (PET)—CT scans (12–15). It is conceivable that the lack of identifiable tumor after a radical resection may potentially result in even greater variations. In the Lung ART study, the use of conformal radiotherapy is mandatory, and the target volumes are tailored based on both radiologic and surgical findings. As a prelude to Lung ART, the present study was designed to identify potential variations in target definitions in an international setting. In addition, the ability of the Lung ART protocol to reduce the potential variations in defining clinical target volumes (CTVs) was studied.

METHODS AND MATERIALS

Study design

Seventeen radiation oncologists in Europe, Asia, Australasia and North America who were considered to be experts in the treatment of lung cancer were invited to participate in this study. Radiation oncologists who were invited to participate had to be members of the International Association for the Study of Lung Cancer and to be also actively involved in research in radiotherapy for lung cancer. All were attached to academic centers, had experience in treating patients with postoperative radiotherapy, and had access to CT-based treatment planning for this purpose. Each participating expert was asked to contour his/her current routine CTV for 2 patients eligible for PORT. For contouring purposes, a CD-ROM–based validated contouring program was provided (16), which contained complete CT datasets (slice thickness 2.5 mm) of both patients and a tutorial regarding use of the contouring program in PowerPoint format (MS Office). In addition, relevant patient details were provided in the first mailing. The CTVs were contoured using standardized window level settings and saved to the CD-ROM, which was then mailed to the study coordinator. Subsequently, details of the contouring protocol for Lung ART were mailed to experts approximately 2 weeks after response to the initial mailing, to derive a second set of contours (protocol CTV) of the same 2 patients. Contours from each observer were copied (made anonymous) to a template CT dataset of the corresponding patient (Fig. 1).

Patient 1 (post-lobectomy). The first patient had undergone a radical right upper lobectomy with a mediastinal lymph node dissection for a stage $pT_2N_2M_0$ tumor. Histology revealed a 3-cm adenocarcinoma with extension to the visceral pleura. Hilar nodes showed no metastases, but two out of seven explored ipsilateral mediastinal nodes (stations 4 and 7 right) showed tumor deposits (17) (Fig. 2). Adjuvant treatment consisted of administration of four cycles of systemic chemotherapy, after which the patient was referred for PORT.

Patient 2 (post-pneumonectomy). The second patient had received induction chemotherapy (three cycles of a platinum-based combination) for a 5-cm nodule in the right upper lobe extending to the visceral pleura, with both ipsilateral hilar and subcarinal nodal disease. As response evaluation revealed a partial response of the tumor and no hilar abnormalities, a right pneumonectomy and mediastinal dissection was performed. Nine lymph nodes were explored: three intrapulmonary and hilar nodes, two subcarinal nodes (station 7), and four paratracheal nodes (2 station 4R and 2 station 2R). Histology revealed a poorly differentiated large-cell carcinoma measuring 4 cm in diameter with 50% necrosis. Metastases were found in a subcarinal node and a right paratracheal node (station 4R). All resection margins were free of tumor, and the patient was referred for PORT for a stage $pT_2N_2M_0$ tumor.

Lung ART contouring protocol (Appendix A). The CTV includes the bronchial stump, the ipsilateral hilar node region, and any possible extension to the mediastinal pleura adjacent to the resected tumor bed. In addition, the mediastinal CTV is to include all the lymph nodes that lie between two noncontiguous nodal stations that have contained metastases at any stage. Based on the surgical literature, subcarinal (LN7) and ipsilateral paratracheal nodes (LN4) are always included in the CTV (Fig. 2). In the case of leftsided tumors, the subaortic and para-aortic nodes (LN 5 and 6) should be included in the CTV (Fig. 2). When metastases are identified in a nodal station, the next nodal station superior to it is included in the CTV, as is the nodal station immediately inferior to the lower involved mediastinal node. However, in some cases the volumes delineated for the CTV could become too large. For instance, in the case of LN7 involvement, LN8 should theoretically be included so that the lower limit will be at the gastroesophageal junction. Therefore, it was decided to define the boundaries more clearly in a table (Appendix B).

Analysis of clinical target volumes

Volumes of the routine and protocol contoured targets of each observer were determined, using a tracing tool in ImageJ (http://rsb.info.nih.gov/ij/). The outlines of all axial two-dimensional contours were traced, and the number of encompassed internal pixels (pixelsize 0.87*0.87 mm) and the number of contoured slices (slice thickness 2.5 mm) were calculated. In addition, both length in three orthogonal directions and center-of-mass (COM) coordinates of each CTV were determined. To determine the coverage of nodal stations to be included in the CTV, a gold standard for mediastinal nodal regions was generated by two clinicians (F.S. and S.S.) at the VU University Medical Center for both patients according to the definitions by Chapet *et al.* (18) using Eclipse v8.1 software (Varian Med. Systems, Palo Alto, CA).

Dosimetric analysis

To evaluate the influence of contouring variation on dose–volume histogram (DVH) statistics before and after use of the protocol, a dosimetric analysis was performed based on both the smallest and the largest target volume. Planning target volumes (PTVs) were generated by expanding CTVs with a margin of at least 5 mm in the mediolateral and dorsoventral directions and of 10 mm in the craniocaudal direction to account for tumor motion and variations in patient setup. A routine conformal treatment plan consisting of five fields using 6- to 15-mV photons was designed in Eclipse v8.1, based on a gold standard CTV contoured by the principal investigator (S.S.). The Lung ART protocol prescribed a dose of 54 Gy in daily fractions of 2.0 Gy. This plan was then projected on each PTV (smallest and largest routine and protocol PTV) and adjusted such that the 95% isodose volume tightly conformed the PTV while respecting dose constraints to organs at risk according to International Commission on Radiation Units and Measurements objectives (19). Specifically, it was aimed to limit the percentage volume of lung tissue outside the PTV planned to receive 20 Gy to 35% ($V_{20} \leq 35\%$) and the maximum spinal cord dose to 50 Gy. The DVHs were calculated to evaluate variability in toxicity

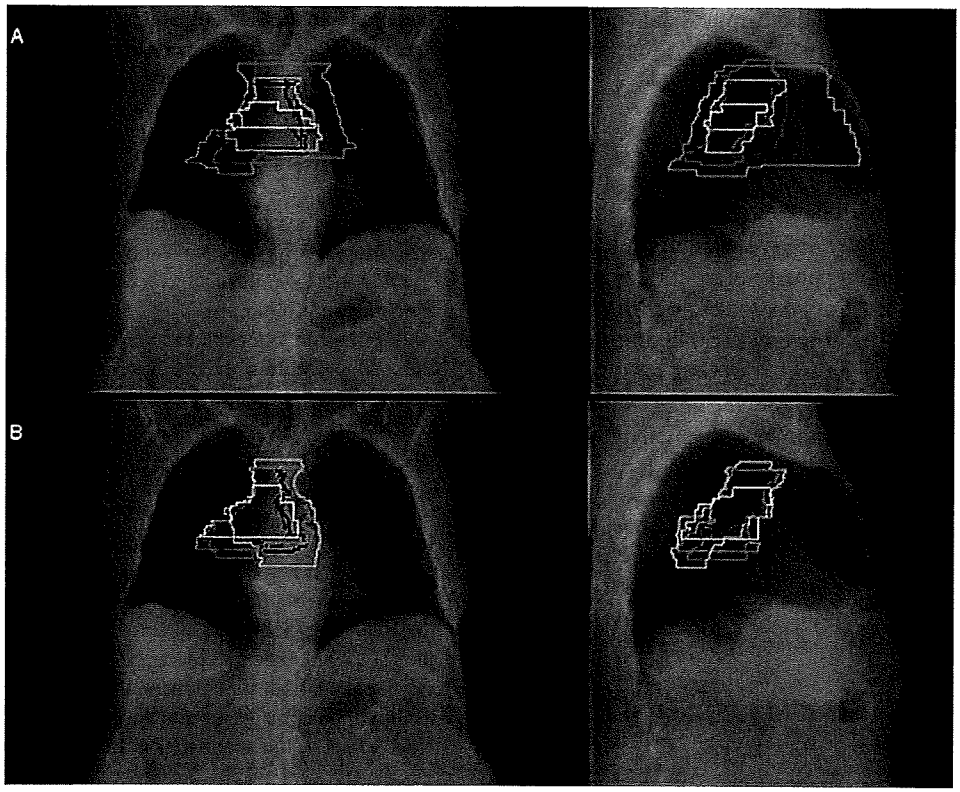

Fig. 1. Routine clinical target volumes (CTVs) (upper panel) and protocol CTVs (lower panel) from six observers projected on a digital reconstruction of a computed tomography dataset from the postlobectomy patient.

profile, and the following parameters were assessed: mean lung dose, total lung volume minus PTV receiving either ≥20 Gy (V_{20}) or ≥5 Gy (V_5), total cardiac volume percentage receiving ≥45 Gy (V_{45}), maximum spinal cord dose, and esophageal length receiving ≥45 Gy.

Statistical analysis

The variance between routine and protocol CTVs of different observers was assessed by constructing a mixed-effects model for each endpoint (*i.e.*, volume, length, or COM position). Contouring procedure and patient identifier were taken as fixed effects, whereas the observer identifier was taken as the random grouping variable. Significance was reported at levels 0.05 and 0.007, with the latter being the adjusted value for multiple testing using the Bonferroni method. Differences in nodal coverage between routine and protocol CTVs were evaluated using an F test in Excel (Microsoft Office 2003).

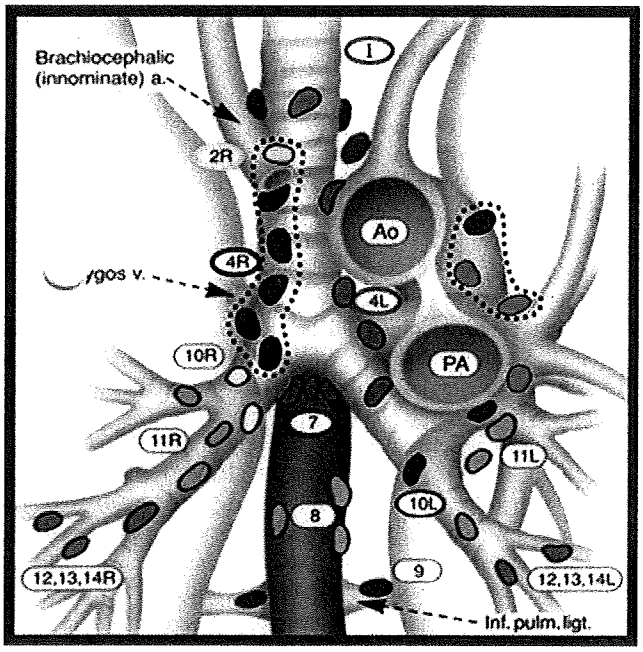

Fig. 2. Nodal staging system (Mountain-Dresler).

RESULTS

Number of datasets received

For each case, a total of 10 clinicians generated routine clinical target volumes (CTV); they included the principal investigator, who had knowledge of the protocol. Both routine and protocol CTV's for both patients were available from six expert observers. One participating clinician returned only a protocol CTV for both cases because the center did not perform routine PORT.

Analysis of clinical target volumes

Regarding experts who returned routine and protocol datasets, for the postlobectomy patient, the median routine CTV was 90.2 cc (range, 36.2–678.4 cc), and the median corresponding protocol CTV was 91.3 cc (range, 60.0–112.4 cc). For the postpneumectomy patient, the median routine CTV was 115.5 cc (range, 48.5–712.1 cc), and the median corresponding protocol CTV was 93.3 cc (range, 78.3–125.3). Regarding all experts, routine CTVs varied up to threefold between clinicians, but this variance was significantly reduced

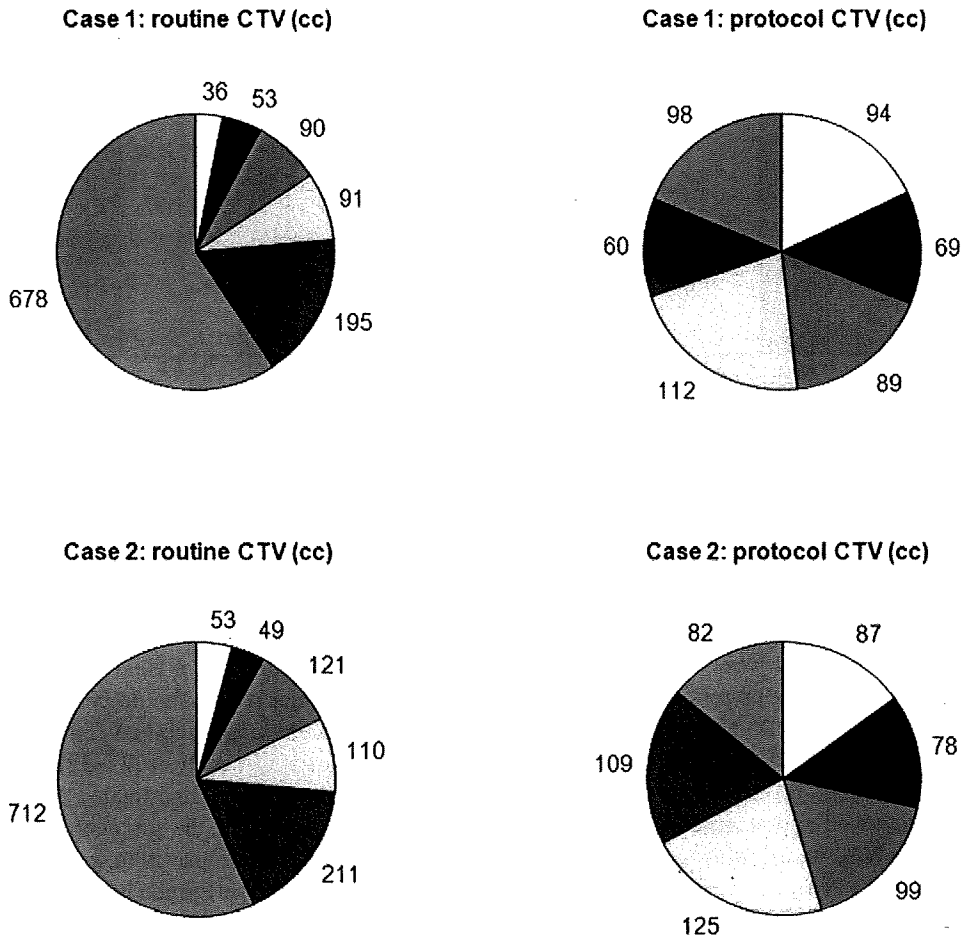

Fig. 3. Routine vs. protocol clinical target volumes (CTVs) (cc) from six observers for the postlobectomy patient (upper panel) and the postpneumectomy patient (lower panel).

for both cases when clinicians used the Lung ART protocol ($p < 0.007$) (Fig. 3). In addition, both the variance in cranial-caudal COM positions ($p < 0.007$) and contoured target lengths along the cranial-caudal Z axis were significantly reduced ($p < 0.05$) using the protocol. All results maintained significance when data of the observer with the most deviating CTV were excluded from analysis.

In both patients, the Lung ART protocol required the CTV to include nodal stations 2 right (LN2R), 4 right (LN4R), 7 (LN7), and ipsilateral hilus. Median coverage of LN4R and LN7 by routine CTVs were 82% (range, 44–97%) and 94% (range, 20–100%), respectively, for the postlobectomy patient. Use of the protocol resulted in an increased median coverage of LN4R ($p < 0.05$) (Fig. 4). Although median coverage did not significantly improve in LN7, the range between observers was much smaller with the protocol (73–100%) compared with routine (20–100%) contoured CTVs (Fig. 4). Similar results were seen in the postpneumectomy patient (Fig. 4). Median coverage of LN2R by routine CTVs was poor in both cases, with values of 0% (range, 0–47%) and 38% (range, 0–62%) in the postlobectomy and postpneumectomy patients, respectively. The results did not significantly improve using the protocol (Fig. 4).

Dosimetric analysis

The difference in 95% isodose volume between the smallest and the largest CTV was reduced from 1,802 cc to 216 cc in the postlobectomy patient and from 1,342 cc to 53 cc in the postpneumectomy patient. Variations in routine CTVs led to important differences in the risk of radiation-induced toxicity; *i.e.*, the V_{20} ranged from 12.7% to 54% in the postlobectomy patient, whereas corresponding values in the postpneumectomy patient ranged from 1.5% to 20.6% (Table 1). Similarly, large variations between experts were observed in mean lung dose, lung V_5, and cardiac V_{45} in both cases. When the protocol was used, differences between observers were significantly reduced, resulting in a more consistent toxicity profile (Table 1). The differences in both spinal cord doses and esophageal length receiving > 45 Gy between routine and protocol CTVs were not as striking as seen with the other parameters.

DISCUSSION

Studies planned to evaluate PORT should use not only modern radiotherapy techniques but also consistent target volume definition. The latter is particularly relevant because the lack of standardized protocol definitions in the past may

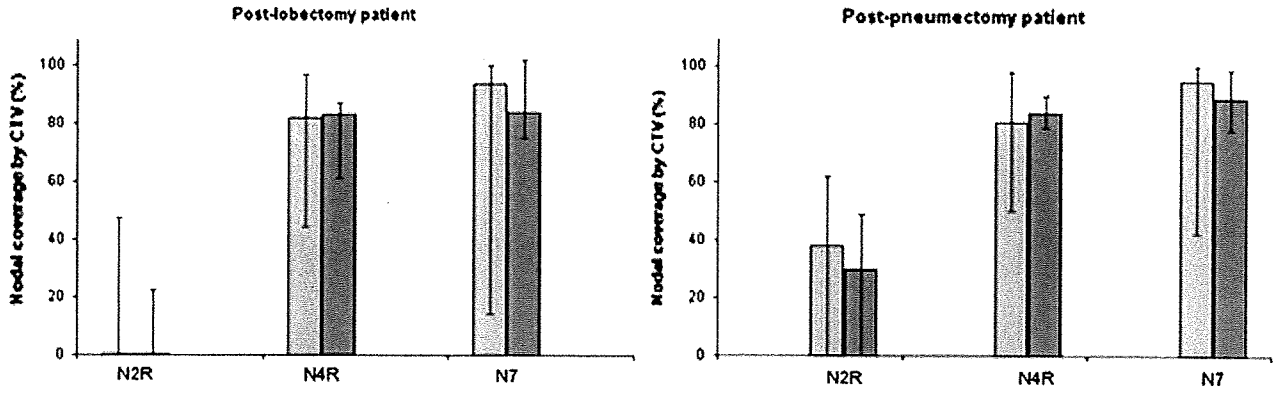

Fig. 4. Nodal coverage (%) by routine and protocol clinical target volumes in the postlobectomy patient (left) and the postpneumectomy patient (right).

have contributed to inconclusive results (10, 20); i.e., the total dose was often not standardized and excessively high (5), with variable field sizes influencing both local recurrence rates and radiotherapy-induced mortality (6). The results of the present study show that even among thoracic radiation oncology experts, large variability was observed in routine target definition for PORT, and the up to threefold variation resulted in important differences in DVH parameters. The potential influence of pulmonary and cardiac toxicity, arising from unnecessarily large fields, on the risk of radiotherapy-induced mortality is now well appreciated (6). Similar concerns are experienced with the use of adjuvant chemotherapy, which is presently the standard of care in patients with non–small-cell lung cancer and resected N1 and N2 disease (21). Follow-up after more than 5 years after adjuvant chemotherapy revealed an increase in mortality (22), a development that highlights the potential for long-term hazards after any adjuvant therapy for such patients.

Before the commencement of the Lung ART trial, protocol target volumes were developed by the Lung ART writing committee based on patterns of local recurrence after surgery (23, 24), lymphatic pathways, and results of the omission of elective nodal irradiation (25, 26). The present study revealed that use of the Lung ART protocol resulted in a large degree of consensus between clinicians. However, residual interobserver variability may still exist as a result of misinterpretation, lack of clear formulation, or ignorance of the protocol. This is supported by the finding that use of the protocol did not improve coverage of the upper para-aortal nodes (LN2R). Consequently, a clear definition of the boundaries of this particular region should be specified in the protocol.

Recent major intergroup trials have also included dummy runs as a part of QA analysis (27–32), but these studies differ from ours in that we investigated interobserver variability both before and after the protocol was provided, allowing for evaluation of the impact of the protocol. In addition, earlier dummy runs were performed using hard copies, whereas we used a CD-ROM–based contouring program containing complete CT datasets that can be run automatically on each Windows-based computer. Our previous study validating this CD-ROM tool has established a more realistic assessment of clinical variations than with hard copies, and it was shown that most clinicians were able to complete the exercise (16).

One limitation of our study is that none of the invited experts from North America finally participated in this study. Furthermore, experts were arbitrarily identified from members of International Association for the Study of Lung Cancer and European Organisation for Research and

Table 1. Variability in planning parameters between the smallest and largest target volumes

	Postlobectomy patient				Postpneumectomy patient			
	Routine		Protocol		Routine		Protocol	
	Range	Difference	Range	Difference	Range	Difference	Range	Difference
Planning target volume (cc)	148–1,342	(1,194)	297–382	(85)	187–1,262	(1,075)	275–308	(33)
95% Isodose volume (cc)	300–2102	(1,802)	518–734	(216)	446–1,788	(1,342)	556–609	(53)
Lung								
Mean lung dose (Gy)	8.0–26.1	(18.1)	11.6–15.3	(3.7)	3.4–13.4	(10.0)	4.0–4.1	(0.1)
V_{20} (%)	12.7–54.0	(41.3)	20.6–29.2	(8.6)	1.5–20.6	(19.1)	2.1–2.9	(0.8)
V_5 (%)	34.7–79.5	(44.8)	52.2–63.1	(10.9)	31.6–59.3	(27.7)	30.4–35.7	(5.3)
Heart								
V_{45} (%)	0–20.5	(20.5)	1.6–5.1	(3.5)	4.3–37.0	(32.7)	7.1–10.0	(2.9)
Spinal cord								
D_{max}	45.3–49.5	(4.2)	47.8–50.0	(2.2)	50.0–51.0	(1.0)	44.8–48.7	(3.9)
Esophagus								
Length receiving 45 Gy (cm)	4.5–11.5	(7.0)	6.8–9.5	(2.8)	5.8–12.0	(6.3)	7.5–10.8	(3.3)

Treatment of Cancer who were active in lung cancer and who were known to the study group. In addition, the participating experts themselves did not perform treatment planning; therefore, interinstitution variability in dose statistics could not be assessed. Instead, dosimetric impact of contouring variability was evaluated by designing a standard plan in our own institution, although we believe that this was of minor influence, as contouring variation seems to be the largest source of systemic errors in lung cancer (33). Furthermore, the results are based on a routine conformal plan consisting of five fields, whereas the use of three fields (which is allowed in the protocol) may have resulted in a more forgiving situation, leading to less striking differences between routine and protocol target volumes. In addition, this study did not account for interobserver variability with respect to shape of the contours, which has been reported to be imprecise between observers (34). Other factors besides the Lung ART protocol could have contributed to the reduction in contouring variability over a period of time, including test–retest reliability. We were unable to study the latter because the logistic difficulties involved in obtaining the full cooperation of all the invited experts were considerable.

This dummy run test was part of the first phase of an external QA program, and the results were sent to the QA team for protocol validation. The magnitude of the observed differences led to a decision to invest in a web-based dummy run for the Lung ART trial. This ongoing study will address the above issues in a more representative population of thoracic radiation oncologists. The next step will include collection of the plans and its verification images for the first patient from each participating center. Subsequently, 15% of the plans will be collected by the QA team to ensure protocol adherence in centers where plans of the first patients were adequate, whereas plans of the patients included in the RT arm will be considered for revision in centers where plans were not adherent to the protocol.

CONCLUSIONS

The large interobserver variation in target definition seen among experts is a confounding factor in clinical outcomes of multicenter clinical trials, emphasizing the need for standardization. A protocol defining target definitions was shown to serve this purpose and is therefore incorporated in the QA program of the Lung ART.

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APPENDIX A: CONFORMATIONAL POSTOPERATIVE RADIOTHERAPY

According to randomization, patients will receive or not receive postoperative radiotherapy (PORT). We recommend that patients randomized in the treatment arm start PORT as soon as possible after randomization. No concomitant chemotherapy is allowed. At least 10 days' interval between the last day of chemotherapy and PORT is requested. This interval may be extended in case radiosensitizing drugs such as gemcitabine have been used, or when the patient does not have full haematologic recovery from the chemotherapy.

Radiotherapy technique

High-energy photons (≥6 MV) should be used. The planned dose to the International Commission on Radiation Units and Measurements reference point is 54 Gy in 27 fractions of 2.0 Gy. The radiotherapy will be given once each day, 5 days per week. The use of conformal techniques is mandatory. A planning computed tomography (CT) scan in treatment position should be used, with a maximal slide thickness of 5 mm for the whole thorax. The use of intravenous contrast is recommended. All target volumes as well as the critical organs should be delineated on this CT scan. Dose–volume histograms (DVH) of all target volumes—resected clinical tumor volume (rCTV), clinical target volume (CTV), and planning target volume (PTV)—and of all critical organs (lungs, cardiac volume, and spine, with or without esophagus) as described in the following section are required. All patients should be treated with a minimum of three fields. All fields should be treated daily.

Definition of volumes

rCTV in the mediastinum. This corresponds to lymph nodes involved according to the pathologic report of the lymph node exploration. The bronchial stump, the homolateral hilar node region, and the eventual extension to mediastinal pleura facing the resected tumor bed completely resected will always be included in the rCTV.

CTV in the mediastinum. In the CTV will be included the rCTV plus a margin corresponding to the upper and lower lymph node station to the involved lymph node area. All the lymph nodes that lie between two noncontiguous node stations that are involved will be included in the CTV. Because of the frequent involvement of subcarinal (LN7) and paratracheal nodes (LN4) on surgical series, these stations will also be systematically included in the CTV.

In the case of a leftsided tumor, the subaortic and the paraaortic nodes (LN 5 and 6) should also be included in the CTV because they are very often involved (as shown in Appendix B). The homolateral supraclavicular region will not be included systematically in the CTV.

PTV. Owing to organ movements and to setup uncertainties, an additional margin of at least 0.5 cm (lateral, anterior, and posterior) and 1 cm (superior and inferior) is recommended. The margins may be individualized according to 4D-CT scan data and/or measurements of the daily setup error. For patients who have had a positron emission tomography (PET)—CT scan before treatment, all data will be collected concerning positive nodes. However, only surgical positive nodes will be included in the rCTV.