



「インテリジェント手術室と高速大容量ネットワーク」
I.臨床
Another EBM
(Engineering Based Medicine)
in TWIns

村垣善浩



EBM:
Evidence Based Medicine
(ガイドライン)

V.S.

もうひとつのEBM
Another EBM:
Engineering Based Medicine
(医工融合)

先端医療は、ナノテク、バイオテクなど理工学を駆使した
技術の集大成

未来医療の現場



脳外科領域

●コンピュータ支援手術の普及度

術中MRI

滋賀医大(2000)、女子医大(2000)、国立癌センター
(2005)、東海大学(2006)、名古屋大学(2006)、
名古屋セントラル病院(2006)、山形大学(2008)、鹿児島大
学(2009)、太田記念病院(2010)

●阻む障害

－ 職人芸、保険点数、コスト、稼働率

●今後の展望

－ 手術プロセスマネージメント(デジタル手術)、
戦略デスク、予測制御型医療

MRI operating theater

Siemens/Erlangen U.



1.5T



I-motion/Calgary U.



0.3T



1.5T



Hitachi/TWMU



Odin/Tel-Aviv U.



0.2T



GE/Harvard U.



0.5T

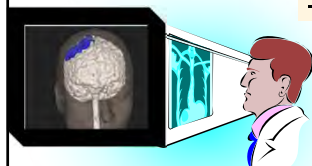


International F1 racing team
in the neurosurgical field

診断と治療の一体化戦略

精密誘導技術

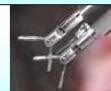
(DDS)



治療計画
(Design)

術中探査/実行
(Sensing/ Procedure)

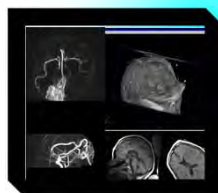
微細領域を
ピンポイントで治療
(Manipulation)



見えない壁で周囲
を守る



(Ablation)



微細治療を安全・確実に支援

悪性脳腫瘍(Glioma)

最大限の摘出 と 最小限の侵襲 による QOTの高い手術治療

悪性脳腫瘍(グリオーマ)摘出のジレンマ 境界不鮮明・周囲正常脳損傷による重篤な合併症

・拡大摘出
生存率↑
合併症↑



・理想的な摘出
生存率↑
合併症↓



・縮小摘出
生存率↓
合併症↓

失語症・片麻痺

言語野・言語神経・運動神経



客観的(可視化)・再現性

適切な術中情報



Controversy of Radical Glioma Resection

- 1990's paper about radical removal and good prognosis

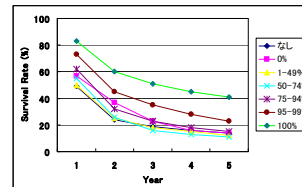
6 papers YES 3 papers NO
 selection bias, methodological flaws
 different method to evaluate removal extent – surgeon?, CT?,
 MRI?

Hess J NeuroOncol (42) 227-231 1999

- 416 GBM, MRI volumetry
 untreated cases $\geq 98\%$: $<98\%$
 all cases $\geq 89\%$

Lacroix et al. J Neurosurg 95:190-198, 2001

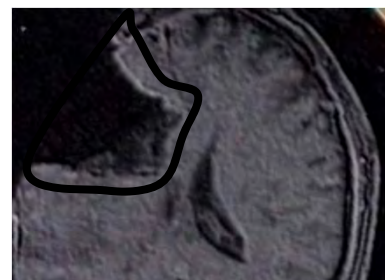
- 6395 malignant glioma, 5-year survival
 total (40%) > 95% (22%) > other



Japan tumor registry

悪性脳腫瘍の生存率を20ポイント向上させるには

- 通常手術 (50 - 75%摘出)
 95%未満摘出
 5年生存率 8-15%
- 術中MRIと形態ナビゲーション
 95%以上摘出
 5年生存率 20%
- 5 ALAと蛍光HivisCASの
 化学ナビゲーション
 100%摘出
 5年生存率 40%



Patho-biological aspects of malignant glioma

Glioblastoma: The Past, the Present, and the Future

Wilson CB: Clin Neurosurg 38, 1992

TABLE 3.1
Assumptions Regarding the Ratio of Tumor Cells to Total Cells at Various Sites and Cell Density in Tumor and Normal Brain

General Assumptions

1 g of tumor = 10^6 cells

1 g of normal brain = 10^6 cells

Whole brain = 1400 g

All tumor cells are viable

Fewer than 1% of tumor cells are clonogenic

Recurrence is a probability function directly related to cell number but modified by local factors, e.g., extracellular matrix.

Assumptions about Tumor Cell to Normal Cell Ratio (T/N)

Enhancing tumor = 1.0

Brain adjacent to tumor (BAT)

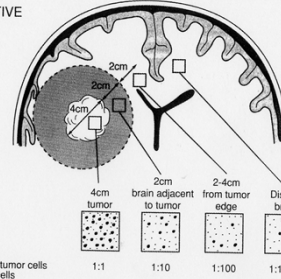
0-2 cm = $1/50$

2-4 cm = $1/100$

>4 cm = $1/1000$

†Alvord's explanation (1) does not explain this; i.e., patients with GBM do not die before the distal cells obtain a footing.

PRE OPERATIVE



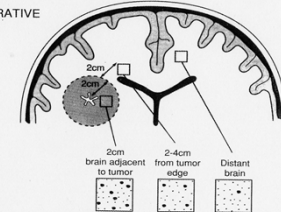
Ratio of tumor cells to total cells

1:1 1:10 1:100 1:1000

A Percentage of tumor cell population

92% 6% 1.8% 0.2%

POST OPERATIVE



Ratio of tumor cells to total cells

1:10 1:100 1:1000

B Percentage of tumor cell population

77% 21% 2%

FIGURE 3.1. Information from biopsy and postmortem examinations provides the basis for estimations of the ratio of tumor cells to normal cells and the percentage of the total tumor cell population before (A) and after (B) nearly total removal of a glioblastoma.

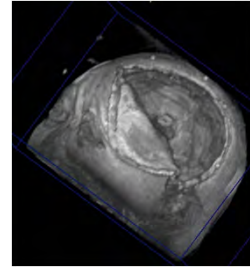
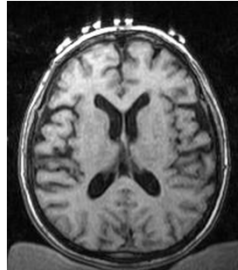


**intraoperative open MRI
advanced Vision**

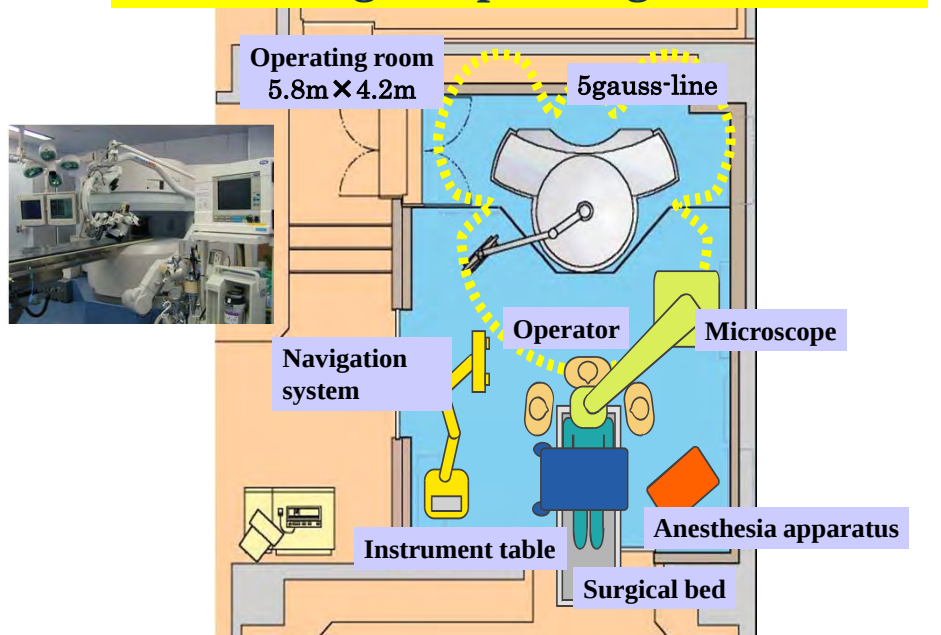
Open configuration MRI

Open MRI (AIRIS II, 0.3 T, Hitachi)

- 永久磁石
- 満足できる画像レベルと機能
 - T1,T2,FLAIR, MRA, 3D, DWI
- 5ガウスライン外で一般手術道具の使用可能



Intelligent operating theater



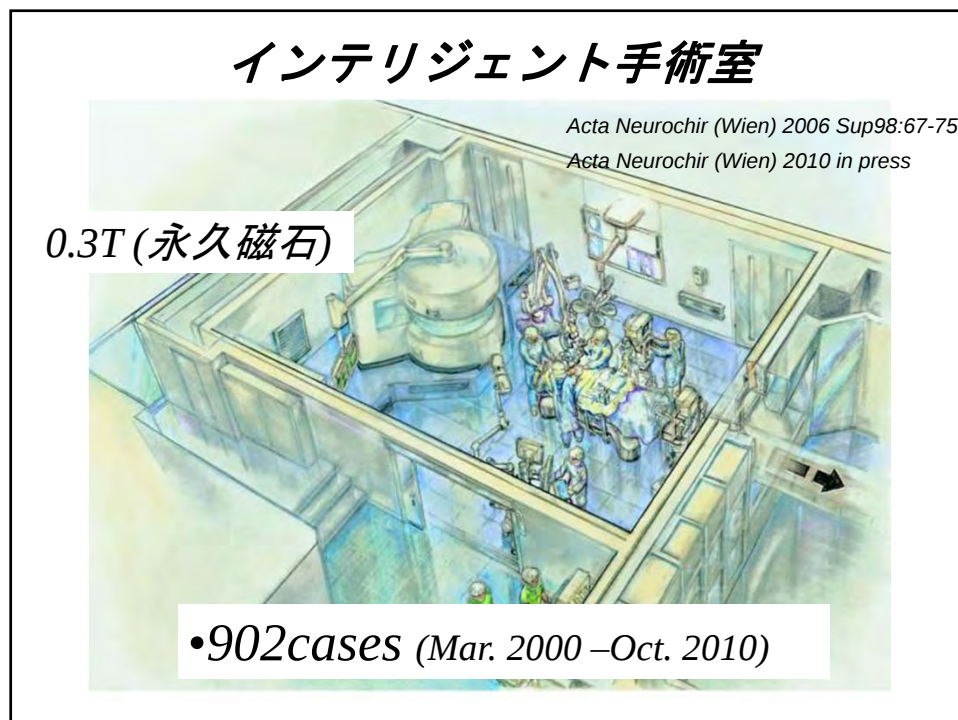
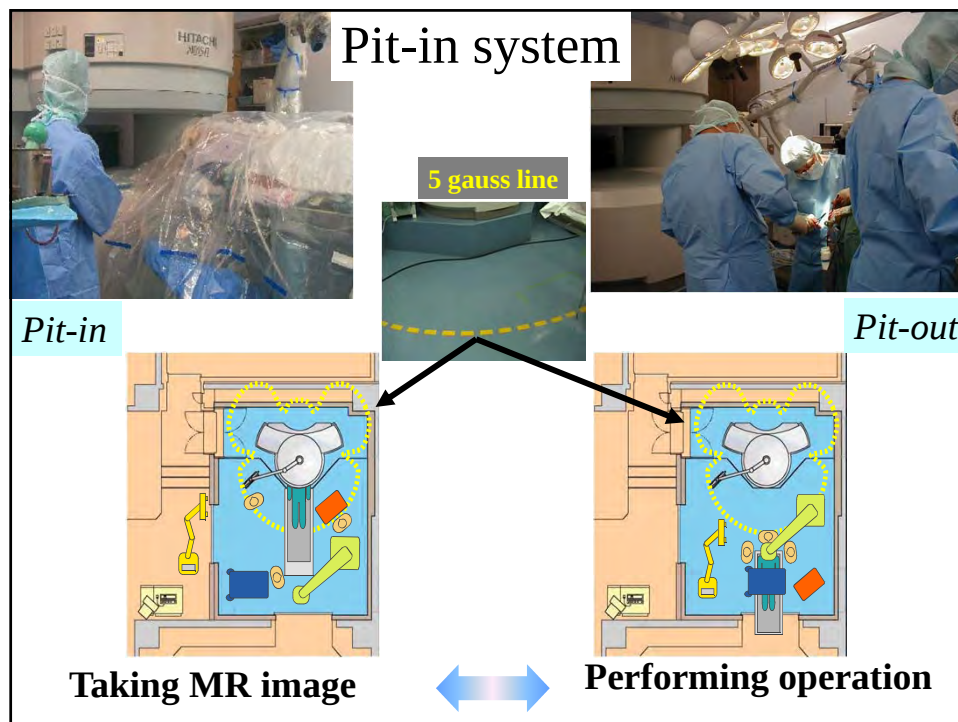
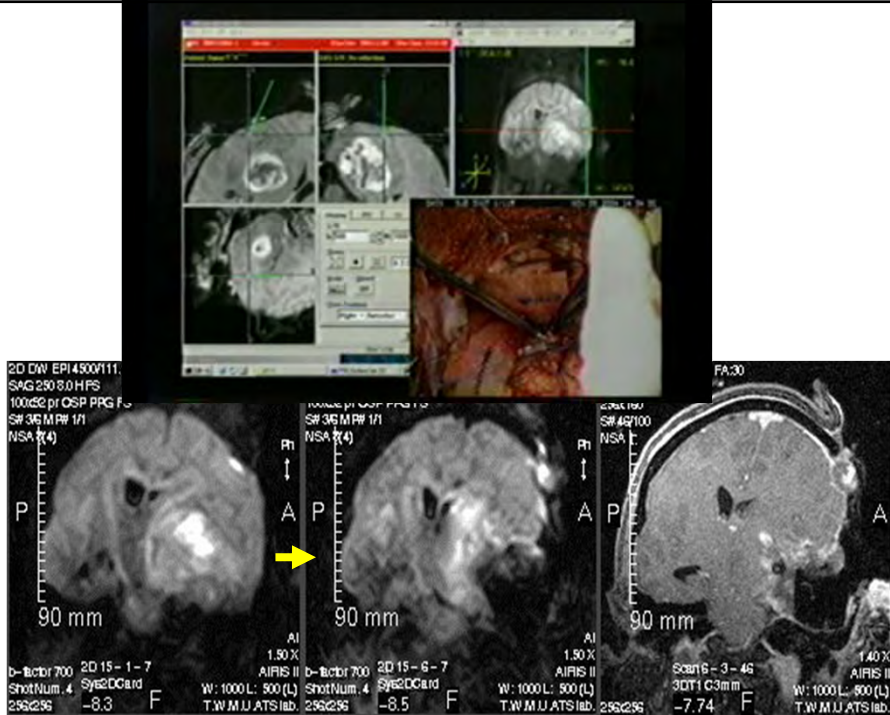


Figure 1 consists of four panels labeled A, B, C, and D, each showing a different MRI slice of a brain. Panel A shows a coronal slice with a green line indicating the location of a lesion. Panel B shows a sagittal slice with a green line indicating the location of a lesion. Panel C shows an axial slice with a green line indicating the location of a lesion. Panel D shows an axial slice with a green line indicating the location of a lesion. To the right of the panels is a software interface with various controls and a 3D model of a brain. The interface includes a 'Display' section with checkboxes for 'F15', 'G1', and 'G2'. Below this is a 'Zoom' section with a 'Zoom' button and a 'Zoom' dropdown menu. The 'Zoom' dropdown menu is set to 'X 2.0'. Below the 'Zoom' section is a 'View' section with a 'View' button and a 'View' dropdown menu. The 'View' dropdown menu is set to 'Right - Anterior'. Below the 'View' section is a 'Tag' section with a 'Tag' button and a 'Tag' dropdown menu. The 'Tag' dropdown menu is set to 'Tag 1'. The 3D model of the brain is shown in the top right corner of the software interface.

拡散強調画像(DWI)による錐体路の術中確認 Real time update navigation との連動



Chemical navigation

5-ALAによるPDD(photo-dynamic diagnosis)
NPe6によるPDT(photo-dynamic therapy)

5-ALAによる術中蛍光診断
スペクトログラムでの高感度測定

5-ALA 5-Amino Levulinic Acid

5-アミノレブリン酸 (ALA)

- ・生体内に含まれる天然アミノ酸
- ・クロロフィル、ヘムの大元の化合物 (生物にとってとても大切な物質)

NC(=O)CC(C(=O)O)C

生体内に含まれる天然アミノ酸

血液、葉緑素の原料のひとつ

5-Amino Levulinic Acid (ALA)

腫瘍集積メカニズム

5-ALA

Tumor cell

ALA synthase

Protoporphyrin IX (Pp IX)

Fe $\rightleftharpoons$ ferrochelatase

Heme

5-ALA

Normal cell

ALA synthase

Pp IX

Fe $\rightleftharpoons$

Heme

PpIX

Absorption spectrum 405nm
Fluorescence spectrum 635nm



細胞内で蛍光物質に代謝

経口投与で吸収

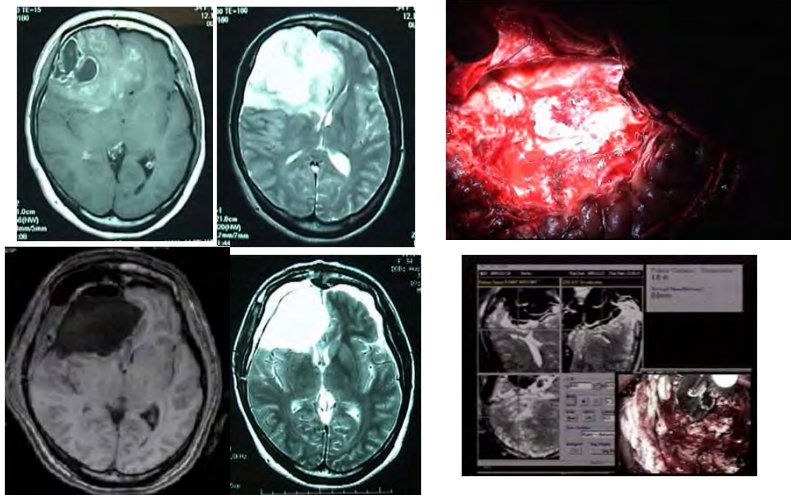
長期間の遮蔽不必要

NC(=O)CC(C(=O)O)C

5-ALA

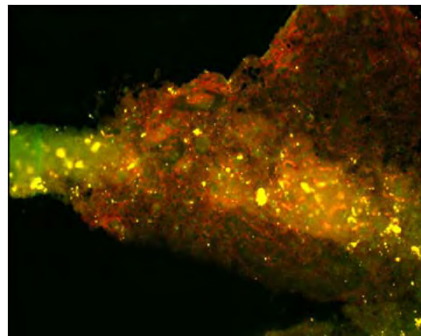
ポルフィリンIX

34 y.o. anaplastic astrocytoma
SEP, 5ALA , iMRI, RUnavigation

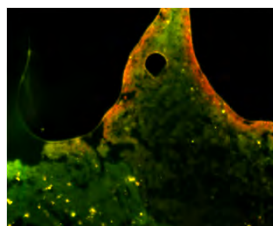


TV(pr) 198ml, TV(po) 0ml, RR 100%

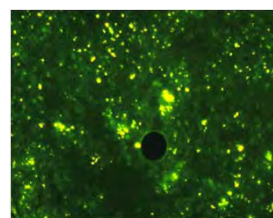
5-ALA fluorescence positive

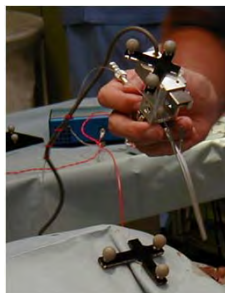


5-ALA boundary



5-ALA negative

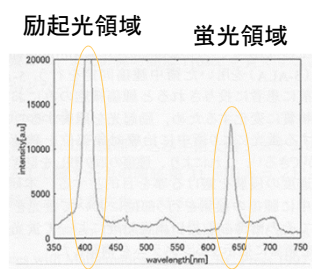




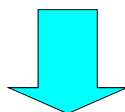
ポイントでの
蛍光分光計測



摘出組織の
蛍光分光計測



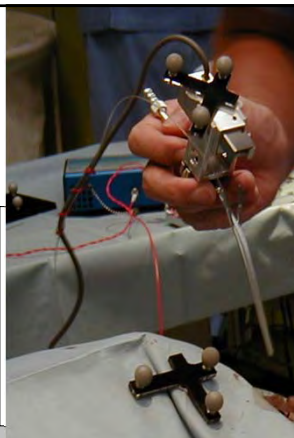
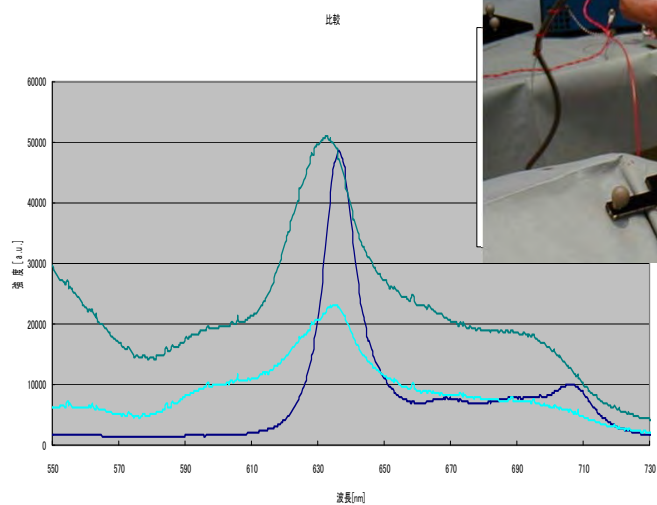
分光光度計による波長分析



高感度かつ分解能の高い腫瘍同定
(空間・波長)

absorption spectrum: 405nm

fluorescence spectrum: 635nm



PDT

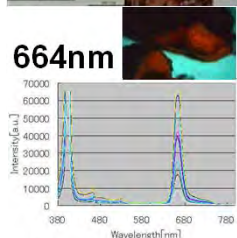
PD-レーザ Talaporfin レザフィリン®

悪性脳腫瘍に対する新治療戦略

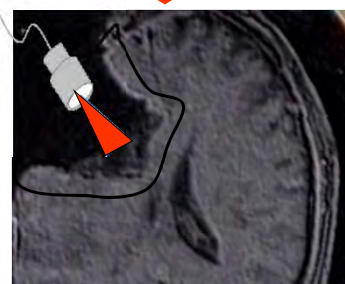
- 術中MRIと
(DWI)ナビゲーション
95%以上摘出



- Talaporfin PD-LASER 664nm
(PDD・PDT)
化学ナビゲーション
100%摘出



- Talaporfin PD-LASER 664nmに
よるPDT
border zone 内の残存腫瘍細胞
レーザーの到達深度 数mm



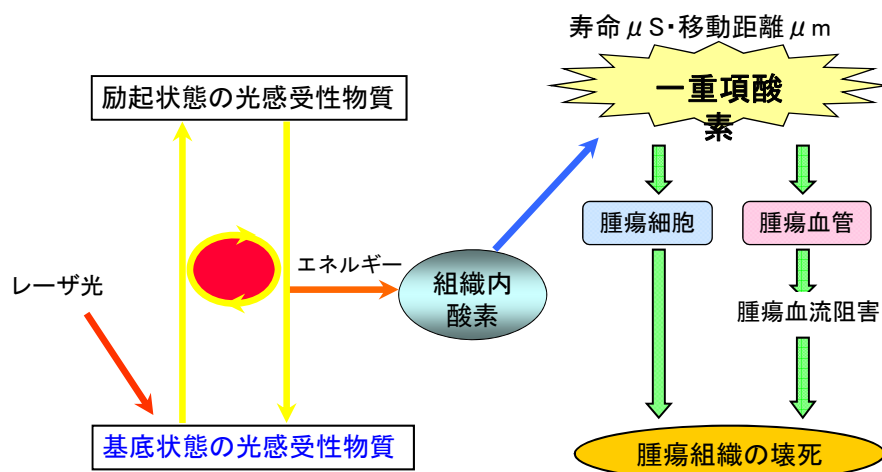
PD-レーザー＋Talaporfin レザフィリン®



松下電器産業株式会社

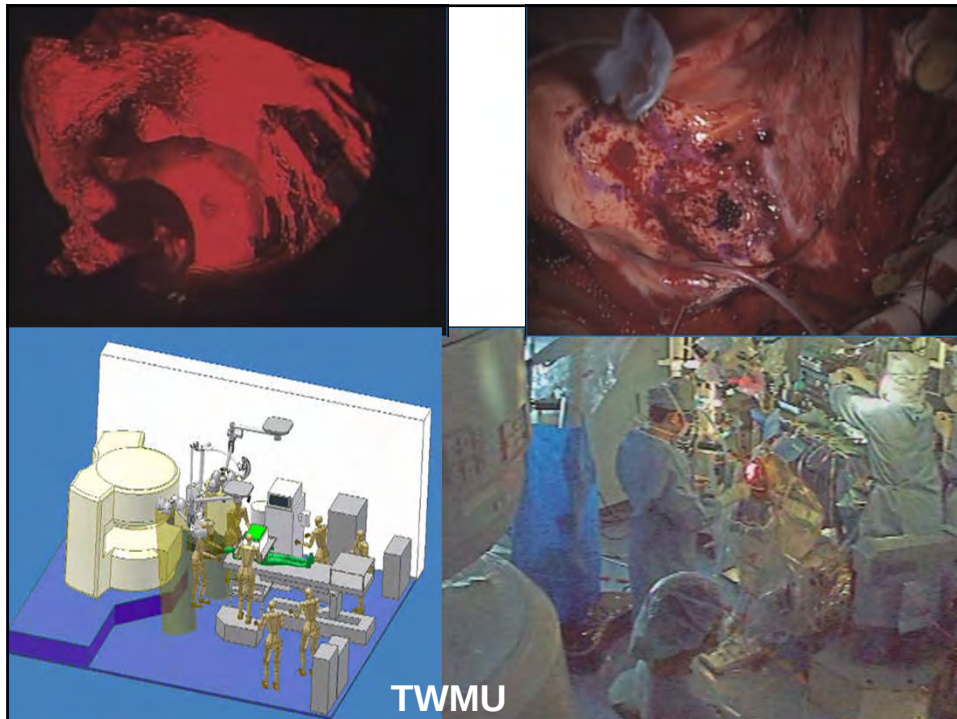
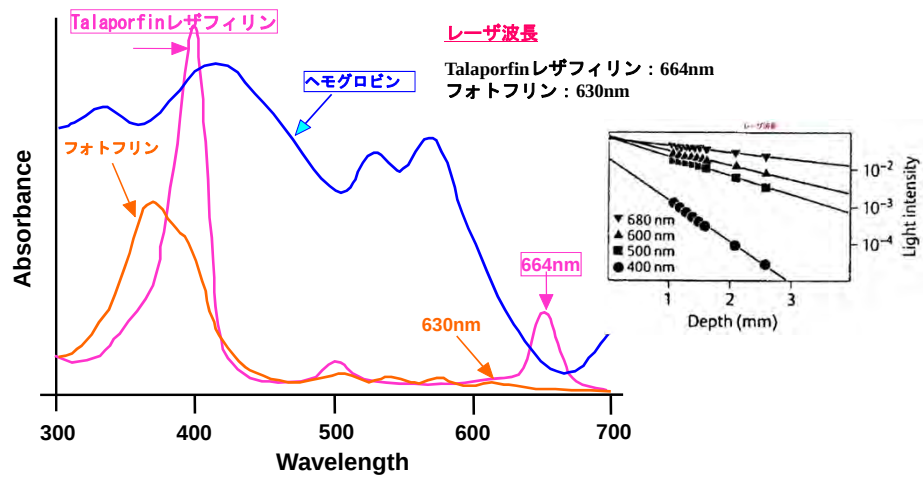
明治製薬株式会社

PDTの原理・作用機序

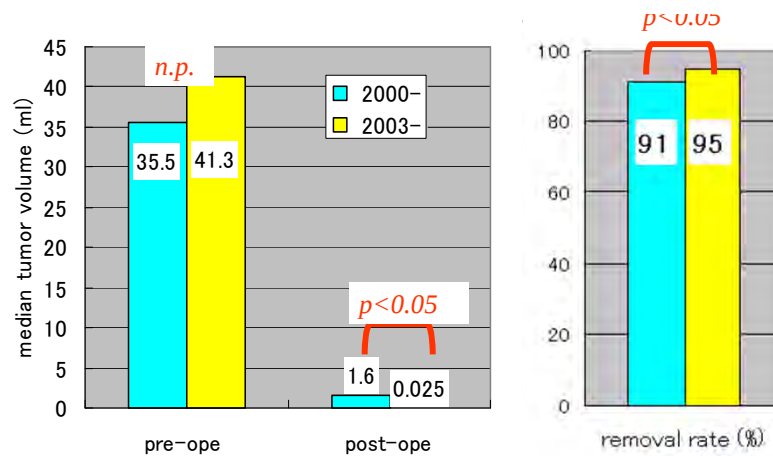


一重項酸素が腫瘍細胞及び腫瘍血管を障害し、抗腫瘍効果を発現

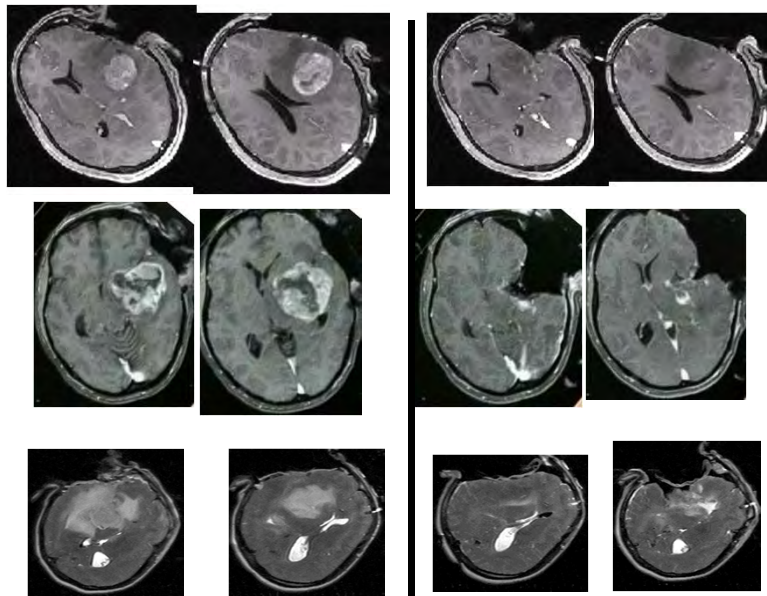
吸収スペクトルの比較



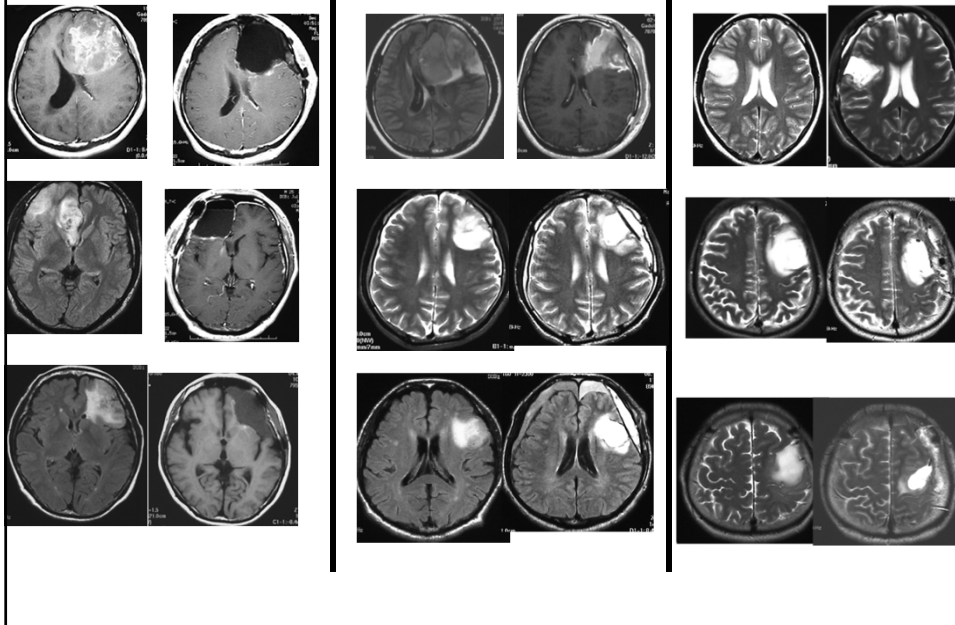
結果 グリオーマの腫瘍量と摘出率
 平均腫瘍量 36.5 ml (28.7-43.9)
 平均残存腫瘍量 0.17 ml (0-0.96)
 平均摘出率 93%
 全摘症例 46% (44/96)



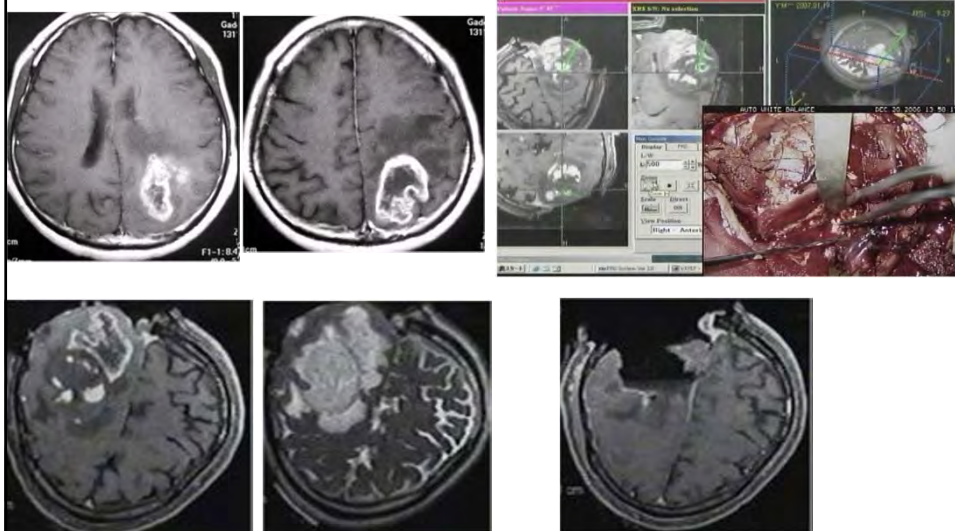
Glioma in Insular and basal ganglia



Glioma near language area

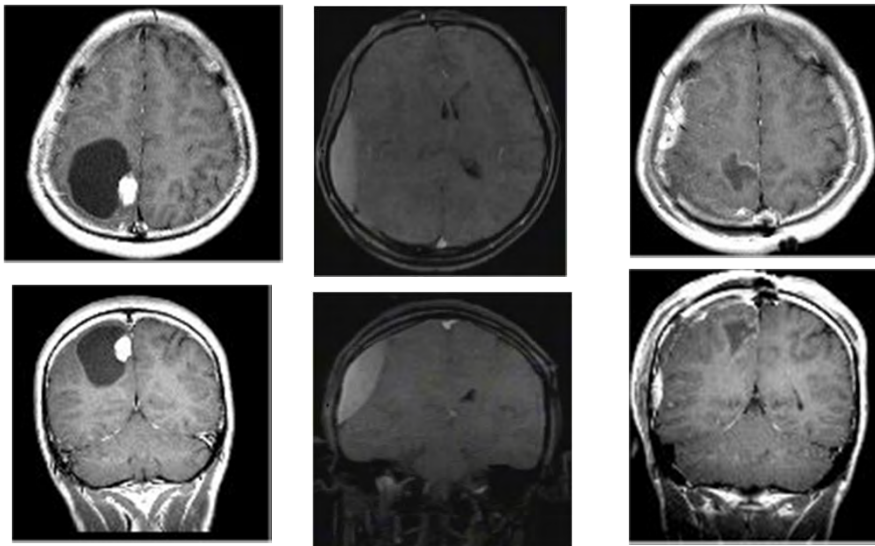


65歳男性 GBM



腫瘍内出血を術中MRIで同定

20歳男性 astrocytoma



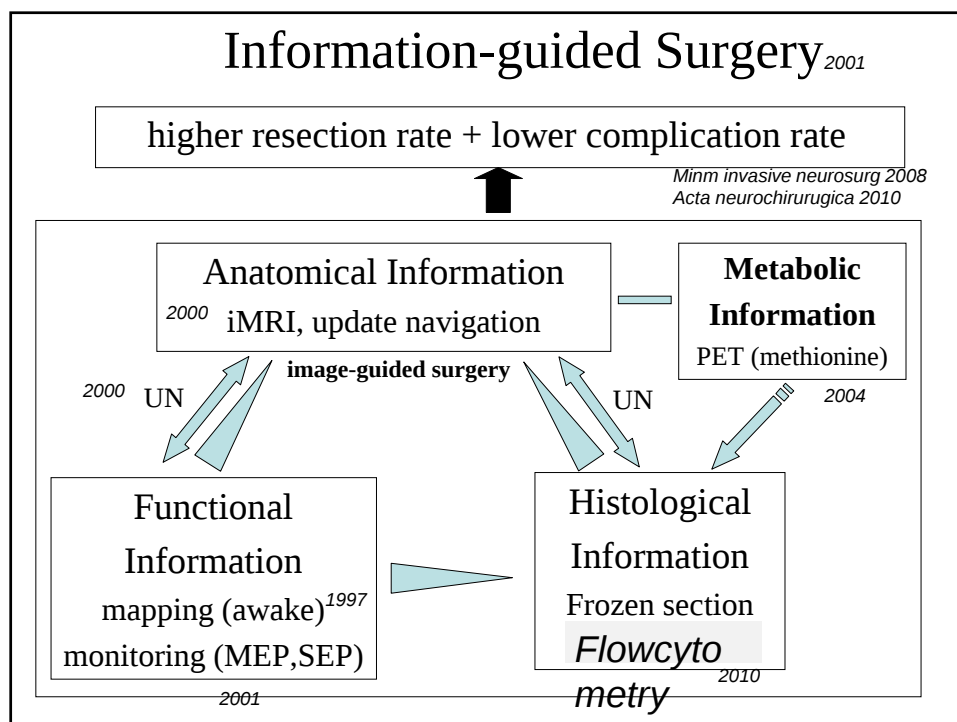
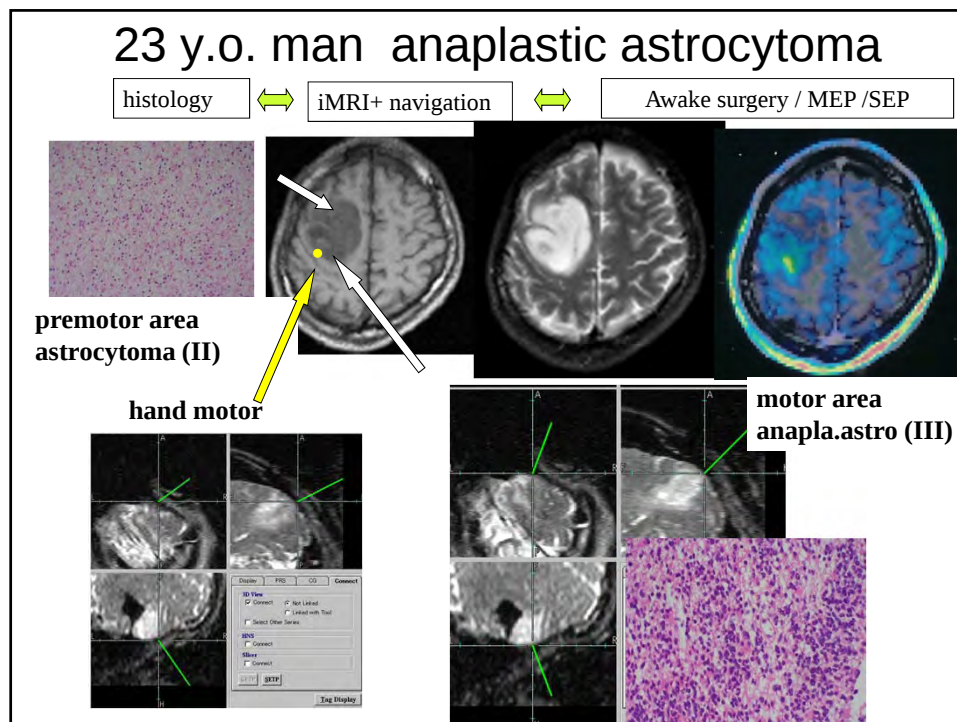
開頭範囲外硬膜外血腫が術中MRIで同定

Survival Rates of Glioma Patients

WHO grade	N	1年	2年	3年	4年	5年
I	5	100	100	100	100	100
II	56	98	93	90	90	90
III	44	95	90	86	78	78
IV	44	62	28	13	13	13
III+IV	88	78	59	50	42	42

astro+oligo+ependy

Japan tumor registry (1990-95)



Open MRI guided robotic surgery 精密誘導手術



Advanced Hands

Computer-aided surgery (CAS)

- Late '80s - now
- Computer integrated
 - Diagnosis
 - Surgical planning
 - Navigation
- Intra-operative imaging
(advanced vision)
- Robotic surgery
(advanced hands for surgeon)
- Strategy desk: Objective assessment & monitoring
(advanced brain)



Robotic surgery

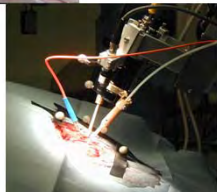
based on W cube(W3)&I

- Wetware (Human)
- Hardware
- Software

Precision-guided surgery

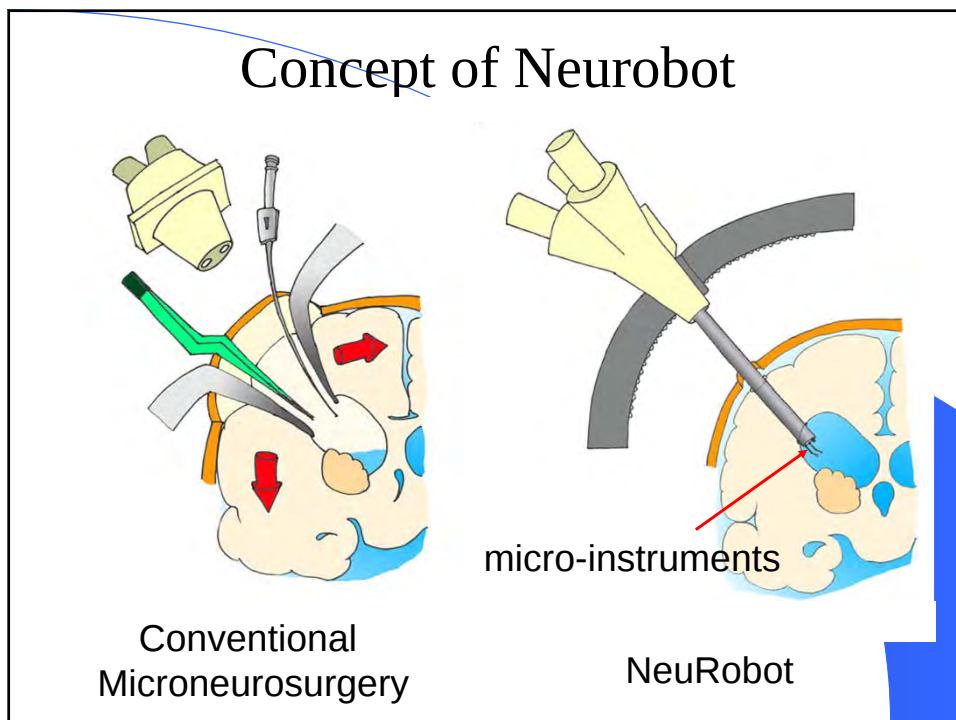
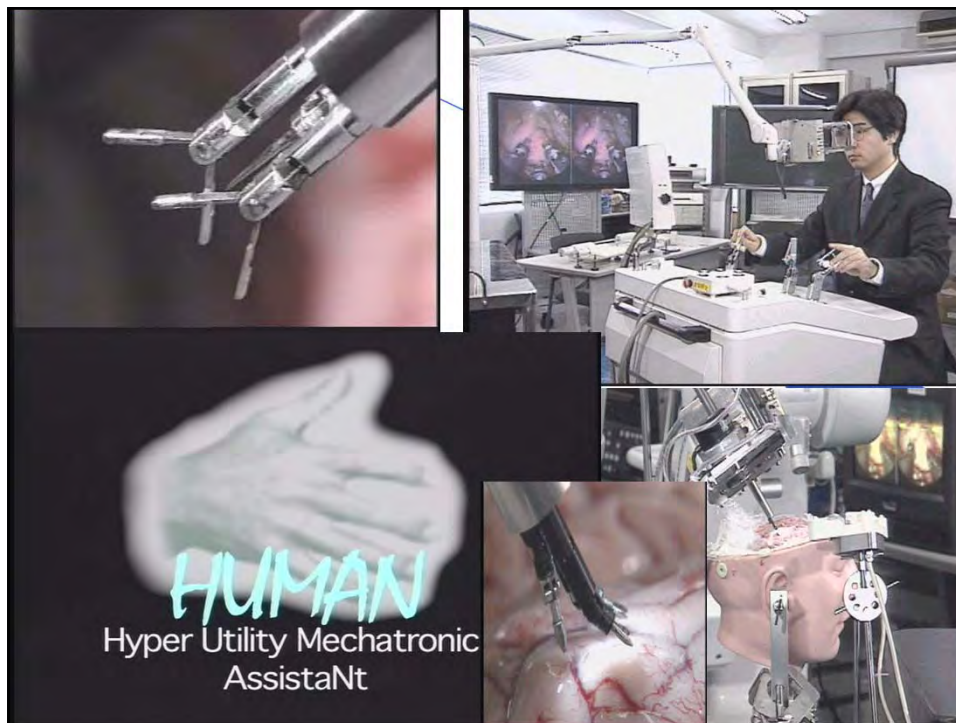
Advanced hands

In
Neurosurgical field



VS



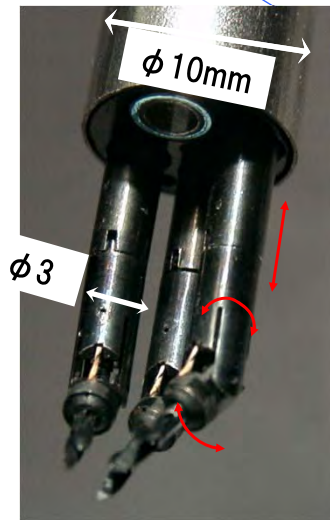


Neurobot

(Shinshu Univ., Tokyo Womens Medical Univ., Waseda Univ. + Hitachi)



KTP laser



3 DOF



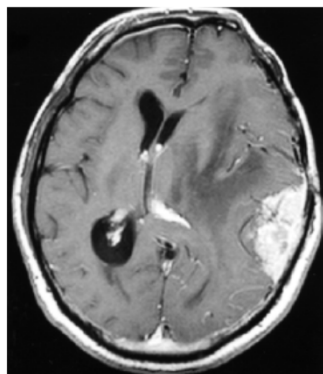
manipulator-
supporting device



Neurosurgery 51:985-988, 2002

First clinical application of robotic telemanipulation system in neurosurgery in August 2002

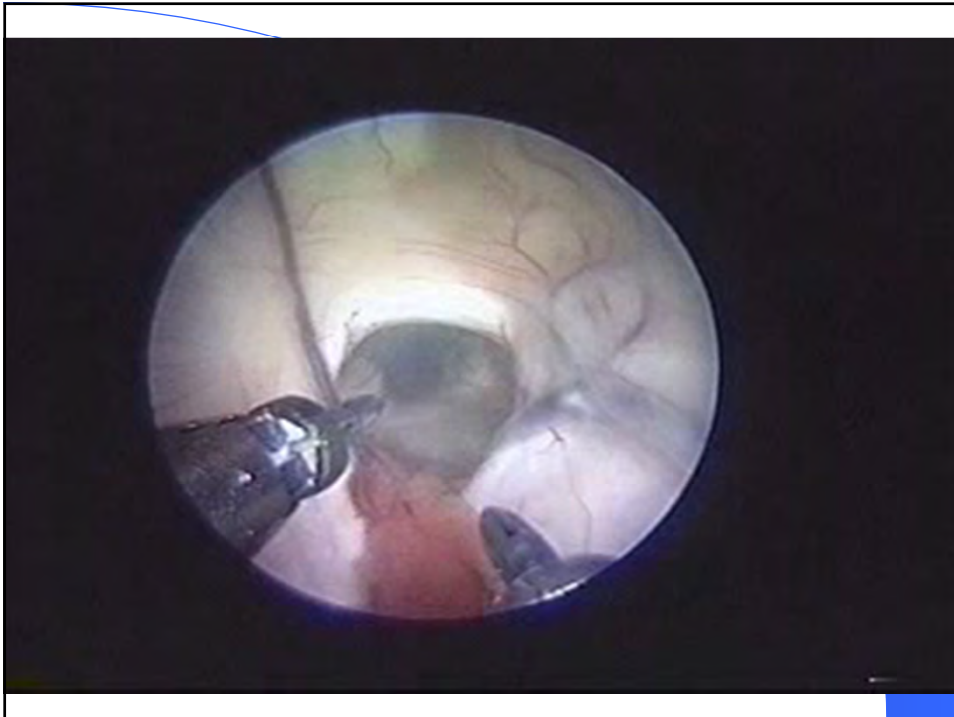
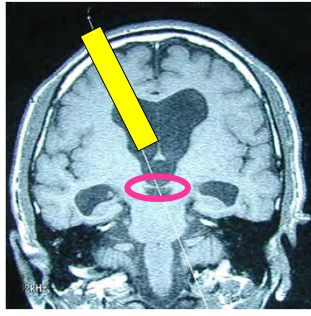
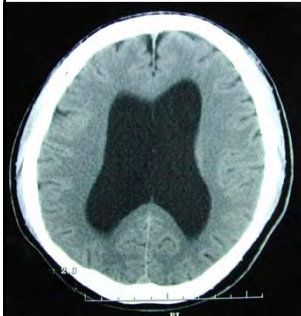
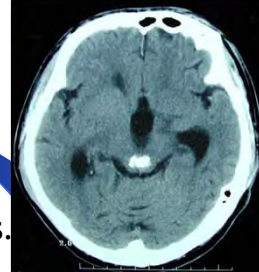
(Shinshu Univ.: Drs Goto, Hongo, Kobayashi)



J Neurosurg 99:1082-1084, 2003

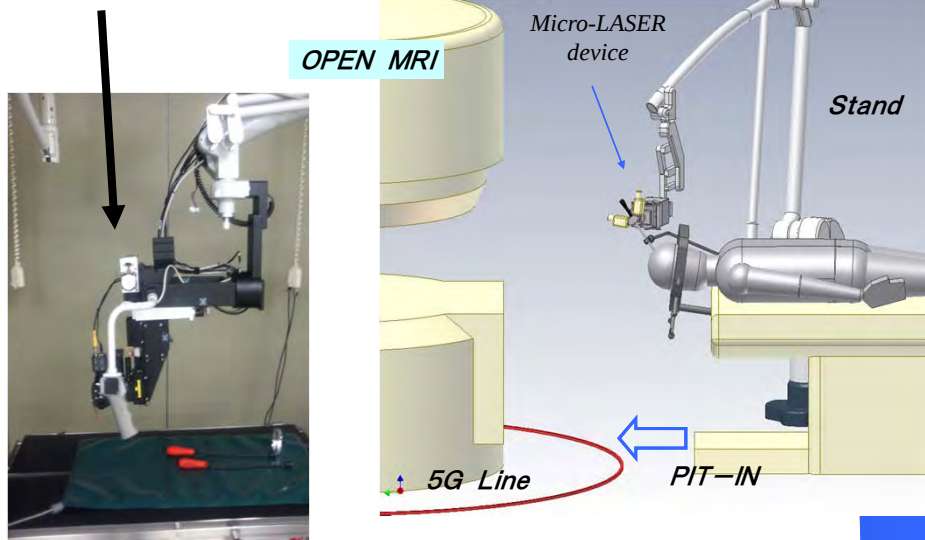
Third case of robotic neurosurgery

- hydrocephalus
- Third ventriculostomy
 - to open the membrane between IIIrd ventr. and subarachnoid space
- Neurobot complete all surgical procedures.



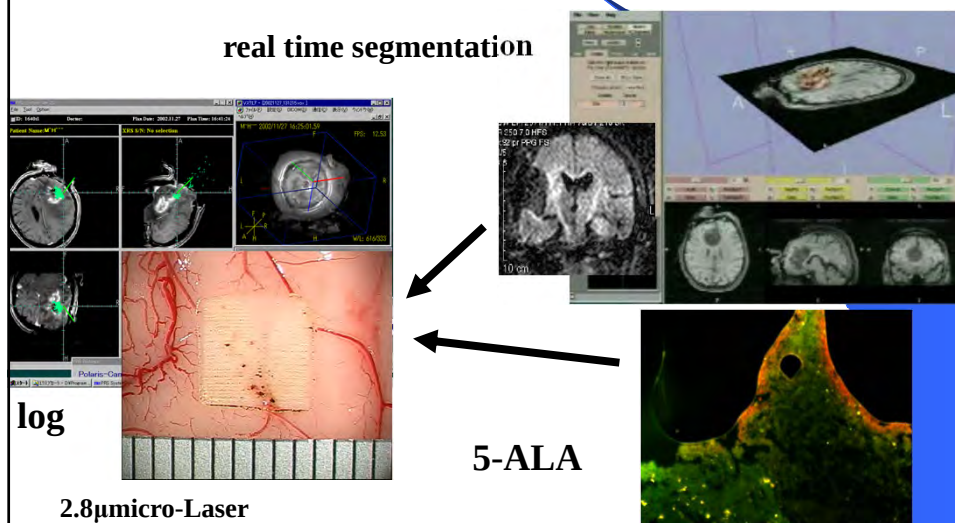
MRI-guided digital surgery

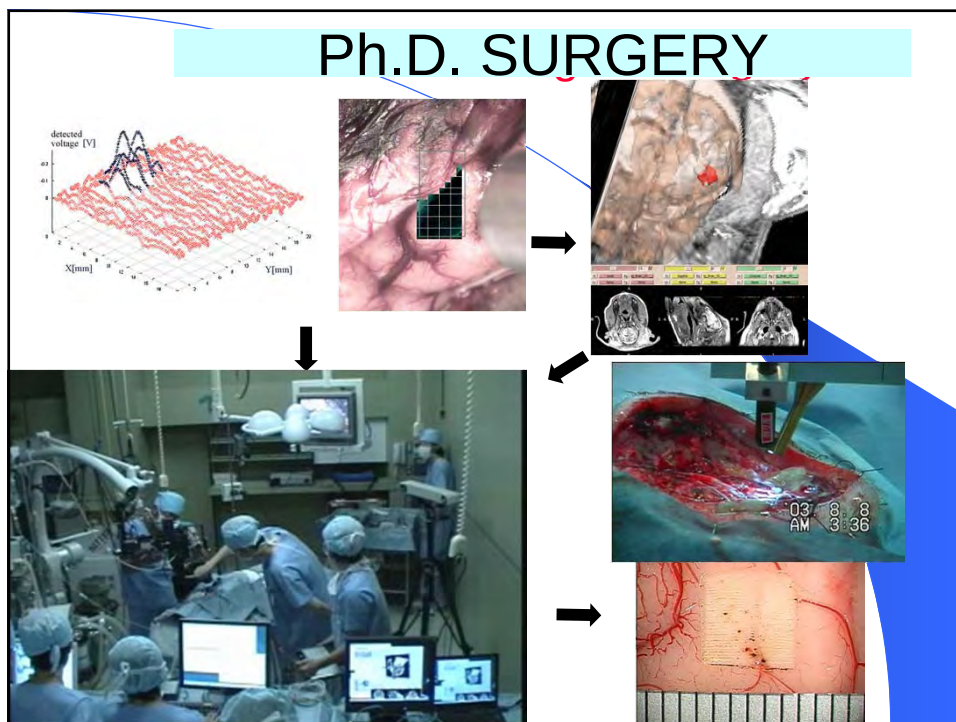
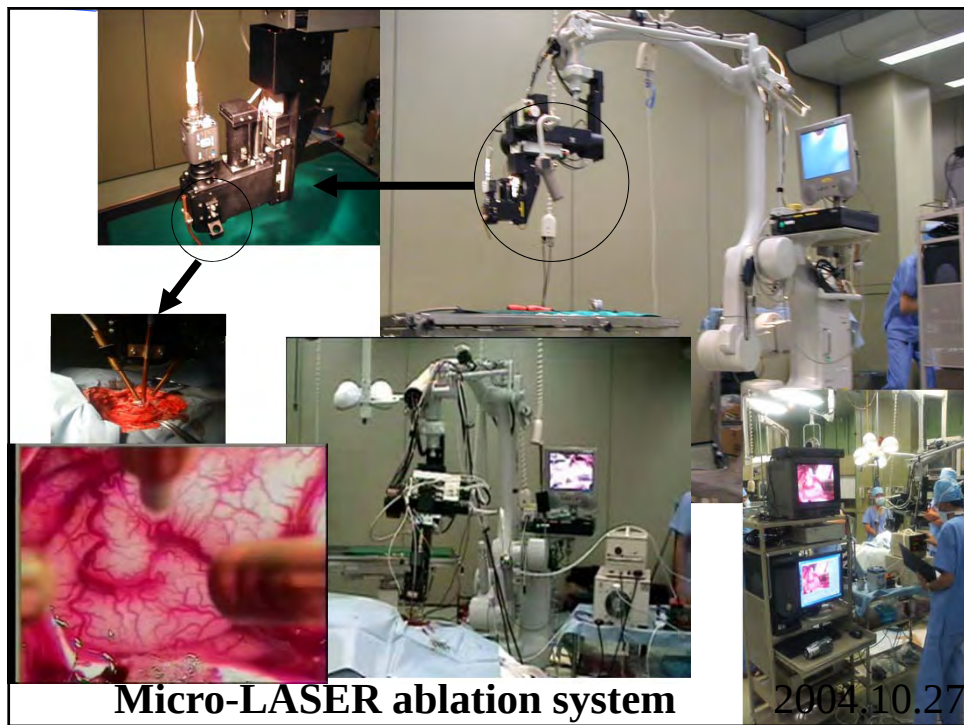
Micro-LASER ablation system



Precision-guided LASER Surgery System

real time segmentation





Tele-robotic surgery

Under radioactive circumstances

