47.8%, respectively). In addition, refinement of the preoperative work-up to screen cN2 disease and distant metastasis also contributed to the higher OS rate of pN2.

We defined four nN categories according to the number of nodes with metastasis and examined the respective survival curves. All the patients were stratified into four prognostically distinct groups by the nN classification. When we tried to validate the results across each pT stage, a clear tendency of deterioration of OS from nN0 to nN3 in the same pT stage can be observed, and the curves were split in pT1 and pT2 stage. The results indicated that nN category was a prognostic factor even in the same pT stage. In the higher pT stage of pT3 and pT4, however, the curves were not apart from each other. In addition to the small number of the cases, the other reason may be that the prognosis of the higher pT stage was always poor regardless of the number of metastatic lymph nodes, so the prognostic effect of nN category was not well demonstrated in these populations.

In a multivariate analysis, the nN category was shown to be an independent prognostic factor for both OS and DFS. Furthermore, the nN category could be used to subdivide pN1 and pN2 patients into two (nN1 and nN2) and three (nN1, nN2 and nN3) prognostically distinct subgroups, respectively. These results showed that the nN category has a powerful discriminative ability with respect to the prognosis and that the pN1 and pN2 categories are prognostically heterogeneous. However, the survival of the nN3 subgroup in pN1 patients was not significantly different from that of the nN1 and nN2 subgroups. It seems that the nN classification does not have as strong a discriminative ability in pN1 as in pN2 patients. It is difficult to explain this finding; however, it may be, in part, due to the small size of the nN3 subgroup ($n = 7$) in pN1 patients. Another possible explanation is that lymph node fragments were removed. During the operation, some of the N1 lymph nodes were most likely removed in fragments instead of intact because of adhesion to the bronchus and lung tissues. Each fragment may have been counted as a single node during the pathologic examination. Thus, the true number of metastatic lymph nodes may have been overestimated, and this would bias the results toward null. In contrast, most of the mediastinal lymph nodes (N2) were removed en bloc with the adjacent soft tissue, and fewer fragments than N1 nodes were produced. All these factors may have contributed to the observed results.

When we subdivided the nN category into pN1 and pN2 subgroups, no significant survival difference was observed between the two subgroups. This indicated that, for metastasis in the same number of lymph nodes, the anatomic location of the positive node (N1 or N2) is not important for postoperative survival. We tend to agree with the opinion that the overall disease burden, rather than the anatomic location of lymph node involvement, has the most important influence on prognosis.[11] Based on the finding in this study that the pN2 stage was accompanied by more lymph node metastasis than the pN1 stage, we postulate that even the slightly higher DFS rate in pN1 than pN2 was attributed to the smaller number of metastatic lymph nodes.

Despite the benefits of nN category for predicting survival, it also has some limitations. As we discussed above, some lymph nodes were inevitably removed in fragments, especially in the N1 region, which could lead to an overestimation of the number of metastatic nodes. Such an overestimation would bias the results of this study toward null, and the true association between the nN category and survival may be stronger than what we observed. However, when the nN category is used clinically as a prognostic tool, the survival risk of patients may be overestimated because of the presence of nodal fragments. To avoid the overestimation, the surgeon should remove the lymph nodes en bloc with the adjacent soft tissue to avoid fragments. If the fragment is inevitable, it is necessary for the operator to put the fragments from one single lymph node into a same bottle and label it definitely.

Second, a sufficient number of retrieved lymph nodes is essential to evaluate the true number of metastatic nodes. In gastric cancer, at least 15 removed lymph nodes are required to assure the reliability of the pN classification.[20] In lung cancer, there have long been controversies regarding the extent of lymphadenectomy.[18,21–23] Some reports have suggested that the optimal number of removed lymph nodes is 11 to 16 to accurately assess stage I lung cancer.[24,25] In the study by Lee et al.,[15] the removal of 11 nodes was set as a threshold for inclusion in their study. In our study, we did not set a threshold. We performed selective lymph node dissection based on the lobe-specific patterns of nodal metastasis for all but the high-risk patients. We think that the number of metastatic lymph nodes should be stable as long as less dissection is based on the idea of the lobe-specific nodal metastasis.[16,17,21,22]

Third, it is difficult to accurately assess the number of metastatic lymph nodes both preoperatively and in nonsurgical patients by CT scan or other methods currently used. Although PET scan can discriminate some metastatic lymph nodes, this is not sufficient to determine the nN category. Therefore, the nN category will contribute less to determine the optimal treatment before surgery. New methods that are capable of identifying each metastatic lymph node for nonsurgical patients will need to be developed.

Finally, the optimal category definition for the number of metastatic lymph nodes needs to be further explored. In this study and previous studies by Lee et al.[15] and Fukui et al.,[9] four categories were defined, and the patients without lymph node metastasis were grouped into a single category. However, for patients with metastatic lymph nodes, the categories had different definitions. Both the other two studies showed the prognostic significance of the number of metastatic lymph nodes based on their category definitions. Because the data are from different institutes, it is difficult to discuss which category definition is the best. Further studies are needed.

In summary, our results demonstrated that the location-based pN stage classification had a poor discriminative ability with regard to the prognosis in resected NSCLC, and patients in pN1 and pN2 are prognostically heterogeneous. Despite the limitations, the nN category as defined in this study is a better prognostic determinant than the location-based pN

stage. The overall disease burden, rather than the anatomic location of lymph node involvement, may have the most important influence on the prognosis. Furthermore, the number of metastatic lymph nodes is a more objective measure than their location, because errors could be made in determining the location of metastatic nodes. Therefore, we believe that the number of metastatic lymph nodes should be considered for the nodal stage classification in the future.

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特集　悪性腫瘍の術中病理診断を効果的に活用する―どこを検索すべきか，どう対応すべきか

肺癌

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臨　床　外　科

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肺癌

Significance of intraoperative pathological examination in lung cancer surgery

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【ポイント】

◆ 進行癌では手術適応の判断のため，早期癌では縮小手術適応の判断のために術中病理診断が行われる．

◆ 術中病理診断の部位には胸水，胸膜結節，原発巣，副腫瘍結節，リンパ節，肺実質・気管支切離断端がある．

◆ 各部位の術中病理診断を十分活用することにより，肺癌に対するより適切な治療法の術中選択が可能になる．

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はじめに

多くの固形癌同様，肺癌に対する治療においても外科切除は重要な役割を担っている．肺癌の外科治療において，完全切除の有無は絶対的な予後因子であり，完全切除可能かどうかの予測はまず画像的に行われるが，画像診断の発達した今日でも，その判断が難しい場合が少なくない．さらに，術中の肉眼所見や触診でも判断しかねる場合には，術中病理診断による最終判断が必要になる．肺癌の手術は基本的に肺実質を減量する手術であり，肺は肝臓のように再生しない臓器であるから，多かれ少なかれ必ず機能低下を引き起こす手術である．したがって，予後を改善しないばかりかQOLも低下させる結果を招く不完全切除は極力回避したい．

進行肺癌の場合，肺全摘術のような肺実質の切除量が多い手術がしばしば必要となるが，これは肺機能低下によるperformance status（PS）の著しい悪化を招き，術後の追加治療にも支障をきたすため，その適応にはきわめて慎重になるべきである．様々な治療法，治療薬が開発されている現代においては，患者にとって肺を切除することが本当に最良な選択肢なのかを真摯に，そして客観的に判断することが重要である．消化管の悪性腫瘍の場合には，切除しないと狭窄による通過障害が生じて逆にQOLが低下するため，不完全切除を覚悟のうえで切除することがあるが，肺癌ではそのような状況は少ない．かつてのように“何が何でも取る”という時代は肺癌の外科治療では過ぎ去っており，術中病理診断の併用は欠かせない．

一方，早期肺癌の場合には，積極的縮小手術が近年広く行われるようになってきている．縮小手術には実質切除量の縮小とリンパ節郭清範囲縮小の2通りがあるが，いずれの場合にも縮小手術の適格性を術中に判断するために原発巣，肺切除断端，摘出リンパ節などの術中病理診断を行うことが多い．

本稿では，一般的な開胸手術の流れに基づいて，迅速病理診断を行う部位選択のポイントおよび，結果をどのように術中判断に反映させるかという点について解説する．なお，本文中のT，N，M各因子の記載およびstage groupingは新TNM分類（第7版）[1]に基づいている（表1）．

術中迅速診断で検索すべき部位と結果のとらえかた

胸水

胸水の病理学的診断には，開胸時にすでに胸腔内に存在した胸水の細胞診（いわゆる開胸時胸水）と，開

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表1　新TNM病期分類（第7版）

病期	T	N	M
潜伏癌	TX	N0	M0
0期	Tis	N0	M0
ⅠA期	T1aまたはT1b	N0	M0
ⅠB期	T2a	N0	M0
ⅡA期	T1aまたはT1b	N1	M0
	T2a	N1	M0
	T2b	N0	M0
ⅡB期	T2b	N1	M0
	T3	N0	M0
ⅢA期	T1aまたはT1b	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N2	M0
	T3	N1	M0
	T4	N0	M0
	T4	N1	M0
ⅢB期	Any T	N3	M0
	T4	N2	M0
Ⅳ期	Any T	Any N	M1aまたはM1b

（文献1より引用）

表2　M因子分類（新TNM第7版）

MX	遠隔転移評価不能
M0	遠隔転移なし
M1	遠隔転移がある
M1a	対側肺内の副腫瘍結節，胸膜結節，悪性胸水（同側，対側），悪性心嚢水
M1b	他臓器への遠隔転移がある

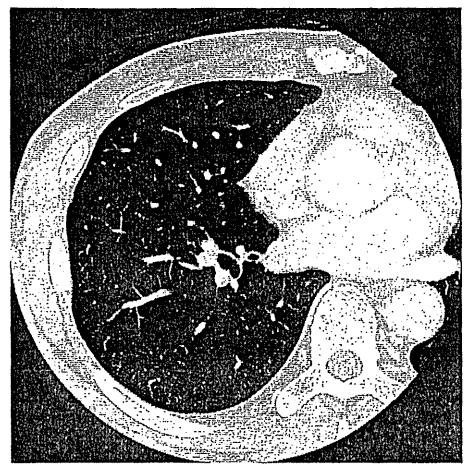

図1　胸膜播種のTSCT画像

胸時に胸腔を洗浄して得られた生理食塩水の細胞診（いわゆる胸腔内洗浄細胞診，pleural lavage cytology：PLC）の2種類が存在する．

開胸時悪性胸水については，従来はT4に分類されていたが[2]，その予後の悪さから新TNM分類では胸膜播種，悪性心嚢水とともにM1aに分類されるようになり[1]，手術非適応因子である（表2）．

一方，PLCについてはたとえ陽性であっても，胸膜播種や胸膜浸潤を病理学的に確認しない限りは，それだけではstagingには反映されず，手術非適応因子とはならないのが現状である．したがって，現時点ではPLCの術中迅速診断を行う必要性には乏しいが，PLC陽性例は陰性例に比べて有意に予後が悪いことが諸家により報告されており[3]，将来的にはTNM分類のstagingに反映される可能性がある．

■胸膜結節

胸膜播種は前述のようにM1aに分類され，手術非適応因子である[1]．しかし，悪性胸水の貯留を伴わない胸膜播種に関しては，現在の高性能CTを用いてもなお術前診断が困難な症例が存在する．原発巣が胸膜直下に存在し胸膜陥入を伴う症例のなかで，特にリンパ節腫脹がないにもかかわらず腫瘍マーカーの異常高値を伴うような場合には，thin-slice CT（TSCT）での胸膜播種巣のチェックが重要である．播種巣が葉間部に存在する場合には，病巣が小さくてもTSCTで容易に確認できることが多いが（図1），葉間部以外の臓・壁側胸膜に微小な播種が存在する場合には，TSCTでも発見が困難である．

当院では不必要な開胸を回避する目的で，開胸に先立ち胸腔鏡を用いた胸腔内の観察（審査胸腔鏡）を施行しているが，2001年1月～2004年12月の4年間に根治切除が予定された原発性肺癌症例1,234例中，胸膜播種を25症例（2%）に認め，化学療法へと方針が変更された．審査胸腔鏡にて播種巣らしき結節を認めた場合には，生検鉗子で組織を採取し迅速組織診断に提出する（図2）．この結果をもとに開胸手術に進むか否かを決定する．

■原発巣

原発巣のチェック項目は，癌細胞の有無，組織型，そして浸潤性の有無（GGO主体の腺癌の場合）の3点である．癌細胞の有無は肺切除術式やリンパ節郭清の要否に大きく関係するため，未確診腫瘍に対する手術に際して必須であるのはいうまでもない．組織型による術式の違いはあまり検討されていないが，たとえば2 cm以下の扁平上皮癌なら縦隔転移のリスクは少ないため，縦隔郭清が省略可能という報告もある[4]．逆

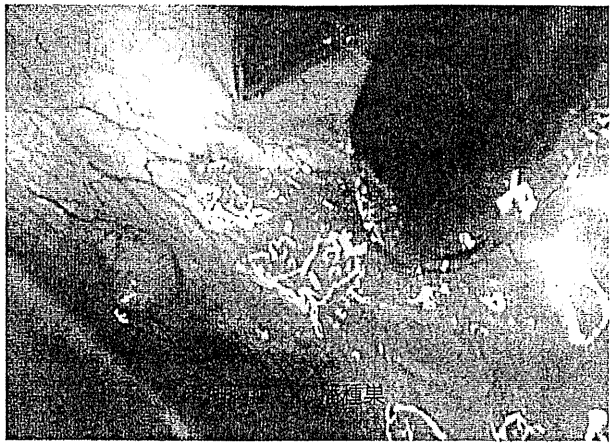

図2　鉗子による播種巣の生検

に，小細胞癌や大細胞癌などの悪性度が高く進行の早い癌に関しては，腫瘍径が小さくても縮小手術は適応となりにくいなど，組織型の病理診断は多少術式の変更に寄与する可能性はある．GGO主体の腺癌における浸潤性の有無の評価については，後述する縮小手術につながる要素であるが，現時点では“浸潤性”の定義が定まっておらず，病理医の間でも見解が分かれることから，統一された定義の制定が待たれているところである．

■副腫瘍結節

新TNM分類でadditional tumor noduleと表現されている用語の訳語が副腫瘍結節である[1]．主病巣のほかに存在する結節が肺内転移と認識される場合には副腫瘍結節として扱われるが，同時多発肺癌として認識された場合には，それぞれが個別に病期分類されることになる．両者の鑑別を的確に行うことは，治療方針の決定や予後の推測において非常に重要である．すなわち異なる肺葉に結節が存在する場合に，原発性多発肺癌であれば，患者の肺機能や全身状態が許せば切除が第一選択になりうる一方，肺内転移であれば進行肺癌であるため切除の対象とはならずに化学療法が治療の主体となり，両者の治療法は全く異なってくる．

しかし，両者の鑑別診断基準は現在まで確定されておらず，特に組織型が同じ場合には，摘出標本を用いた病理検索や分子生物学的検索でも両者の鑑別は困難なことが多い．実際にはCT画像所見，腫瘍マーカー値，N因子の有無などの臨床的背景を加味して総合的に判断することもしばしばある．

原発性多発肺癌か肺内転移かの鑑別には，Martini and Melamed[5]によって報告された診断基準（以下M & M基準）がこれまで広く用いられてきた．この基準によれば，異時性多発肺癌の診断は，

A．組織型が異なる

B．組織型が同じで以下のいずれかの条件を満たす

①少なくとも2年以上の間隔をおいて発生している

②上皮内癌から発生している

③第2癌が異なる肺葉あるいは肺から発生しているが，両者に共通なリンパ経路に転移がなく，胸郭外への転移がない

とされている．一方，同時性多発肺癌の診断基準は，

A．組織型が異なる

B．組織型が同じで以下のいずれかの条件を満たす，

①上皮内癌から発生している

②両者に共通なリンパ経路に転移がなく，胸郭外への転移がない

とされている．

これらの項目であれば，術中迅速診断にて原発巣の組織型とリンパ節転移の有無をチェックすれば術中判断も可能であるが，実際の臨床ではM & M基準では十分ではなく，脈管侵襲の有無，細胞の分化度，組織形態などの病理学的所見を加えた方法が提唱されている．さらに近年では，p53変異を用いた鑑別[6]，EGFR/KRAS変異を用いた鑑別[7]など分子生物学的手法を用いた方法も報告されているが，いずれも術中病理診断は不能である．

特にわが国では近年，HRCTスキャンの普及が進み，多発肺結節の発見頻度が飛躍的に増加しているため，世界的に統一された鑑別診断基準が早急に策定されることが望ましい．

副腫瘍結節（肺内転移）のT因子分類に関する取り決めであるが，新TNM分類（第7版）では副腫瘍結節が主病巣と同一の肺葉内に存在する（PM1）場合にはT3，同側の他肺葉に存在する（PM2）場合にはT4，そして対側肺に存在する（PM3）場合にはM1aとされることになった（第6版ではそれぞれT4，M1，M1であった）（表3）[1,2]．特に同一肺葉内転移が存在してもリンパ節転移を認めない場合には，T3N0M0 stage IIBに分類され，手術後の長期予後が期待できる病期に分類されるため，積極的に肺葉切除を考慮してもよ

表3　副腫瘍結節（肺内転移）とT因子

	新TNM（第7版）	旧TNM（第6版）
同葉内の肺内転移	T3	T4
同側異葉の肺内転移	T4	M1
対側の肺内転移	M1a	M1

いと考えられる.

■肺門・縦隔リンパ節

肺癌手術患者においてはN因子が最も予後に影響する因子であり，N2, 3症例は原則適応外である．術前のN因子診断には造影CTスキャン，PETスキャン，時にはEBUS，縦隔鏡などが行われるが，cN0症例の約20%が実際には肺門または縦隔のリンパ節転移を有する[4]．ただし，cN0-pN2症例の予後は比較的良好であり，通常の肺葉切除に関しては術中リンパ節転移が判明したからといって，必ずしも切除を中止する必要はないと考えられる．

一方，肺全摘術は肺葉切除に比べると術後のQOLが著明に低下する術式であり，術後合併症も多く，しかも分岐部切除を伴う場合などにはsurgical mortalityも相当高くなる．したがって，それらに見合うだけのoncological benefitが期待される症例のみが肺全摘術の対象となりうる．腫瘍を完全切除するためには肺全摘が避けられない，という状況に出くわしたときに，これを完遂するべきか否かの術中判断を行うに当たって，N因子の術中評価は重要である．そして予後とQOLの両者を考慮したとき，縦隔リンパ節転移のある場合には原則として全摘は勧められない．特に70歳以上の患者においては残存呼吸機能が十分でないことが多く，また心負荷も大きいため原則適応外となる．特に術前cN1例と診断された例では肺全摘または二葉切除となる可能性が高く，しかも腺癌の場合にはpN2である率が60%と高値であり，注意が必要である[8]．

ところで，近年多く発見されるようになった早期肺癌に関しては，縦隔リンパ節郭清も拡大郭清から選択的郭清へと変遷しつつあるが，選択的郭清の標準術式と呼ばれるものは現在のところ存在しない．RIを用いたセンチネルリンパ節の技術も確立されたものではない．ただし，過去の肺癌における肺門・縦隔リンパ節転移経路を詳細に調査した結果，選択的リンパ節郭清法についてわが国を中心にいくつか報告されており[9~11]，改定された肺癌取扱い規約でも選択的郭清について記載されている[12]．すなわち，右上葉，左上区域原発の肺癌においては気管分岐部リンパ節（#7）の郭清が，また両側下葉原発の肺癌においては上縦隔のリンパ節郭清が，いずれも状況により省略可能である．このような選択的郭清を行うにあたっては，可能ならばリンパ節を迅速診断に供しておくほうがよいだろう．転移しやすいルート上の肺門・縦隔リンパ節をいくつか選んで提出することになるが，提出部位や個数については定められた方法はなく，各施設の判断に任されているのが現状である．

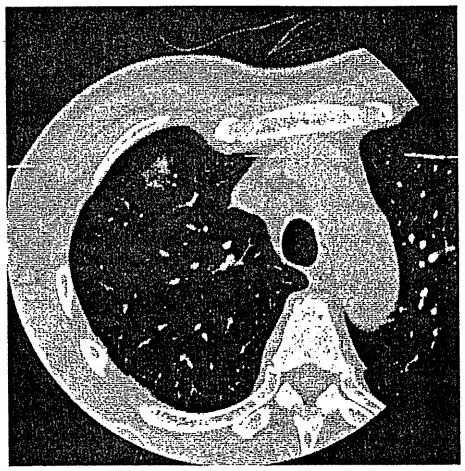

図3　GGO部分の比率が50%を超える早期腺癌のCT写真

■肺実質切除断端

1960年Cahan[13]が，肺門および縦隔の所属リンパ節郭清を伴った肺葉切除をradical lobectomyとして報告して以来，肺葉切除術＋肺門・縦隔リンパ節郭清が肺癌に対する標準術式として定着した．1980年代に入りCTが実用化され，比較的小型の肺癌が発見されるようになってきたことから，北米ではLung Cancer Study Group（LCSG）が，臨床病期IAの肺癌に対して標準手術である肺葉切除を施行した群と縮小手術（肺部分切除または区域切除）を施行した群の多施設共同無作為化比較試験を1982~1988年にかけて行った[14]．その結果，縮小手術群には肺葉切除に比べて3倍もの高い局所再発率が認められた．そのほか欧米で同様の報告が相次ぎ，いずれも縮小手術群に6~24%の高い局所再発率がみられた[15,16]．また，上述のLCSGの報告は3 cm以下の末梢型肺癌すべてを対象とした結果であったが，2 cm以下の肺癌に限ったsubgroup解析でもほぼ同様の結果であった．したがって，腫瘍が小さいという理由だけでは縮小手術の適応にならないことが判明し，肺葉切除＋リンパ節郭清術は50年以上を経た現在に至るまで肺癌根治手術の基本であり，これまでは低肺機能などのpoor risk症例に対してのみ縮小手術が行われてきた（消極的縮小手術）．

しかし，近年わが国では，ヘリカルCTの広汎な普及やマルチスライスCTの出現とともに，きわめて早期の肺癌が数多く発見されるようになり，それに対する根治を目的とした積極的縮小手術も再び見直される

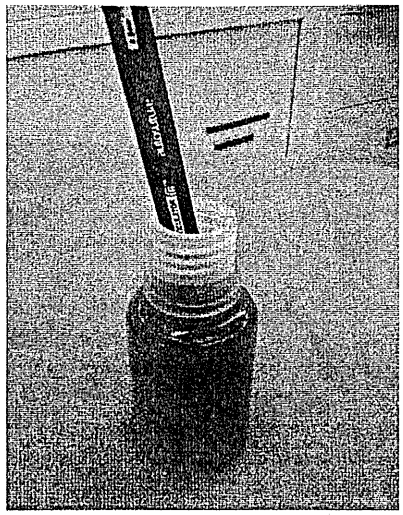

図4　ステイプラーの洗浄細胞診

ようになってきた．特に図3のようにGGO部分の比率が50％を超え，画像上，早期の腺癌と思われる症例に対しては，積極的縮小手術が行われるようになってきた[17,18]．

現在わが国では，Japan Clinical Oncology Group（JCOG）を中心として縮小手術の妥当性に関する大規模臨床試験（JCOG0802，JCOG0804）が進行しており，将来的には縮小手術が標準となる可能性がある．ただし前述のように，現時点での肺癌に対する標準手術はあくまで肺葉切除であり，積極的縮小手術の適応については，今のところ十分なコンセンサスは得られていない．したがって，積極的縮小手術の施行に当たっては，摘出した原発巣における前述した浸潤性のチェックや，周囲リンパ節のチェックのほかに，肺実質断端部のチェックを術中迅速診断に取り入れることで，再発率がより低下すると考えられる．

術中に切除断端におけるcancer cellの有無を調べることは再発率を減少させる重要な要素と思われるが，切除断端すべてを術中に細かく組織診することはかなり多くの手間と時間を要するため，事実上不可能である．また，自動縫合器による肺実質の挫滅などにより術中診断に難渋することも多い．したがって，断端部評価のために擦過細胞診やスタンプ細胞診，ステイプラーの洗浄細胞診（図4）などを術中病理診断項目に取り入れている施設もある[19,20]．

細胞診はすべての局面からまんべんなく採取できるので，定性的ではあるが断端に悪性細胞があるかどうかの判定に関しては，組織診に比べ感受性が高いと推定される．Sawabataら[21]は原発性肺癌に対して肺部分切除を行い，摘出標本の断端（staple line）全体をプレパラートに擦過して細胞診を行ったところ，陰性例8例は全例再発を認めなかったのに対して，陽性例7例のうち4例で断端再発したと報告している．Higashiyamaら[22]は，肺部分切除に用いた自動縫合器を洗浄し細胞診を行ったところ，原発性肺癌112例中11例（10％）で陽性であり，このうち4例で再発を認めたが，陰性例にはいずれも再発は認めなかったと報告している．以上のように，切除断端細胞診陰性の確認が再発率を減少させる重要な要素と推定されるが，現時点ではそれを術中迅速病理診断に用いることの臨床的意義についてはいまだ不明のことが多く，研究の必要がある．

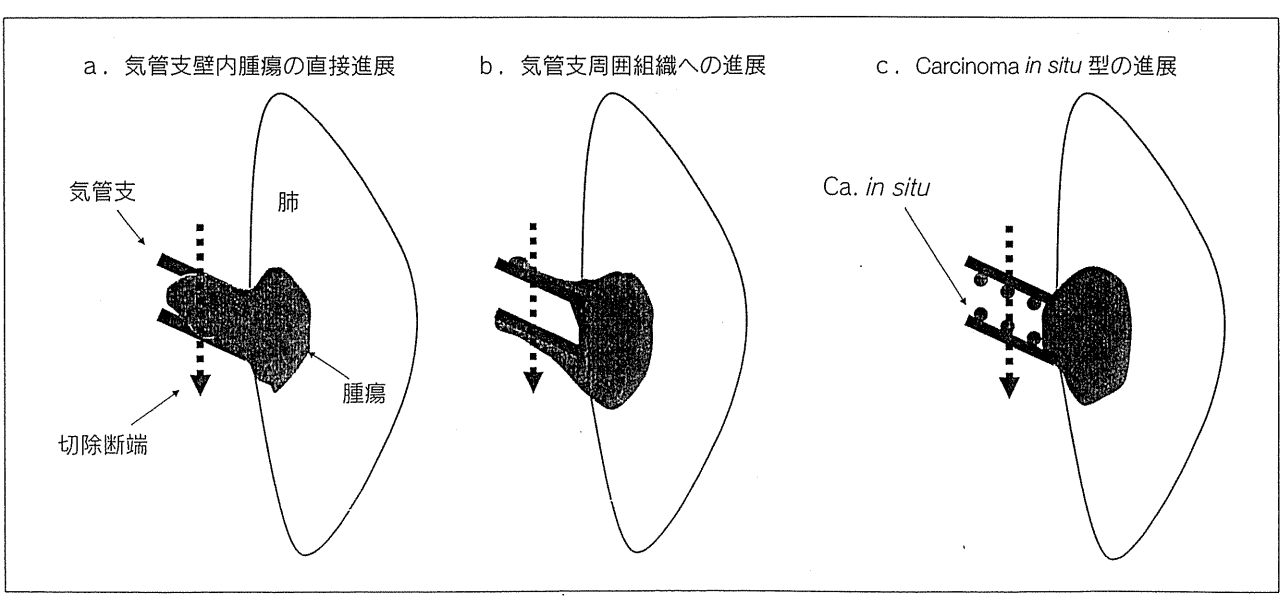

図5　気管支断端陽性例における3種の進展様式

■気管支切離断端

気管支切離断端の術中チェックは，特に中枢型肺癌において重要である．その結果によっては，通常の切除からスリーブ切除に術式変更したり，スリーブ切除の範囲を切り足すなどの必要性がしばしば生じる．気管支断端陽性には次の3パターンがある．すなわち，①気管支壁内に存在する腫瘍の直接進展（図5a），②気管支周囲組織（peribronchial tissue）への腫瘍の進展（図5b），そして③carcinoma *in situ* 型の腫瘍の進展（図5c）である．このうち，②の気管支周囲組織における断端陽性が断端陽性例のなかでは最も頻度が多いが，これは気管支周囲組織内リンパ管への癌細胞の進展を意味しており，多くの場合にはその先に存在する縦隔リンパ節にもすでに転移をきたしており，予後が悪いことが明らかとなっている[23]．したがって，その場合には縦隔リンパ節の迅速診断も併用し，スリーブ切除を行うことが本当に予後を改善するかを検討する必要がある．

おわりに

以上，通常行われる開胸手術の流れに基づいて，迅速病理診断に提出する部位選択およびその意義を解説した．術中病理診断を活用することにより，肺癌に対するより適切な治療法選択の判断（decision making）が可能になると考えられる．

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Wireless Modification of the Intraoperative Examination Monitor for Awake Surgery

—Technical Note—

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Abstract

The dedicated intraoperative examination monitor for awake surgery (IEMAS) was originally developed by us to facilitate the process of brain mapping during awake craniotomy and successfully used in 186 neurosurgical procedures. This information-sharing device provides the opportunity for all members of the surgical team to visualize a wide spectrum of the integrated intraoperative information related to the condition of the patient, nuances of the surgical procedure, and details of the cortical mapping, practically without interruption of the surgical manipulations. The wide set of both anatomical and functional parameters, such as view of the patient's mimic and face movements while answering the specific questions, type of the examination test, position of the surgical instruments, parameters of the bispectral index monitor, and general view of the surgical field through the operating microscope, is presented compactly in one screen with several displays. However, the initially designed IEMAS system was occasionally affected by interruption or detachment of the connecting cables, which sometimes interfered with its effective clinical use. Therefore, a new modification of the device was developed. The specific feature is installation of wireless information transmitting technology using audio-visual transmitters and receivers for transfer of images and verbal information. The modified IEMAS system is very convenient to use in the narrow space of the operating room.

Key words: awake craniotomy, intraoperative cortical mapping, intraoperative monitoring, cerebral glioma, surgery

Introduction

Current management strategy of cerebral gliomas emphasizes the importance of maximal possible surgical resection with minimal risk of postoperative morbidity,[7,11,12] but this goal cannot be attained without use of the advanced computer-assisted intraoperative technologies, because of the typical infiltrative growth and unclear borders of primary parenchymal brain tumors, as well as the common effects on functionally-important cerebral structures, which create a significant challenge for differentiation between the margin of the lesion and adjacent viable normal tissue. Various technological adjuncts directed at facilitation of surgery for intracranial neoplasms are currently incorporated into neurosurgical practice.[4,5] Particularly, the technique of awake craniotomy is widely used for intraoperative brain mapping during resection of lesions located in or in the nearest vicinity to eloquent cortical areas.[8,9,16,20]

Around a decade ago, the dedicated intraoperative examination monitor for awake surgery (IEMAS) was developed by our group.[5,6,11,19] The clinical experience with this device was generally very successful, but a few minor problems still appeared. First, carrying of the IEMAS in and out of the operating room between surgeries easily damaged the connecting cables and attachments, which sometimes resulted in highly undesirable mechanical problems during tumor resection. Sec-

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ond, the quantity of medical information displayed on the screen of IEMAS was not considered adequate by the operating surgeon in some cases. Therefore, the device was improved by modifications. The details of its initial clinical testing was reported previously and published elsewhere.[21] Here we present our clinical experience with routine use.

Materials and Methods

IEMAS was designed as an information-sharing device for use during awake craniotomy for intracranial lesions.[6] The device provides simultaneous real-time visualization of a wide spectrum of intraoperative data. For example, the patient's mimic and face movements during answering specific test questions, type of the examination test, position of the surgical instruments and cortical stimulator in the surgical field, parameters of the bispectral index monitor, and general view of the surgical field through the operating microscope, can be presented compactly in one screen with several displays (Fig. 1). Moreover, this combined image can be projected on several in-room liquid crystal display (LCD) monitors, so the integrated real-time information can be easily distributed and quickly analyzed by all members of the surgical team, practically without interruption of the surgical manipulations.

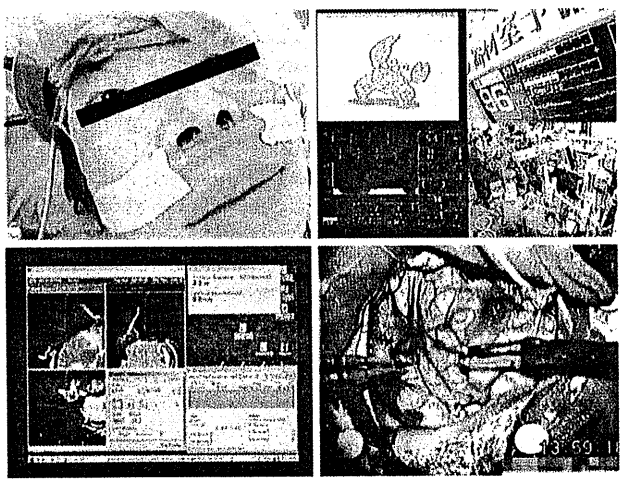

Fig. 1 Integration of multiple intraoperative parameters on the screen of the wireless intraoperative examination monitor for awake surgery. On the *upper left* display, the patient face and eyes can be seen to facilitate checking of the consciousness status and mimics during response to test questions. On the *lower left* display, the anatomical data from the real-time updated neuronavigation system is shown, which can localize the exact position of the cortical stimulator. On the *lower right* display, the view of the surgical field through the operative microscope during brain mapping is seen, which can be helpful for precise identification of the timing of stimulation. On the *upper right* display, 4 different types of information are presented, which are (*clockwise*): the test object provided for a patient for naming, parameters of the bispectral index monitor reflecting the patient's awake state, general view of the operating theater, and parameters of the heart beat monitor. In total, 7 different intraoperative parameters are integrated in real-time on one screen.

The specific feature of the new modification of the IEMAS system is the installation of wireless information transmitting technology using audio-visual transmitters and receivers for transfer of images and verbal information.[21] The general technical characteristics are presented in Table 1. The device consists of 3 main parts: patient monitor, operator monitor, and control box (Fig. 2).

The patient monitor is a 3.5-inch LCD with a small

Table 1 Technical parameters of the latest modification of intraoperative examination monitor for awake surgery

Size (mm)	390 × 1100 × 1300
Power supply (V)	AC 100; DC 12
Frequency range of audio-visual transmitters	1.2 GHz (1 channel) and 2.45 GHz (2 channels)
Camera and monitors	CCD camera 3.5 inch LCD monitor (patient monitor) 7.5 inch LCD monitor (operator monitor)
Degrees of freedom in monitors positioning	6 (self-controlling)

AC: alternating current, CCD: charge coupled device, DC: direct current, LCD: liquid crystal display.

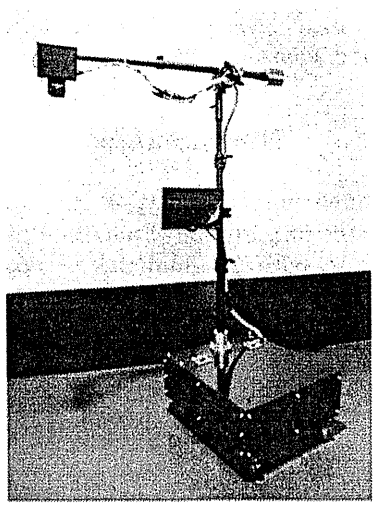

Fig. 2 General view of the wireless modification of intraoperative examination monitor for awake surgery. Three main parts of the device are seen, patient monitor, operator monitor, and control box.

charge coupled device (CCD) camera and incorporated highly sensitive microphone. The test questions for the patient are displayed on this monitor, and the camera images the patient's face simultaneously with the verbal response to tests. The operator monitor is a 7.5-inch LCD, which can project various intraoperative parameters. The whole combined image is constructed with a special divider of the recording system. In the modified IEMAS, 7 separate windows can be created on this screen, compared with 5 on the previous version of the device. The image of this monitor is recorded on the hard disk of the recording system, which is located outside the operating room (Fig. 3). The control box contains a down scan converter, alternating current power supply, and audio-visual transmitters and receivers. Metal poles connecting all 3 components of the device are made from the recreated parts of the commercially available tripod.

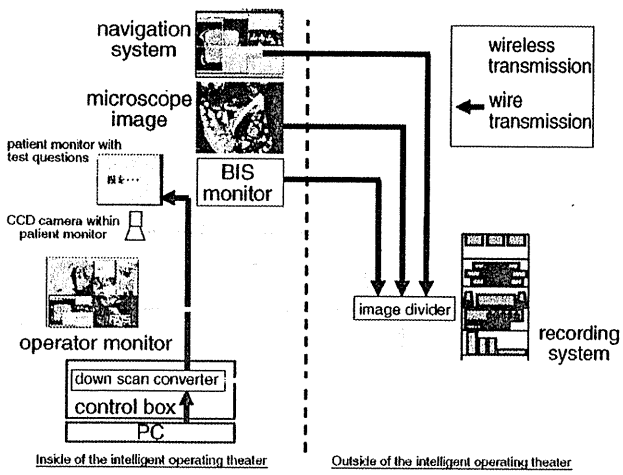

Fig. 3 Scheme of information transfer during use of intraoperative examination monitor for awake surgery and signal exchanging system provided by audio-visual transmitters and receivers. BIS: bispectral index, CCD: charge coupled device, PC: personal computer.

In the operating theater, the compact device is located beside the operating table and controlled by the assistant in charge of brain function monitoring (Fig. 4), whose main tasks include providing of the test questions for the patient simultaneously with electrical stimulation of the cerebral cortex performed by the operating surgeon, and checking the appropriateness of response by evaluation of both the verbal answer and movements of the facial muscles and eyeballs.

Results

A total of 939 neurosurgical procedures for resection of intracranial gliomas were performed in the intelligent operating theater of the Tokyo Women's Medical University from March 2000 to January 2011. Awake craniotomy was performed in 220 cases, and the initial modification of IEMAS was used 186 times.

The clinical testing of the new modification of the device was initiated on February 1, 2010, and immediately revealed the presence of crossed line effects, which resulted in impaired quality of visual and auditory data. This technical trouble was caused by imperfect design of the control box, with close vicinity of the several transmitters and receivers within the same tight space, as well as by use of a similar frequency (2.4 GHz) for all transmitters. Change of the

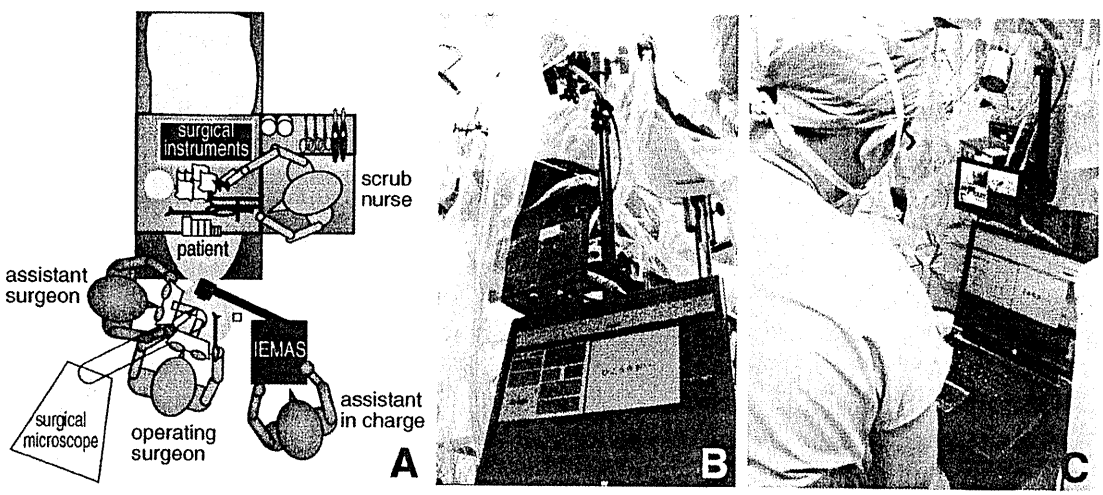

Fig. 4 Schematic (A) and real (B) demonstration of the position of the intraoperative examination monitor for awake surgery (IEMAS) during resection of glioma, and its use by the assistant in charge of brain mapping (C).

Table 2 Possible problems with identification of the speech areas with intraoperative electrical stimulation of the cerebral cortex during awake craniotomy and technical solutions required for their elimination*

Problem	Solution
Speech arrest during intraoperative cortical mapping may be similarly caused by stimulation of the different cortical areas, namely motor cortex, negative motor cortex, and speech area itself, which requires their precise discrimination. Presence of the surgical drapes separating the patient face and examination monitor from the examiner of the cortical functions may result in problems with identification of important neurological signs appearing during cortical stimulation, and with assessment of the appropriateness of visualization of the examination task by the patient.	Monitoring of the patient face, its mimics, and involuntary movements of the facial muscles at the time of speech arrest during cortical stimulation may be extremely helpful for ruling out both false positive and false negative identification of the speech area and for its precise localization.
Insufficient awakening of the patient from sedation and suboptimal level of his or her conscious may result in poor response to examination tasks and pseudo speech arrest, which may result in false positive identification of the cortical speech area.	Information on the patient sedation level should be integrated with details of his or her response to the examination tasks and those data should be provided both for the surgeon and examiner of the cortical functions.
It may be difficult for the surgeon to assess correctness of the patient response to examination task, since at the same time he or she performs electrical stimulation of the cortex. The examiner of the cortical functions providing the examination tasks for the patient cannot see the nuances of the cortical stimulation performed by the surgeon, which may create problems with precise interpretation of the patient responses.	The information on the cortical stimulation observed by the surgeon through the operating microscope and data on the type of examination task providing for the patient and his or her response should be integrated in real-time. Moreover, this information should be preferably provided not only for the surgeon and examiner of the cortical functions, but for all other members of the surgical team in order to prevent loss of the important information and its correct interpretation.
Even if according to the intraoperative cortical mapping it can be suspected that speech area is localized correctly, it may be difficult for a surgeon to integrate precisely its positioning with the anatomical details of the tumor location.	The information on the electrical cortical stimulation during intraoperative brain mapping should be integrated with the data of intraoperative neuronavigation with three-dimensional visualization of the tumor location.

*According to Yoshimitsu et al.[21] and Sakurai et al.[19]

wireless connections between the image divider and operator monitor to cables was successfully done initially,[21] but simple reduction of the frequency of this transmitter from 2.4 GHz to 1.2 GHz was soon found to be adequate for full resolution of the problem. The wireless modification of IEMAS was used during 34 subsequent awake craniotomies without technical problems during the 12 subsequent months.

Discussion

Precise intraoperative localization of the eloquent cortical areas is of paramount importance during resection of cerebral gliomas. However, the anatomical location has individual variations.[13–15,17,18] Moreover, indolent tumor growth may result in further shift of the functional cortical centers away from the mass. Therefore, intraoperative mapping of cortical and, sometimes, subcortical cerebral structures is essential, which is frequently performed during awake craniotomy with the conscious communicating patient during direct electrical stimulation of the specific brain areas.[1,3,8–10,16,20] Several problems may arise with identification of the cortical speech areas using such technique and require specific solutions (Table 2).[19,21] Particularly, elimination of the anarthria produced by positive motor response of the tongue and face or from the negative motor response of the tongue during cortical stimulation is extremely important for precise evaluation of the language function.[2,10]

Our IEMAS may significantly facilitate cortical brain mapping during awake craniotomy and definitely proved its usefulness.[5,6,11,19] However, sometimes appropriate use suffered from occasional interruption of the connecting cables or detachment. Moreover, the operating surgeon had complained on several occasions of the limited number of intraoperative parameters visualized on the screen of the monitor. While those problems were definitely minor, anxiety and irritation can result for members of the surgical team due to more or less prolonged interruption of the tumor removal. The latter is definitely highly undesirable taking into account the awake condition of the patient.

Modification of the device was directed on installation of the wireless transmitting functions and increase of the number of windows on the operator monitor screen. Some technical problems appearing during initial clinical testing were resolved quickly. Our experience with the modified IEMAS suggests complete elimination of minor problems associated with the previous version. The compact and wireless structure is very convenient to use in the narrow space of the operating room. Further efforts with im-

provement of the IEMAS will include development of a more comfortable user interface and installation of the auto-tracking mechanism in the CCD camera of the patient monitor for automatic correction of its positioning during cortical mapping.

Acknowledgment

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ORIGINAL ARTICLE

Stereotactic radiosurgery of essential trigeminal neuralgia using Leksell Gamma Knife model C with automatic positioning system

Technical nuances and evaluation of outcome in 130 patients with at least 2 years follow-up after treatment

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Abstract The objective of the present study was the evaluation of outcome in 130 patients with essential trigeminal neuralgia, who were treated using Leksell Gamma Knife model C with automatic positioning system and followed at least 24 months thereafter. Radiosurgery was guided by fused thin-sliced magnetic resonance (MR) and "bone window" computed tomographic (CT) images. In all cases, retrogasserian part of the trigeminal nerve at the level of trigeminal incisura was selected as a target, and one 4-mm collimator was used for delivery of the maximum irradiation dose of 90 Gy. The coordinates of the isocenter were adjusted for positioning of the nerve in the center of 80% isodose area, and were corrected in each individual case with regard to presence of distortion artifacts on MR images. Initial relief of the typical paroxysmal facial pain was marked in 127 patients (98%) within a median interval of 3 weeks after treatment. However, in 23 patients the pain re-appeared later on. Overall, at the time of the last follow-up 112 patients (86%) were pain-free, including 86 who remained both pain- and medication-free after initial radiosurgery. In 31 cases (24%), treatment was complicated by facial hypesthesia and/or paresthesia. In conclusion, radiosurgery of essential trigeminal neuralgia

The results of this study were presented during the 9th Biennial Congress of the International Stereotactic Radiosurgery Society (June 7–11, 2009; Seoul, South Korea).

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results in a high rate of initial pain relief, but pain recurrences and associated complications are not uncommon. The outcome may be influenced by various technical nuances; therefore, treatment should be preferably done in specialized clinical centers with sufficient expertise in the management of this disorder.

Keywords Trigeminal neuralgia · Treatment · Stereotactic radiosurgery · Gamma Knife surgery · Automatic positioning system · Outcome

Introduction

Stereotactic radiosurgery has become the standard management option for medically resistant essential trigeminal neuralgia if surgical procedure(s) is ineffective or could not be done due to any reason. According to multiple reports, in 61–98% of cases the treatment results in satisfactory control of paroxysms of the facial pain regarding both their intensity and frequency [2–4, 6–10, 18–47, 49, 51–54, 56].

During 10-year period from 1998 till 2008, the first author (M.H.) performed Gamma Knife surgery (GKS) in 303 patients with essential trigeminal neuralgia. The main principles of the applied radiosurgical strategy and overall results in these cases were reported previously [11–17]. The objective of this retrospective study was the evaluation of outcome in a selected cohort of patients, who underwent treatment using Leksell Gamma Knife model C with automatic positioning system [APS] (Elekta Instruments AB, Stockholm, Sweden), and were followed for at least 2 years thereafter.

Methods

From January 2003 to September 2008, a total of 4,105 radiosurgical procedures using Leksell Gamma Knife model C with APS were performed in the Department of Neurosurgery of the Tokyo Women's Medical University and in Saitama Gamma Knife Center. In 262 cases, GKS was performed for management of essential trigeminal neuralgia. From this cohort, 130 patients were followed at least 2 years after treatment and constituted the clinical basis of the present analysis. The demographic characteristics of this group were similar to the residual cases, which also underwent GKS, but had insufficient length of follow-up. All clinical, radiological and radiosurgical data were extracted from the prospectively maintained computer databases.

During the same time span, 41 surgical microvascular decompressions (MVD) were performed in both clinics for primary management of essential trigeminal neuralgia, whereas no other type of procedures were used for such a purpose.

General data

There were 72 women and 58 men. Their age varied from 31 to 88 years (mean, 68 years). Seven (5%) patients were younger than 50 years, 17 (13%) were between 50 and 59 years, 50 (39%) were between 60 and 69 years, 33 (25%) were between 70 and 79 years, and 23 (18%) were older than 80 years.

The duration of symptoms before first visit to radiosurgical outpatient clinic varied from 1 to 497 months (mean, 98 months). In all cases, there was a typical clinical presentation of essential trigeminal neuralgia characterized by paroxysmal "electric discharge"-like facial pain with certain unilateral topographical distribution within one or more divisions of the trigeminal nerve. The attacks of pain were triggered by facial stimulation, such as mastication, tooth brushing, face washing or touching, speech. Their daily frequency varied from 10 to uncountable number. All patients characterized their pain as intolerable and associated it with at least 8 out of 10 points on the Visual Analogue Scale. No one patient had other type of facial pain (i.e., continuous pain), sensory disturbances on the face and cornea, or history of multiple sclerosis. In all cases, magnetic resonance imaging (MRI) excluded the presence of structural intracranial lesion.

All patients noted at least partial effect of carbamazepin (Tegretol®) for facial pain control either before or at the time of radiosurgery. The length of medication trials before GKS varied in our hospital from 1 to 24 months (mean, 12 months). If carbamazepin was well tolerated, its dose in cases of suboptimal pain control was steadily increased from 200 to 600 mg/day.

The indications for radiosurgical treatment included:

(1) Insufficient control of pain, defined as less than 80% of its intensity and frequency reduction with prescription of carbamazepin at the optimal dose and schedule of administration [15]
(2) Allergy, side effects, or complications associated with administration of carbamazepin
(3) Inability to perform MVD due to any reason

The duration of medical treatment failure before radiosurgery depended inversely on pain intensity, but, in general, at least 3 months of observation was recommended before decision was made on surgical management. As a rule, all patients and their nearest family members were provided with detailed information on the various possible treatment options, including MVD, percutaneous ablative procedures, and GKS. Advantages and risks of each technique were clarified, taking into consideration peculiarities of the individual case with regard to age, medical comorbidities, pain severity, and previous treatment. MVD was usually strongly recommended for younger individuals

(less than 50 years old), whereas radiosurgery was suggested for older ones (more than 70 years old). Nevertheless, the final decision on the preferred modality was made by the patient himself or herself. Informed consent was provided before treatment in each case.

Radiosurgery

On the day of radiosurgery, a Leksell G stereotactic frame (Elekta Instruments AB) was fixed on the patient's head under local anesthesia in such a way as to make it parallel to the intracisternal portion of the trigeminal nerve, which was attained by correspondence of the plane of the frame base to the orbitomeatal line. This option provides an opportunity to follow the whole length of the nerve in one axial MR image [15–17, 29]. The projection of the trigeminal incisura of the petrous bone was localized 1.5 cm anterior and 1.5 cm superior to the external auditory meatus, and this point was positioned close to the center of the *Y*-axis with appropriate adjustment in *Z*-axis (Fig. 1).

Axial thin-sliced (1.0 mm) contrast-enhanced and "bone window" computed tomography (CT), and axial thin-sliced (0.5 mm) heavy T_2-weighted MR images were obtained in stereotactic conditions, using zero degree gantry tilt for all investigations. Radiological data were transferred to Leksell Gamma Plan version 5.34 or, later, version 8.3 (Elekta Instruments AB).

Radiosurgical treatment planning was done by reference to a simultaneous onscreen display of all obtained images within the three-dimensional workspace. First, trigeminal nerve, brain stem, and adjacent vascular structures were determined and accurately delineated with different colors. Postcontrast CT images were used to distinguish the non-enhanced Meckel's cave from enhanced cavernous sinus and tentorium. In all cases, the retrogasserian part of the trigeminal nerve at the level of trigeminal incisura on the side of the facial, pain was selected as a target (Fig. 2). One 4-mm collimator was used constantly for delivery of maximum irradiation dose of 90 Gy at 100% isodose line. Using advantages of APS, which provides 0.1 mm positioning accuracy, the coordinates of the isocenter were carefully adjusted for positioning of the nerve into the center of not just 50%, but 80% isodose area. The dose to the brain stem was kept below 18 Gy, which corresponded to 20% isodose line. A dose-volume histogram was generated to assure that 1 mm^3 or less of the pons had received such irradiation dose. In cases of narrow cerebellopontine cistern, the beam plugging technique was used to avoid excessive dose delivery to the brain stem (Fig. 3). After completion of the treatment plan, the coordinates of the isocenter were adjusted according to the presence of distortion artifacts evaluated three-dimensionally in each individual case using fused "bone window" CT and MR images [11–17]. In few cases with poor visualization of the trigeminal nerve or contraindications for MRI, the radiosurgical target was set according to the location of the trigeminal incisura and Meckel's cave, which were defined, correspondingly, on "bone window" and postcontrast CT (Fig. 4).

Neither steroids, nor anticonvulsants were routinely administered at the time of GKS.

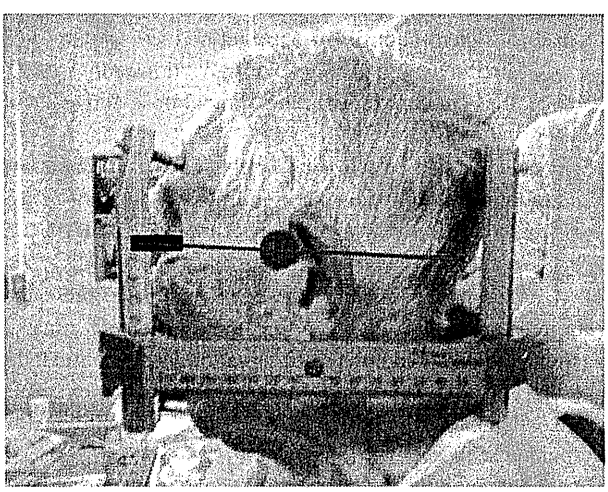

Fig. 1 Fixation of the stereotactic frame on the patient's head in parallel to the intracisternal portion of the trigeminal nerve (*red line*) attained by correspondence of the plane of the frame base to orbitomeatal line, and positioning of the projection point of the trigeminal incisura (*red spot*) close to the center of the *Y*-axis with appropriate adjustment in *Z*-axis

Follow-up

All patients were followed by the treating neurosurgeon with regular clinical examinations, which were scheduled every 3 months during the first year after treatment, every 6 months during the second and third years, and yearly thereafter. Each patient was advised to make a non-scheduled outpatient visit in case of exacerbation of pain or any other clinical deterioration. Routinely, MRI investigations were not done after GKS. The length of follow-up varied from 24 to 66 months (mean, 38 months).

Results

Pain response to treatment

Relief of the typical paroxysmal facial pain (more than 80% of its intensity and frequency reduction) at some time point after initial radiosurgical treatment was marked in 127 out of 130 patients (98%). The time interval to such an effect varied widely (Table 1), and in median constituted 3 weeks (Fig. 5).

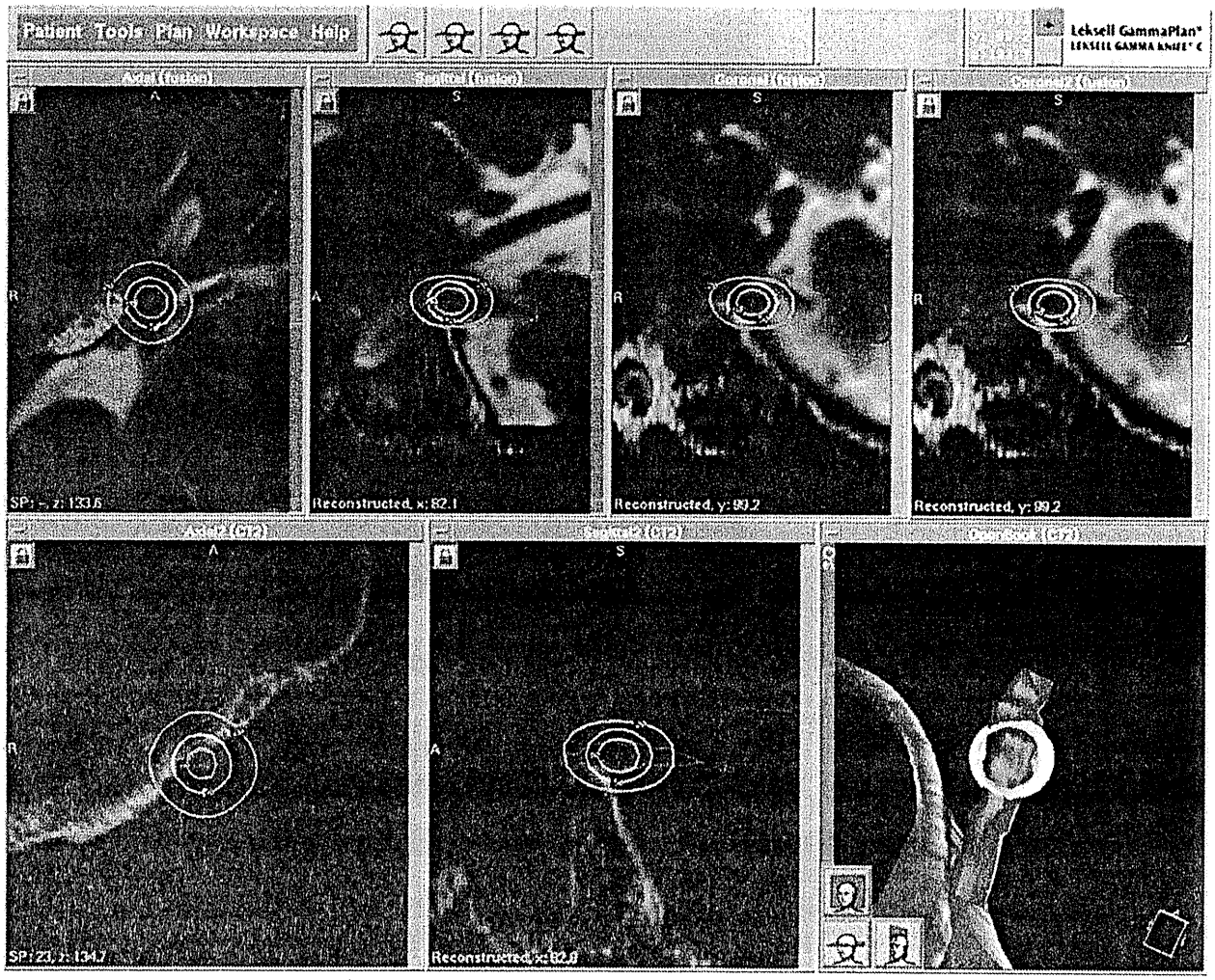

Fig. 2 Radiosurgical treatment plan for essential trigeminal neuralgia. Trigeminal nerve (*blue*) and brain stem (*red*) are delineated. Retrogasserian part of the nerve at the level of the trigeminal incisura was selected as a target using one 4-mm collimator, which coordinates were carefully adjusted for positioning of the nerve into the center not just of 50% (*yellow circle*), but of 80% isodose area

Treatment failures, recurrences, and salvage treatment

In three out of 130 patients (2%), typical paroxysmal facial pain did not respond to treatment at all.

Sixty-one out of 127 patients (48%) with pain relief experienced persistent paroxysms of facial pain during the first 6 months after treatment, which, however, showed 60–80% reduction in intensity and frequency compared to pretreatment period and did not require any additional treatment, were therefore not considered as treatment failure or recurrence. The latter was defined as re-appearance of regular pain attacks 6 months and more after GKS, but, in fact, was never noted within first year after treatment. It was observed in 23 out of 127 patients (18%) who had initial pain relief. In 15 cases the recurrence was considered as minor and did not require pursuing further surgical intervention, whereas in eight it was viewed as major since it necessitated additional surgery [44].

All 26 patients who did not respond to radiosurgery or experienced pain recurrence underwent salvage treatment. Administration of carbamazepin was more or less effective in 18 of them. In eight other patients, percutaneous radiofrequency rhizotomy (six cases), microvascular decompression (one case) and second GKS (one case) were performed due to insufficient efficacy of the medical treatment.

Outcome

Overall, 112 out of 130 patients (86%) were pain-free at the time of the last follow-up (Fig. 6). In 104 cases the disappearance of pain followed initial radiosurgery, and 86 of these patients were medication-free, whereas 18 still

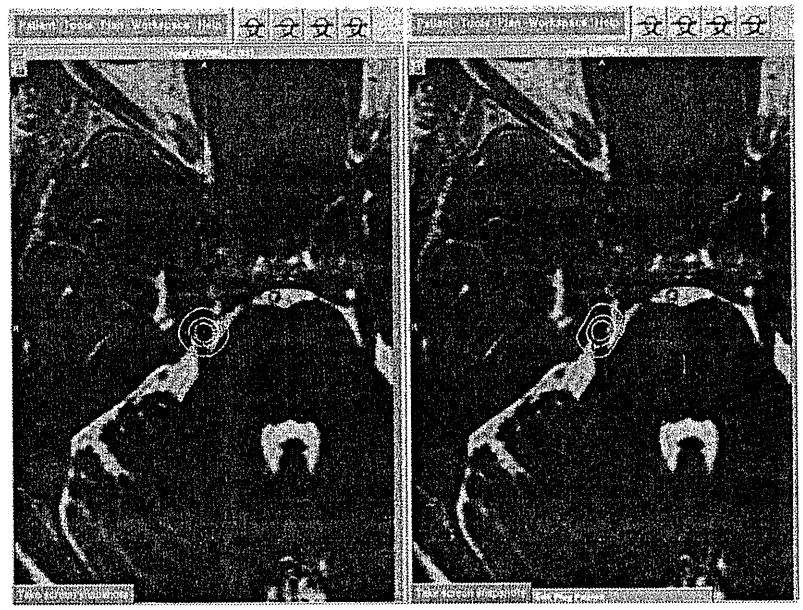

Fig. 3 Modification of the 20% isodose line corresponding to 18 Gy irradiation dose using beam plugging technique for avoidance of the excessive irradiation of the brain stem in case of the narrow cerebellopontine cistern

used carbamazepin. Eight additional patients became pain-free after salvage treatment, while 18 (14%) continued to suffer from more or less severe facial pain.

Complications

Acute complications were not noted in any case of the present series. In 31 out of 130 patients (24%), the treatment was followed by development of facial hypesthesia and/or paresthesia, and in 16 of them it was marked as bothersome. Since in all latter cases the facial numbness was severe enough to interfere with activities of daily life, it was assigned a Barrow Neurological Institute score of grade IV [47, 51]. The median time to development of the complication was 6 months (Fig. 7). Other types of complications were not noted during follow-up.

Patients' age and results of treatment

Results of GKS for trigeminal neuralgia in various age groups of patients are presented in Table 2. Chi-square test for trend revealed that initial treatment failure was more

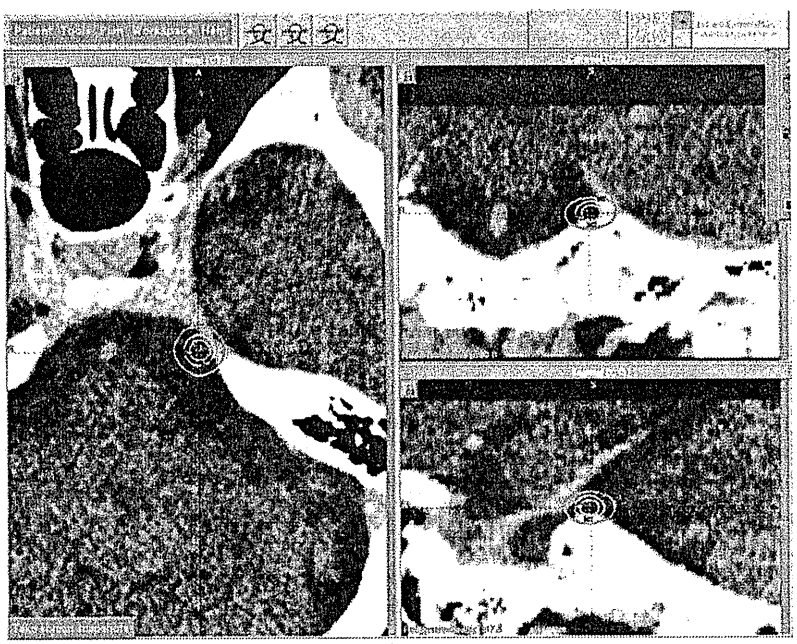

Fig. 4 Radiosurgical treatment plan for essential trigeminal neuralgia in a case with contraindications for MRI investigation. The target was set according to location of the trigeminal incisura and Meckel's cave defined on contrast-enhanced CT

Table 1 Time interval to relief of the typical paroxysmal facial pain after Gamma Knife surgery for essential trigeminal neuralgia

Time interval until pain relief after treatment	Number of patients[a]
0–3 days	38 (29%)
4 days–1 month	57 (44%)
1–3 months	22 (17%)
More than 3 months	10 (8%)
Total	127 (98%)[a]

[a] In three other patients (2%) of the present series, typical paroxysmal facial pain did not respond to treatment at all

typical for younger individuals (P=0.0264), whereas the rates of recurrence, excellent outcome, total and bothersome facial numbness did not show any statistically significant association with patient's age.

Discussion

It is widely recognized that GKS can be effectively used for management of medically resistant essential trigeminal neuralgia, alternatively to transcutaneous ablative procedures or such non-destructive technique as MVD. The latter, however, still represents the gold treatment standard, particularly for younger patients, with limited comorbidities, and reasonable life expectancy. Compared to radiosurgery, MVD definitely provides superior immediacy of response and early results, better durability of pain relief, and lower rate of facial numbness [24, 37, 43, 52]. Meanwhile, the necessity to perform craniotomy under general anesthesia may in some way interfere with the patient's daily activities. Moreover, while rather rare in experienced hands, open surgery may be associated with several complications, such as non-specific headache, diplopia, trigeminal nerve dysfunction, facial palsy, deafness, CSF leak, infection, intracranial hemorrhage, stroke, pneumonia, and deep venous thrombosis [24, 37, 43, 52]. Even a very low risk of postoperative mortality also cannot be ignored. In contrast, radiosurgery represents a nearly non-invasive 1-day treatment, which does not require any significant activity restrictions. Compared to other transcutaneous ablative techniques it has lower immediacy of response, but comparable efficacy, and a definitely lower complication rate [21, 24, 27, 52]. Roughly, from one- to two-thirds of patients have a chance to attain freedom both from pain and medication after GKS [2–4, 6, 8, 10, 18, 19, 21, 22, 24–37, 39–47, 50, 51, 53, 56], which also usually leads to definite improvement in quality of life, even if pain-free status is not achieved [2, 25, 38, 40, 44]. While reduction of the dose to the trigeminal nerve at the time of initial irradiation may not only decrease the risk of facial numbness, but result in suboptimal long-term pain control, it should be emphasized that radiosurgery may be repeated, if necessary, and does not preclude from further management with other techniques [19, 21, 25, 26, 48]. Probably due to these reasons, there is a growing number of patients with medically resistant trigeminal neuralgia who nowadays prefer sterotactic irradiation as a primary treatment option [43]. It fully corresponds with our recent practice, since during the study period 262 individuals underwent GKS and only 41 MVD, which means that in approximately six out of seven cases the former method was chosen.

A number of factors associated with favorable outcome after radiosurgery for trigeminal neuralgia were identified previously. Those ones include older age [10, 23, 44, 45, 50, 53], presence of typical symptoms [23, 28, 40, 45, 47, 51,56], right-sided facial pain [49, 50], pain in a single trigeminal nerve distribution [21], shorter duration of the

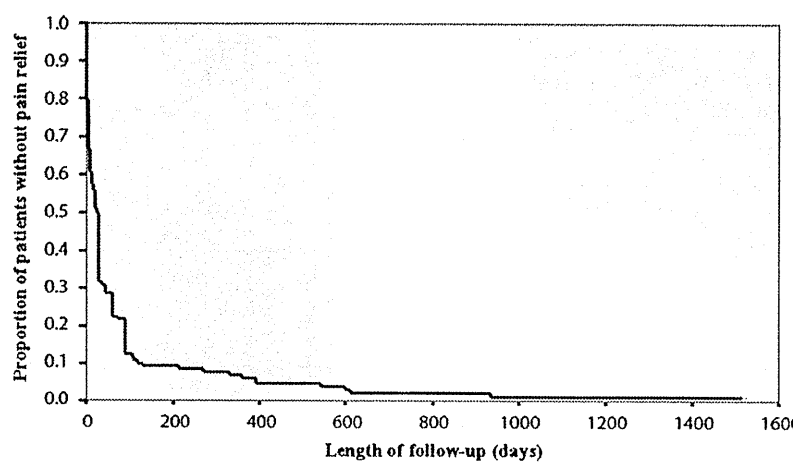

Fig. 5 Kaplan–Meier curve reflecting relief of paroxysmal facial pain after Gamma Knife surgery for essential trigeminal neuralgia. The median period to pain relief after treatment constituted 3 weeks