



Associazione Italiana
di Radioterapia Oncologica

RADIOTERAPIA STEREOTASSICA ENCEFALICA CON GAMMA KNIFE: INDICAZIONI CLINICHE, PROBLEMATICHE E DIFFERENZE CON ALTRE METODICHE STEREOTASSICHE

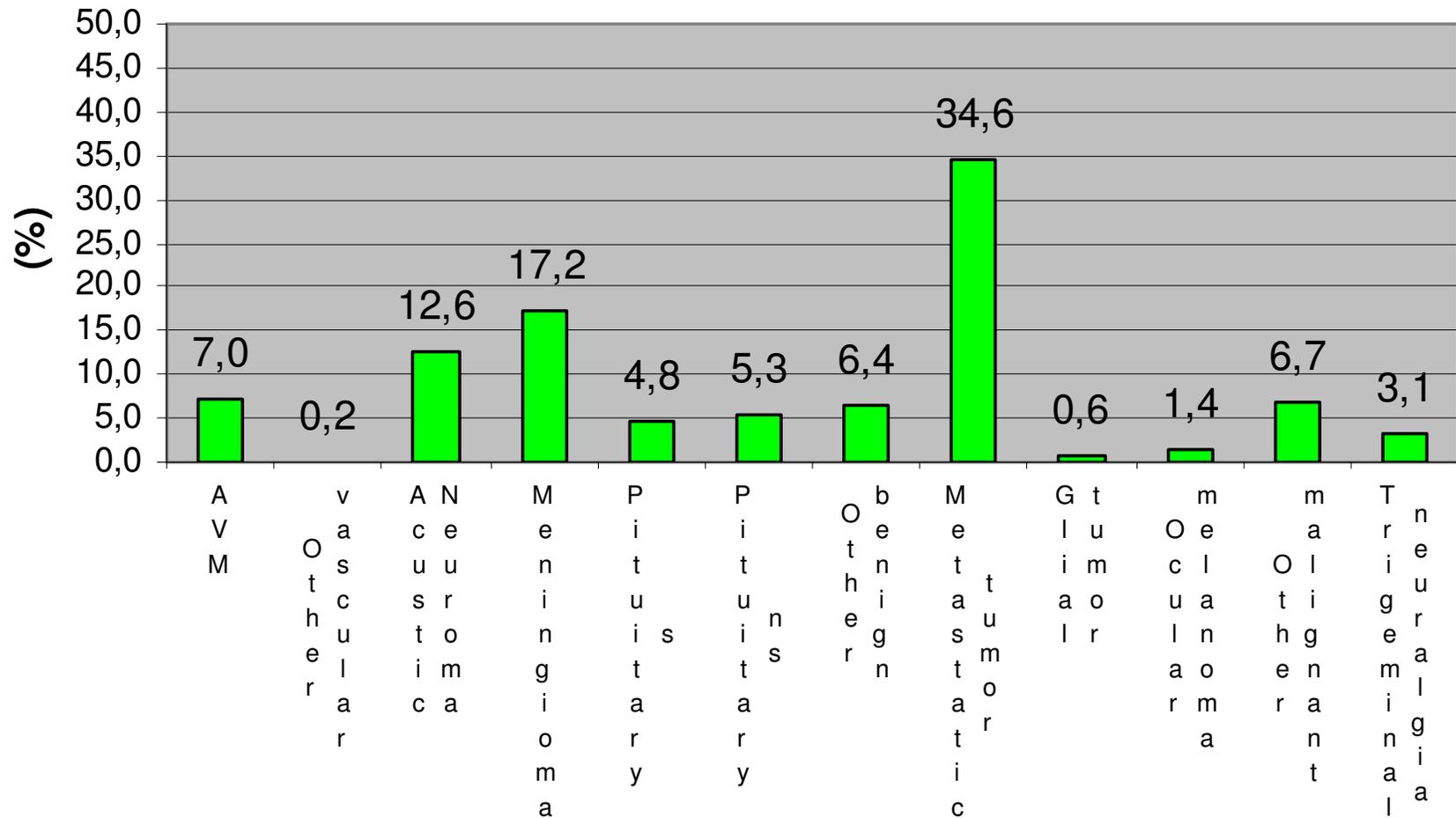
Micaela Motta - HSR, Milano

*IX CORSO PARTENOPEO DI RADIOTERAPIA: RADIOTERAPIA HIGH TECH: CHE COSA C'E' DI NUOVO?
NAPOLI, 08 e 09/06/2009*

Gamma Knife® surgery, is a non-invasive method for treating brain diseases. It is the delivery of a **single, high irradiation dose** to small and critically located intra-cranial volumes through the intact skull.

At the beginning it was used only for brain disorders, now above all for tumors.

hSR activity



Prescription Dose (50%)

	Gy
Adenoma NS	15
Adenoma S	25
AVM	18 - 22
Uveal Melanoma	35
Meningioma	15
MET	16 - 25
Acoustic Schwanoma	13
Trigeminal Neuralgia	35 - 40

The procedure

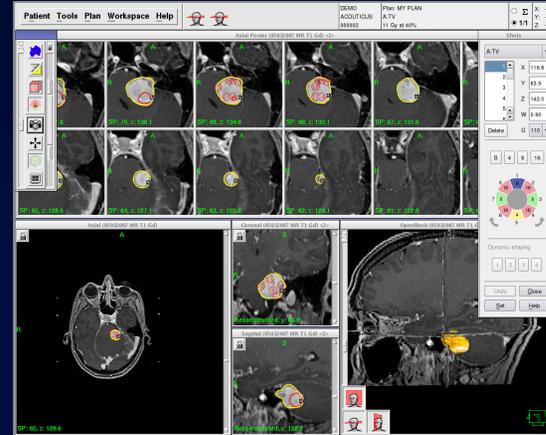
1. Coordinate System



2. Imaging



3. Treatment Planning



4. Patient Docking (Clearance Run)



5. Therapeutic Procedure

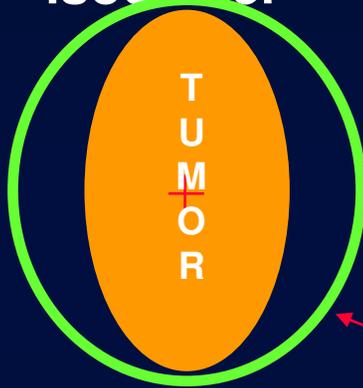


NOT NECESSARY QA PATIENTS !!



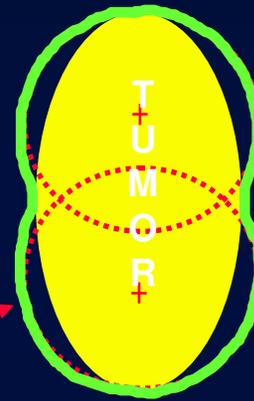
Conformity of dose to target

Single
isocenter



$$\text{PIV/TV} = 2.7$$

Two isocenters

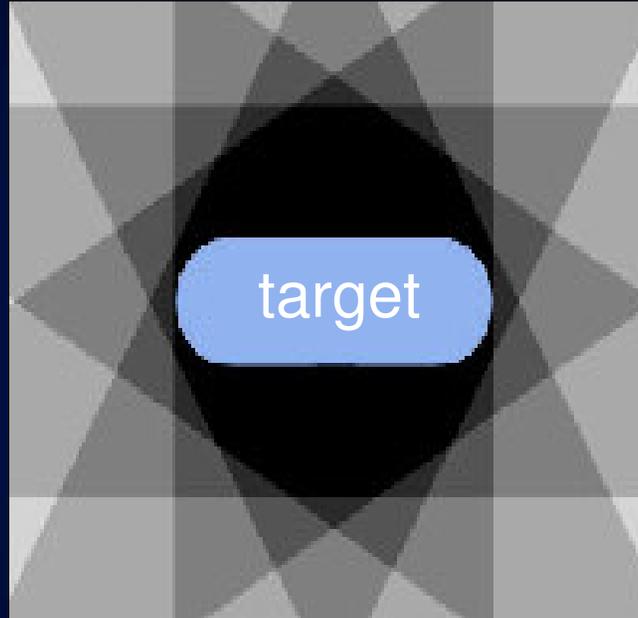
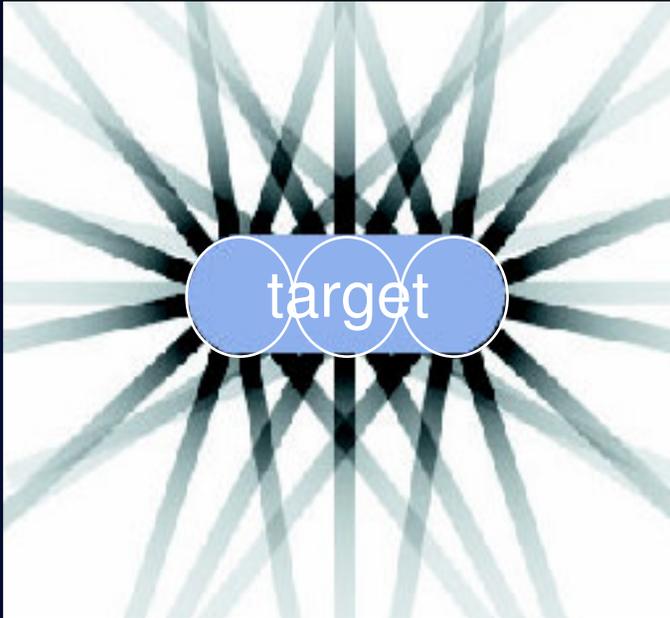


$$\text{PIV/TV} = 1.4$$

Prescription
isodose volume

PIV/TV = Conformity of the prescribed dose to the target volume

Conformity of dose to target



The two pictures show the necessity for multiple isocenters in order to minimize dose delivered to normal tissue.

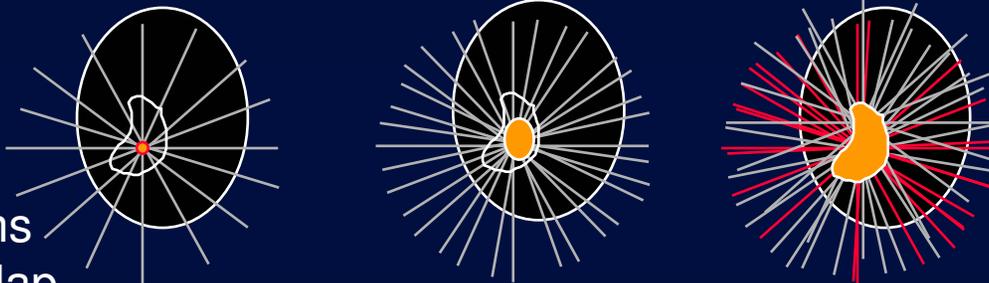
Importance of narrow beams



Target in head

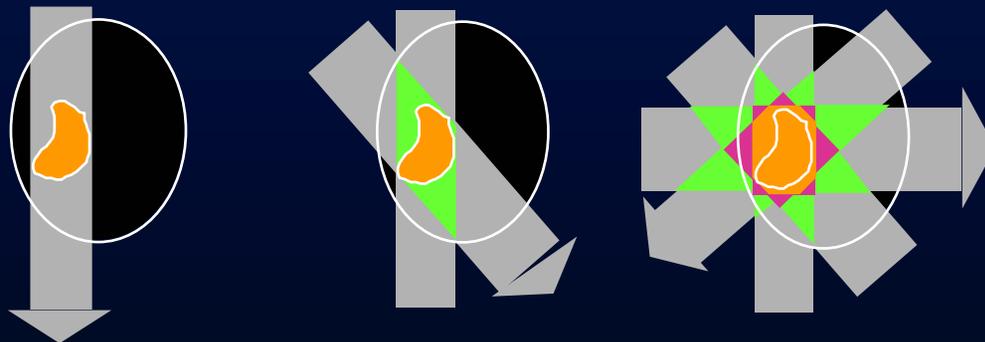
Leksell Gamma Knife[®]

Multiple isocenters using narrow beams = small beam overlap



Linac μ MLC

One isocenter with several wide beams individually shaped = large beam overlap



Time

QA program

Mechanical positioning repeatability < 0.05 mm

Diode Tool repeatability < 0.1 mm

Film Holder repeatability < 0.1 mm

Absolute positioning accuracy PPS < 0.3 mm

Axial radiological accuracy < 0.4 mm

System accuracy < 0.5 mm

Composite shots

Patient Tools Plan Workspace Help

Patient Selected: Composite PERFECTION
x: --
y: --
z: --

▼ Axial Poster (Leksell)

SP: -, z: 107.0 SP: -, z: 106.0 SP: -, z: 105.0 SP: -, z: 104.0

SP: -, z: 103.0 SP: -, z: 102.0 SP: -, z: 101.0 SP: -, z: 100.0

SP: -, z: 99.0 SP: -, z: 98.0 SP: -, z: 97.0 SP: -, z: 96.0

SP: -, z: 95.0 SP: -, z: 94.0 SP: -, z: 93.0 SP: -, z: 92.0

▼ Coronal (Leksell) ▼ Shots

	X	Y	Z	W	G
1	100.0				
2		100.0			
			100.0		
				1.00	
Delete					90

B 4 8 16

1
8 4 16 4 2
7 16 16 3
6 4 16 4 4
5

Dynamic shaping
1 2 3 4

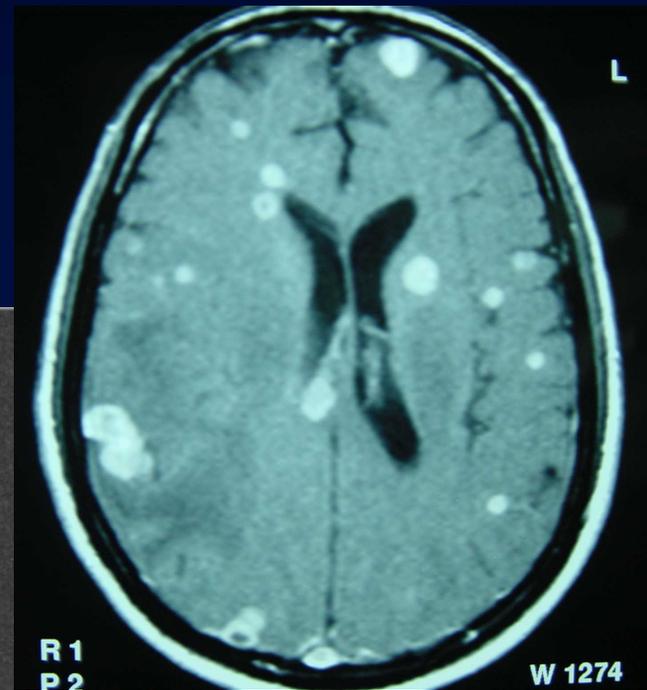
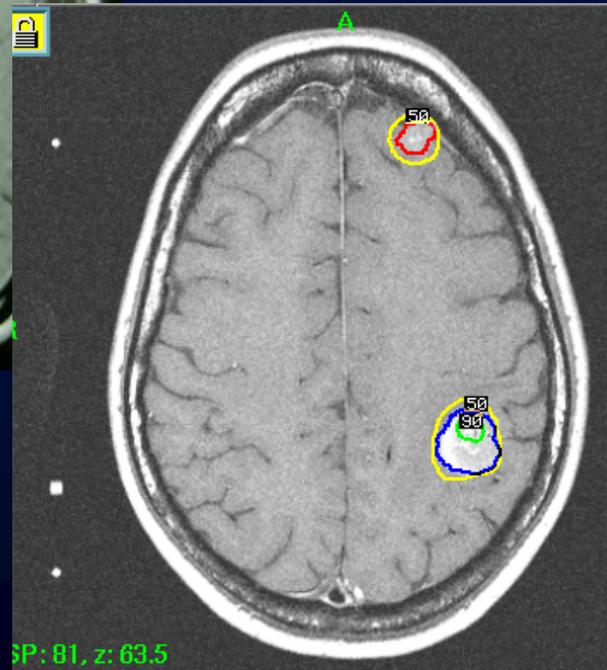
Undo Close
Set Help

Reconstructed, y

Reconstructed, x: 100.0

▼ OpenBook (Leksell)

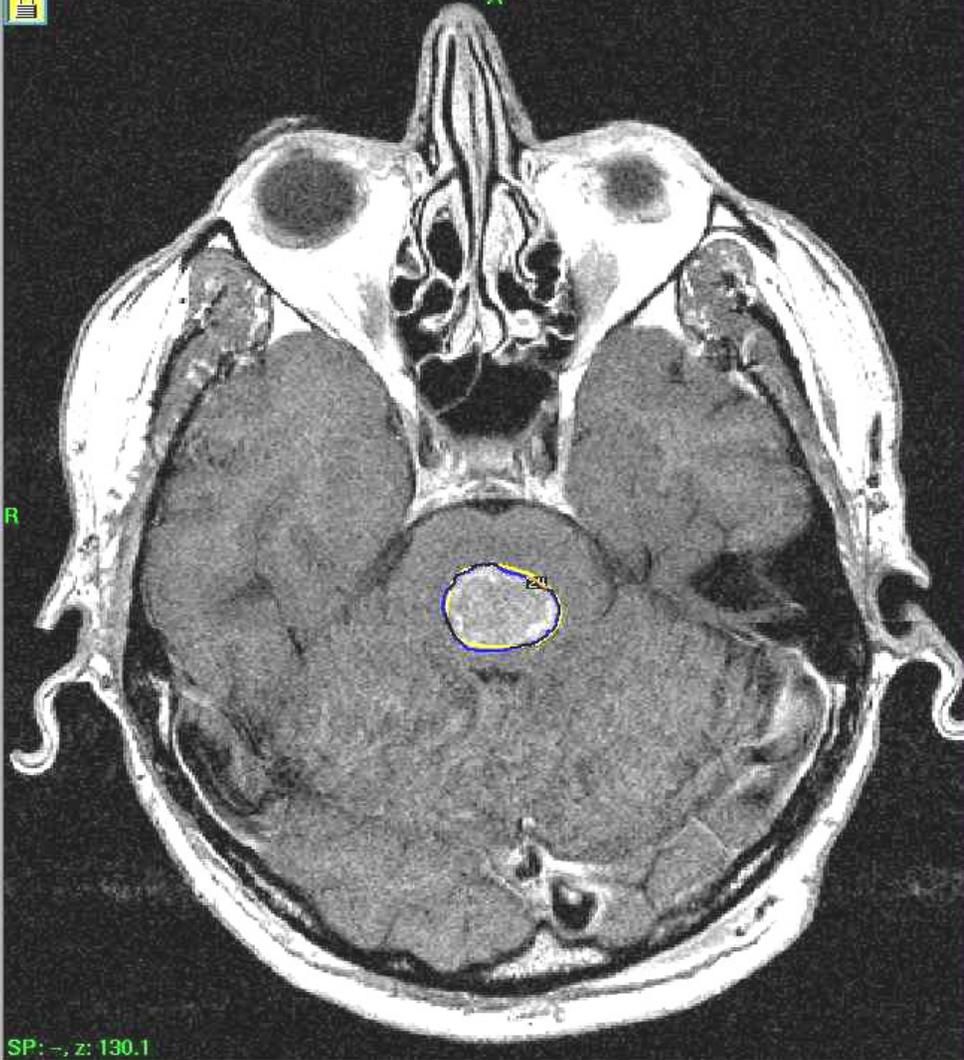
Brain metastases





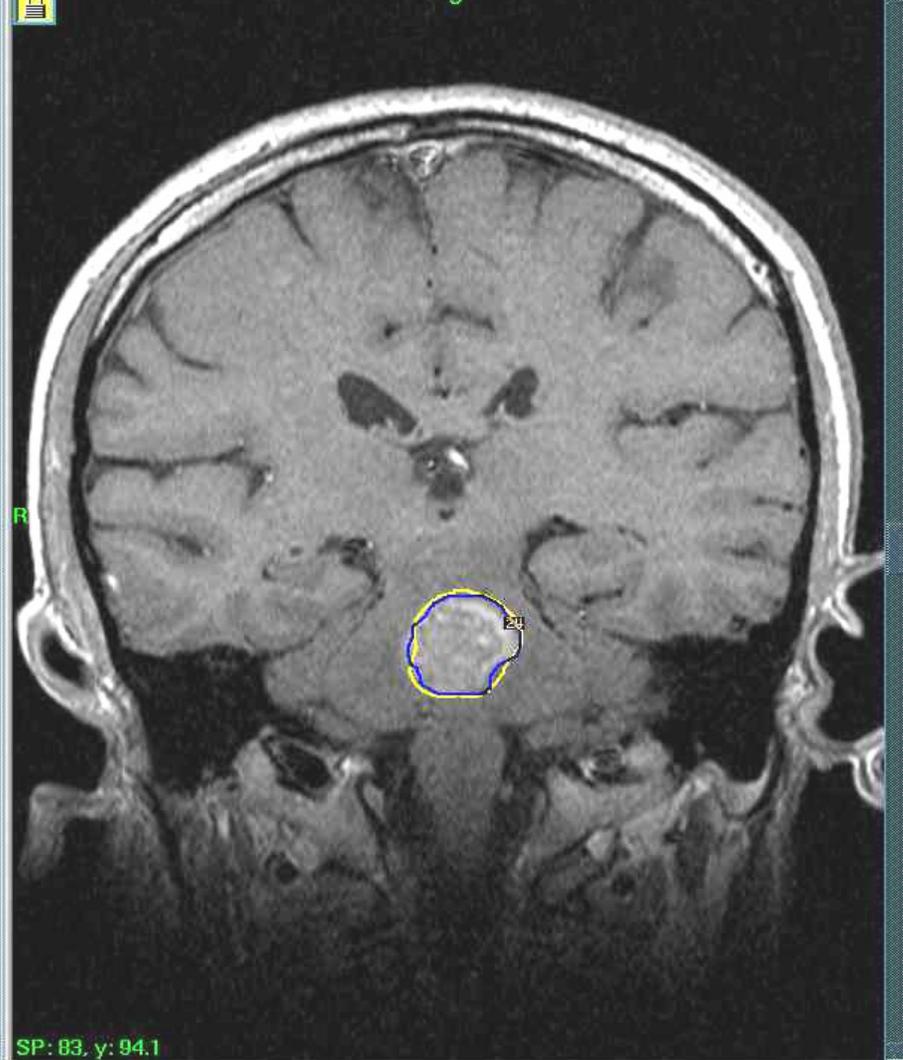
Axial (comb)

A



Sagittal (comb)

S



Nov 28



LGP

One

Two

Three

Four

EXIT

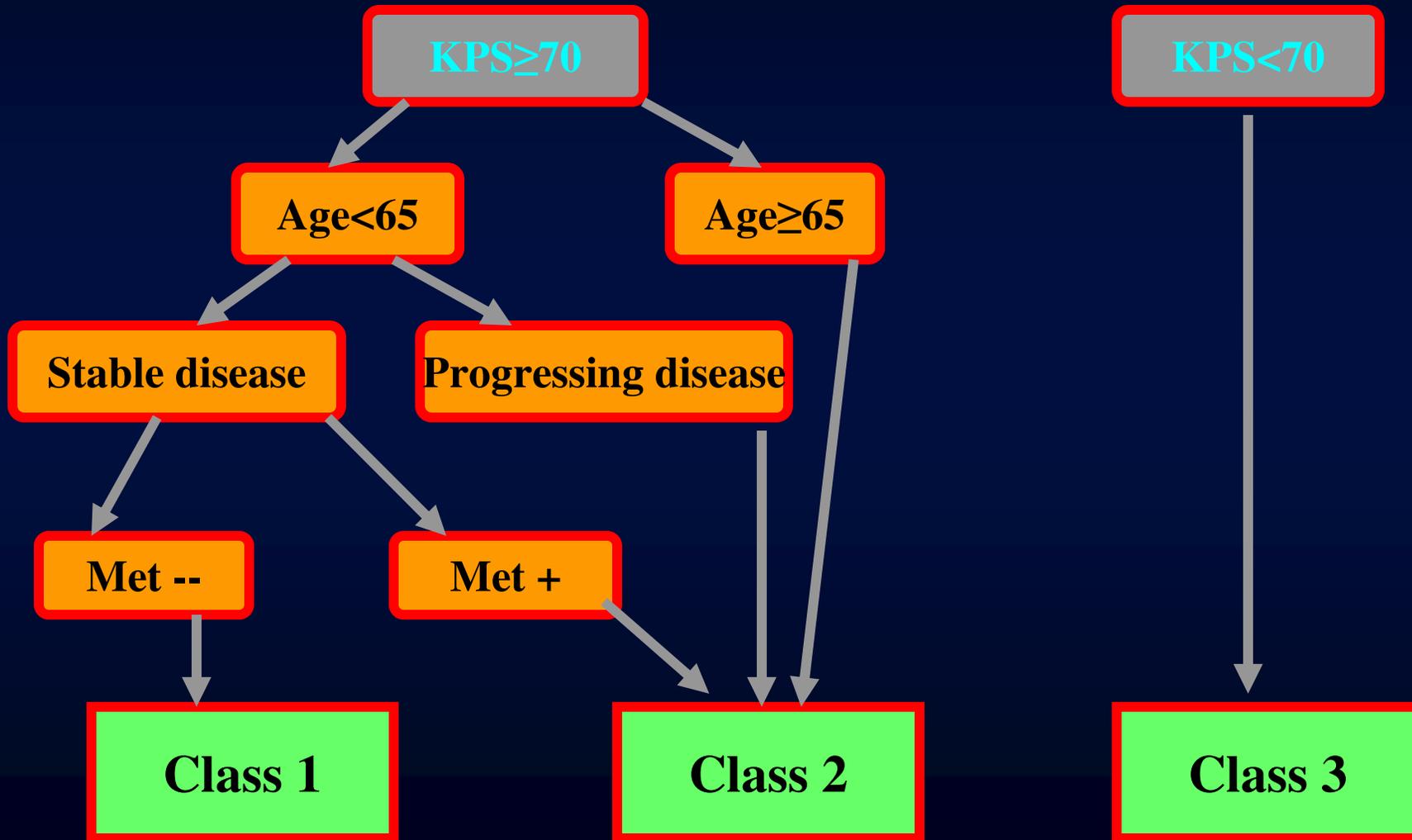
HELP



Incidence

- Lung
- Breast
- Melanoma
- Kidney
- Gastroenteric
- Thyroid
-

Brain Metastases RPA Classification



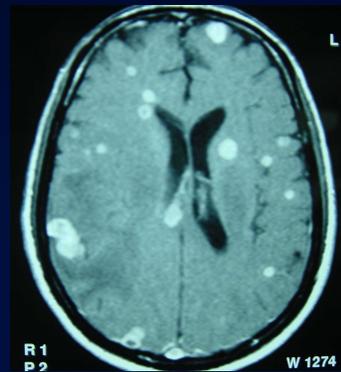
Flow chart

1. BRAIN MRI
2. TAC W.B
3. BONE SCAN
4. BIOPSY
5. KPS



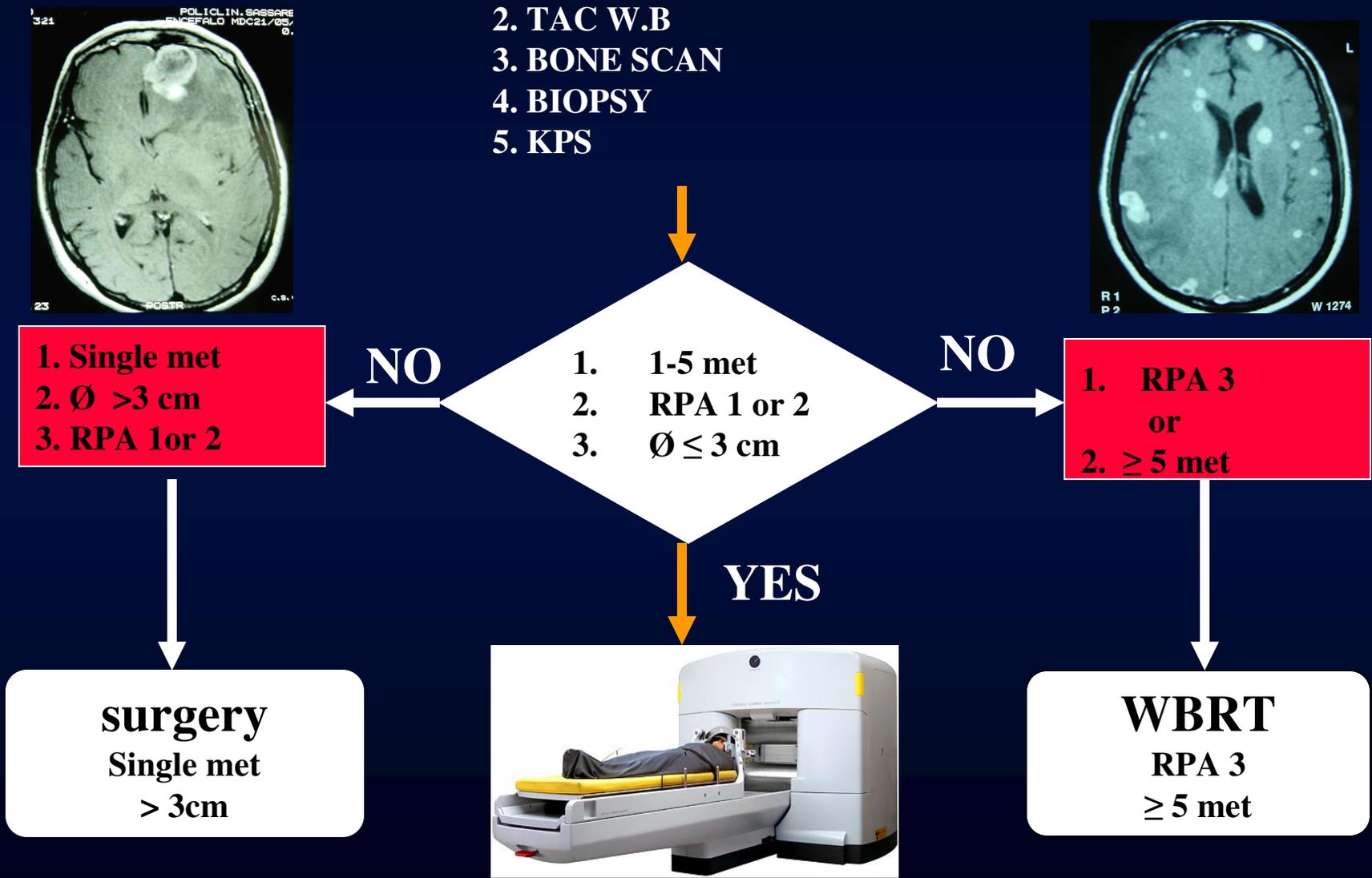
- 1. Single met
- 2. $\emptyset > 3$ cm
- 3. RPA 1 or 2

surgery
Single met
> 3cm



- 1. RPA 3
or
- 2. ≥ 5 met

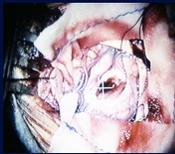
WBRT
RPA 3
 ≥ 5 met

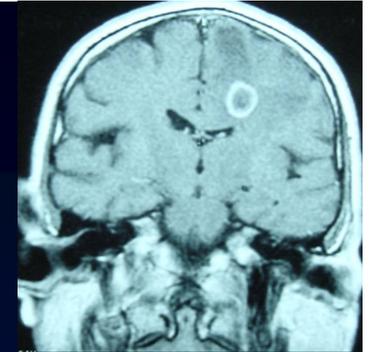
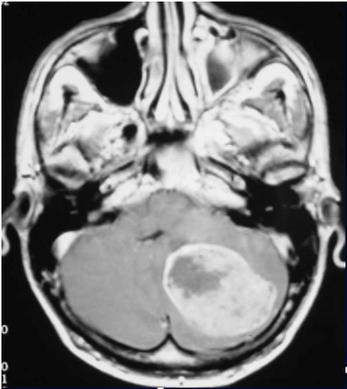




Number of METs



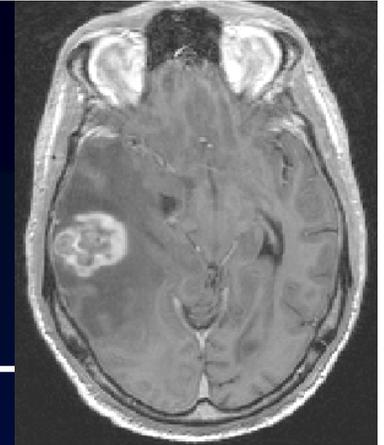
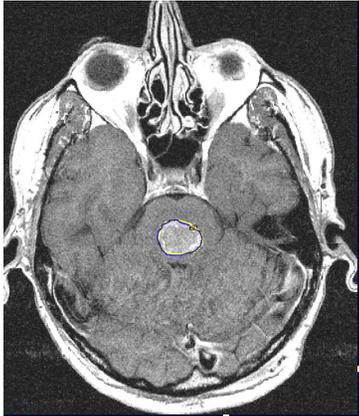
		Number
RADIOSURGERY		4-5
SURGERY		1
WBRT		∞
SURGERY + WBRT		1-2



Dimensions

		Diameter
RADIOSURGERY		< 3 cm
SURGERY		No limits
WBRT		No limits (better if < 1 cm)
SURGERY + WBRT		No limits

Localization



RADIOSURGERY



No limit

SURGERY



crucial

WBRT



No limit

**SURGERY
+ WBRT**



crucial

Treatment

- Radiosurgery (single fraction)
- Dose 20 - 25 Gy
- Lesions $\emptyset \leq 3$ cm (volume 15 cm³)

Also for radioresistant tumors

melanoma-kidney

A photograph of a university campus. In the center, a large, modern bell tower with a cross on top stands on a green lawn. Behind it is a large, multi-story building with a curved facade. To the left, a tall tower has the letters 'HSR' on top. In the foreground, there is a wooden fence and a large green bush. The sky is clear and blue.

EXPERIENCE AT HSR -MILAN

517 pts (Jan. 2001- Jan 2005)

Primary site

• NSCLC in 264 pts	51%
• BREAST in 98 pts	19%
• KIDNEY in 47 pts	9%
• COLON in 36 pts	7%
• MELANOMA in 31 pts	6%
• MISCELLANEOUS in 64 pts	7%

All pts stratified according to RPA classes

Inclusion criteria

- Less than five metastases;
- Diameter of the lesion ≤ 3 cm (volume 15 cm^3)
or
total tumor volume in multiple metastases
 $< 20 \text{ cm}^3$;
- patient in RPA class 1 or 2.

Methods

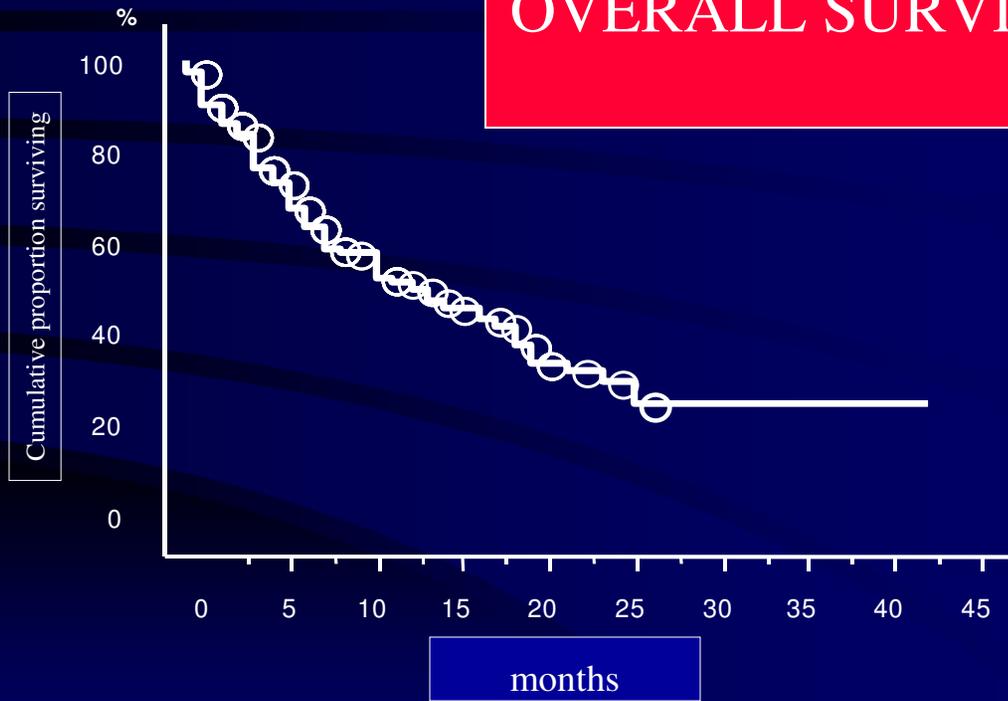
- Treatment performed in a single fraction.
- Dose prescription: 20-25 Gy at isodose 50%.
- Mean tumor volume : 2.47 ml (0.01 - 30.9 ml).
- Mean prescription dose to tumor margin :
22.6 \pm 3.4 Gy (range 9 – 25 Gy).

Results - 1/3

- Mean follow up :16 months.
- Overall median survival : 12 mos
- One year survival rate : 52 %
- Two years actuarial survival rate: 32 %
- 1-year local control : 89%
- **Complications: (radionecrosis) 8.6%**

Results – 2/3

OVERALL SURVIVAL



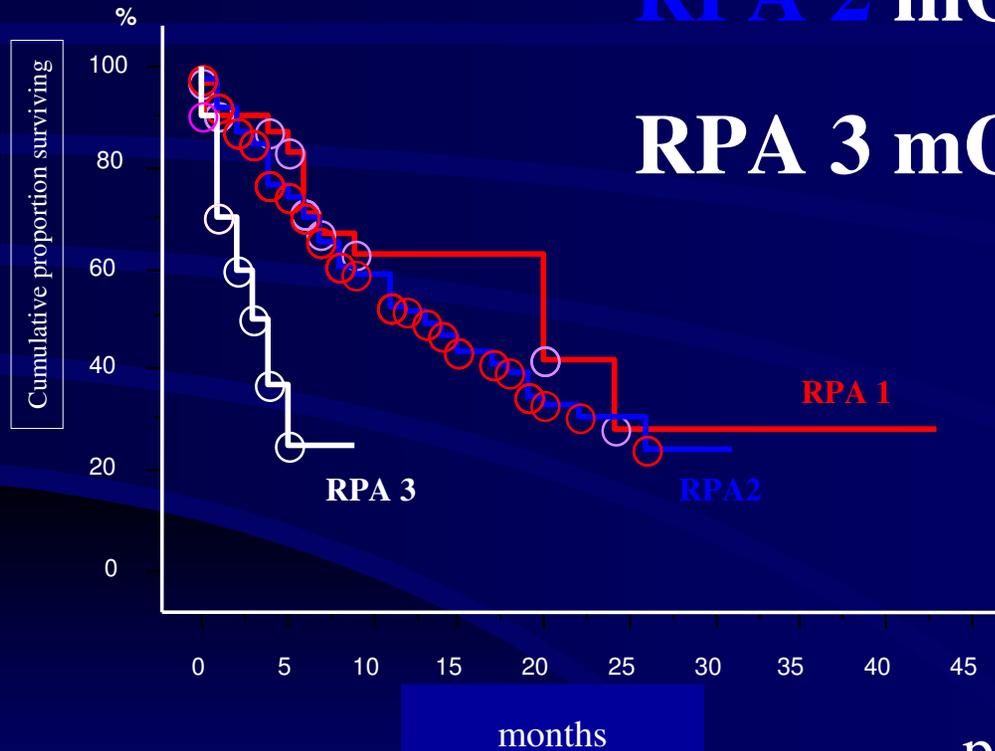
Results - 3/3

OVERALL SURVIVAL
ACCORDING TO RPA CLASSES

RPA 1 mOS = 21 mos

RPA 2 mOS = 13 mos

RPA 3 mOS = 3,5 mos

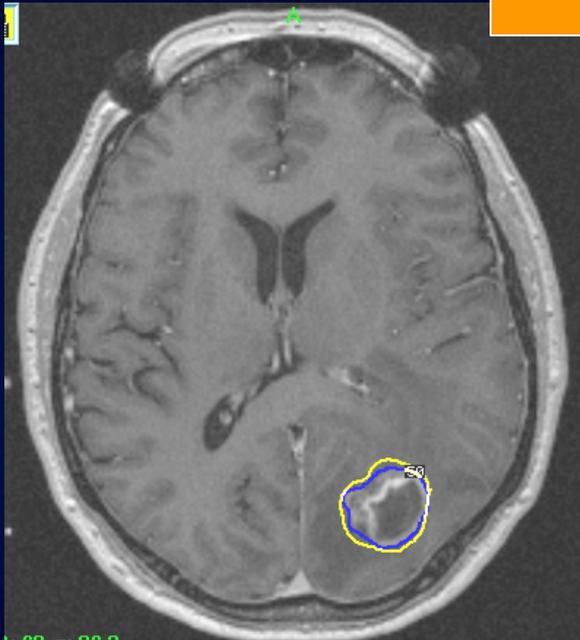


$p = 0.0003$

RS Results (HSR 517 pz)

1st Author/Inst	FFP by lesion	Median survival (mo)	Necrosis %
Moriarty (JCRT)	88% (1yr)	10.5	6%
Goodman (UCSF)	82% (1yr)	9.1	—
Young (5 instit)	91%	7.0	<4%
Chen (USC)	89%	7.8	?0%
Gerosa (Verona)	88% (1yr)	9.2	—
Pirzkall (Heidelberg)	92%	5.5	2%
Kihlstrom (Karolinska)	94%	7.0	5%
Flickinger (Pittsburg)	89%	10.0	1%
Fukuoka (Sapporo)	96%	8.0	5%
Joseph (Stanford)	94%	7.4	17%
Simonova (Prague)	94%	9.0	10%
Aucher (4 instit)	86%	12.9	?0%
Present series (HSR)	89% (1yr)	11.5	9%

Results ...

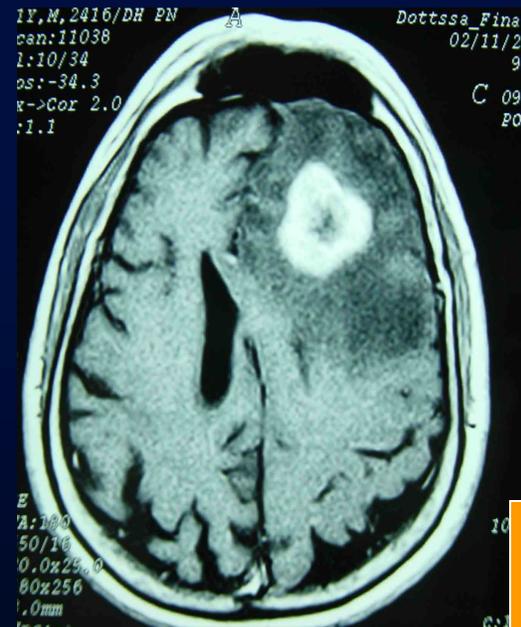
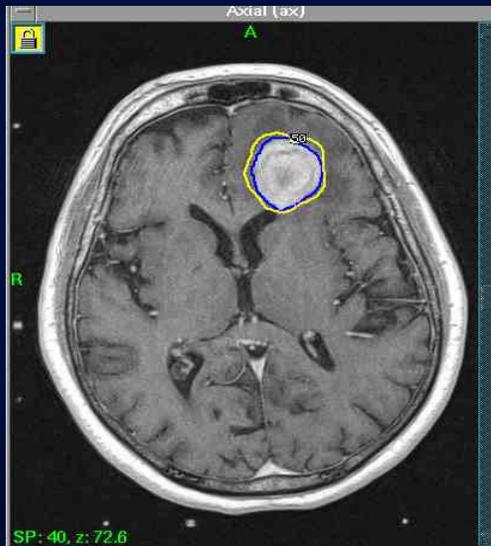


6 MONTHS AFTER RADIOSURGERY

Complications:

TREATMENT

Radionecrosis
after 4 months



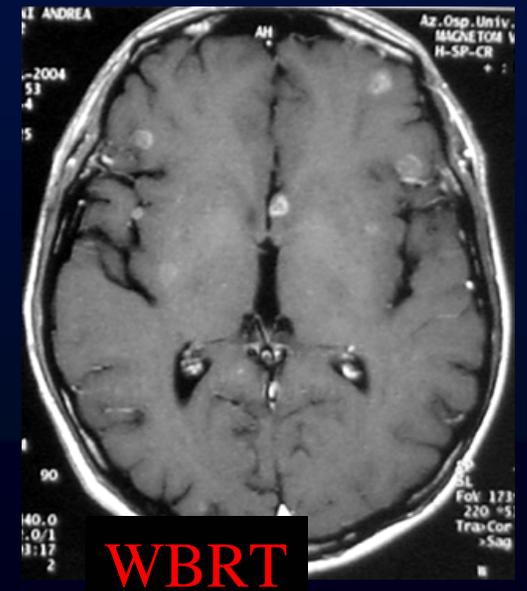
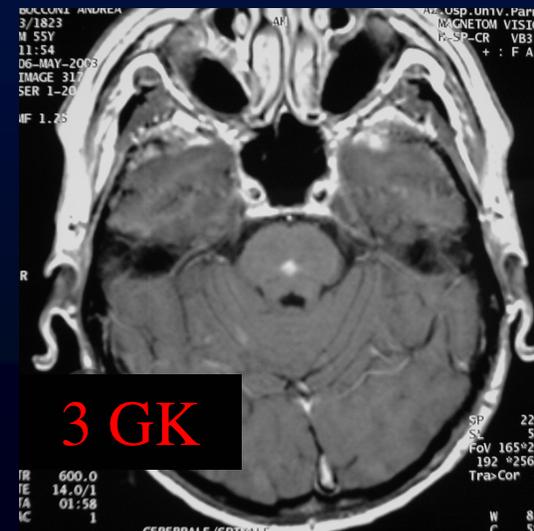
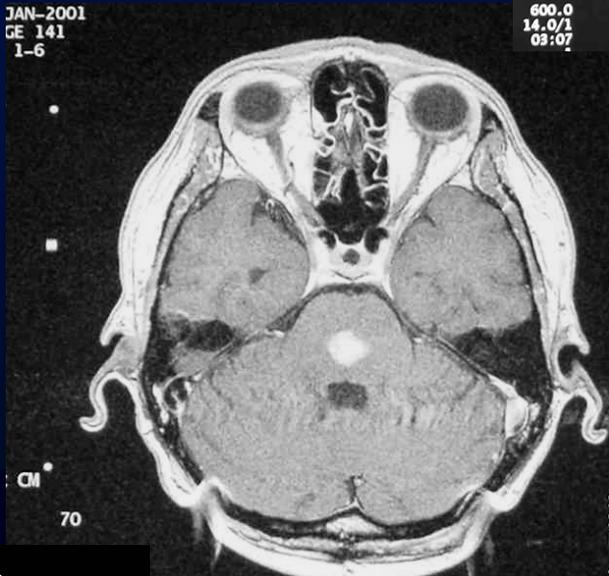
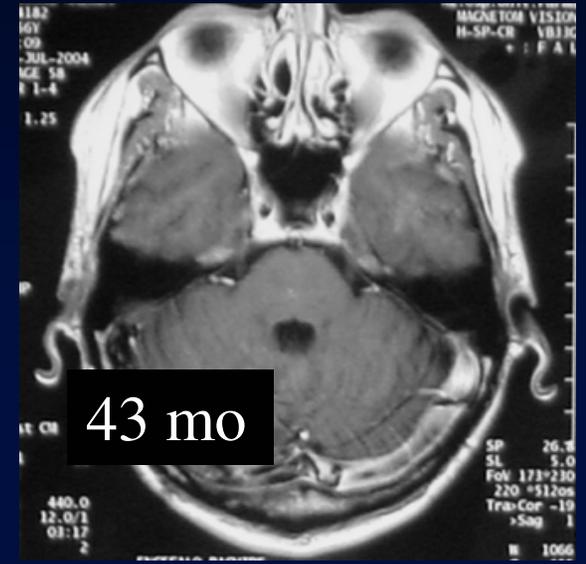
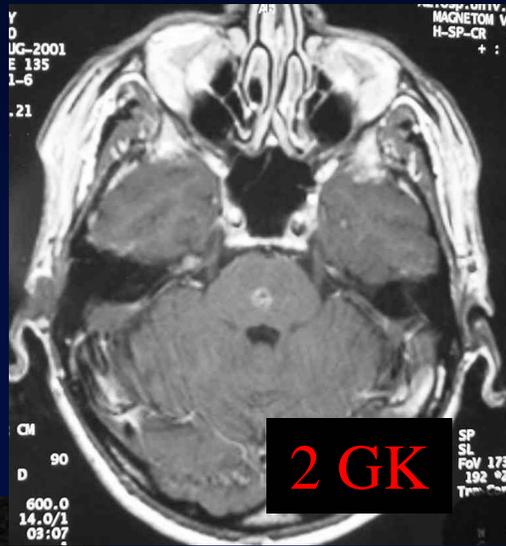
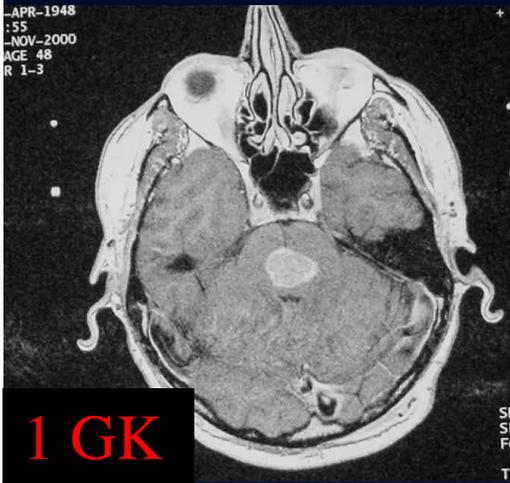
Surgery!

Mortality

	Mortality
RADIOSURGERY	0%
SURGERY	2-8%
WBRT	0%
SURGERY + WBRT	2-8%

**What to do in the case of
recurrence / new lesions
after gamma knife?**

What to do? Re-treat!



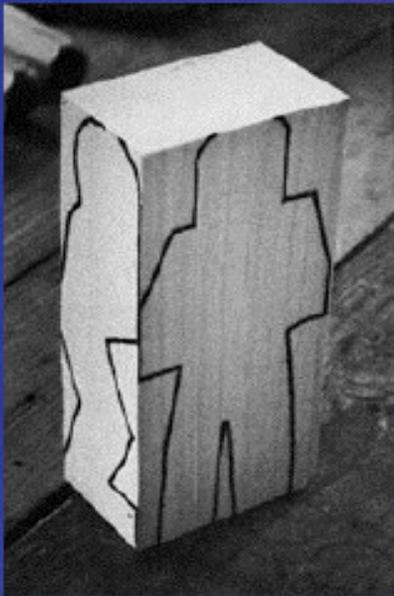
ALTRE METODICHE
TECNOLOGICHE

E

LORO APPLICAZIONI...

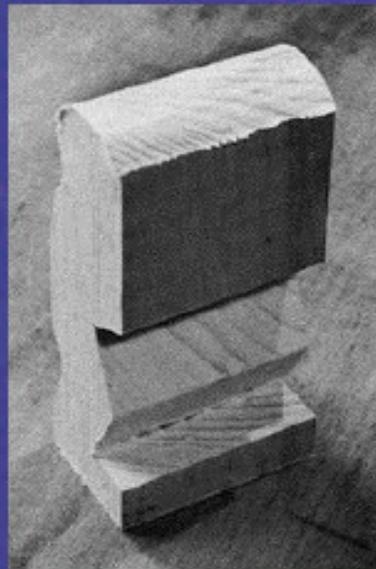
Dose Sculpting

2-D Planning

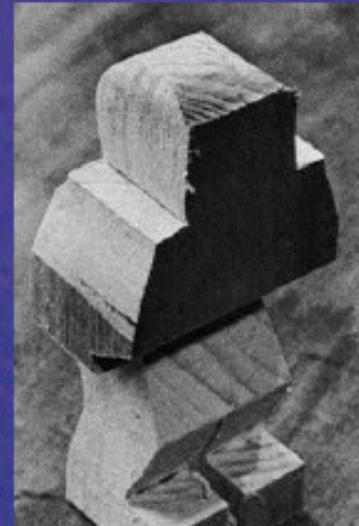


3-D

Conformal



IMRT



Courtesy of J. Schreiner Kingston Regional Cancer Centre, Ontario

SRS and SBRT*

- SRS= brain, 1 fraction
- SBRT= others, 1-few fractions
- stereotactic equipment (frame based or frameless)
- image guidance (planning and treatment)
- multiple beams (photons or particles)
- organ motion control
- mechanical tolerances ≤ 2 mm

*ASTRO/ACR guidelines. Int J Rad Oncol Biol Phys 2004;60: 1026-1032

SRT MACHINES (1/2)

- **SRT WITH LINAC**

SRT MACHINES (2/2)

- CyberKnife is a dedicated SRT machine that is not designed to provide radiotherapy capability. Small, precise beams and long treatment delivery times.
- Tomotherapy is a linac that images and delivers treatment through a rotational gantry (like CT). Provides image guidance with every treatment and can simultaneously treat multiple targets quickly.

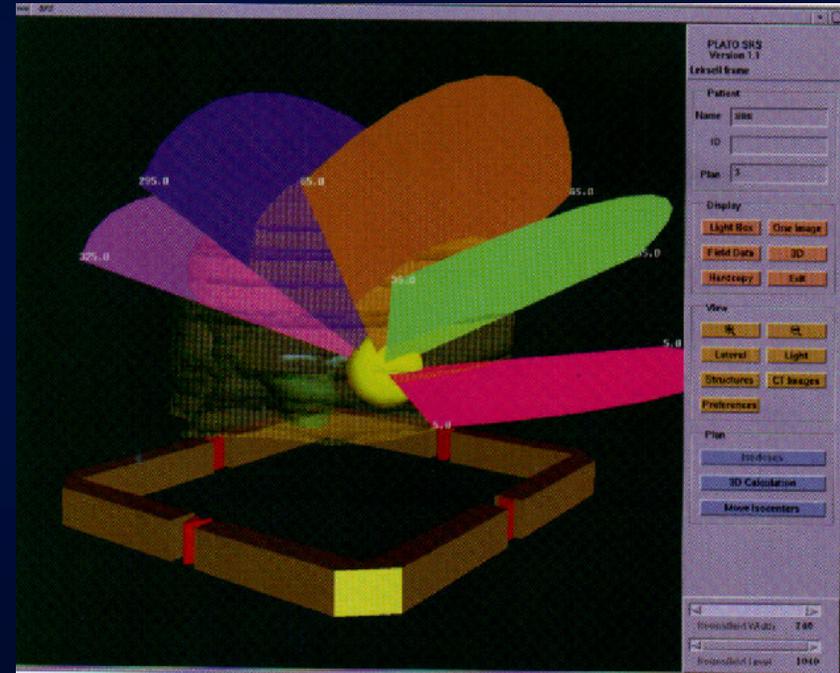
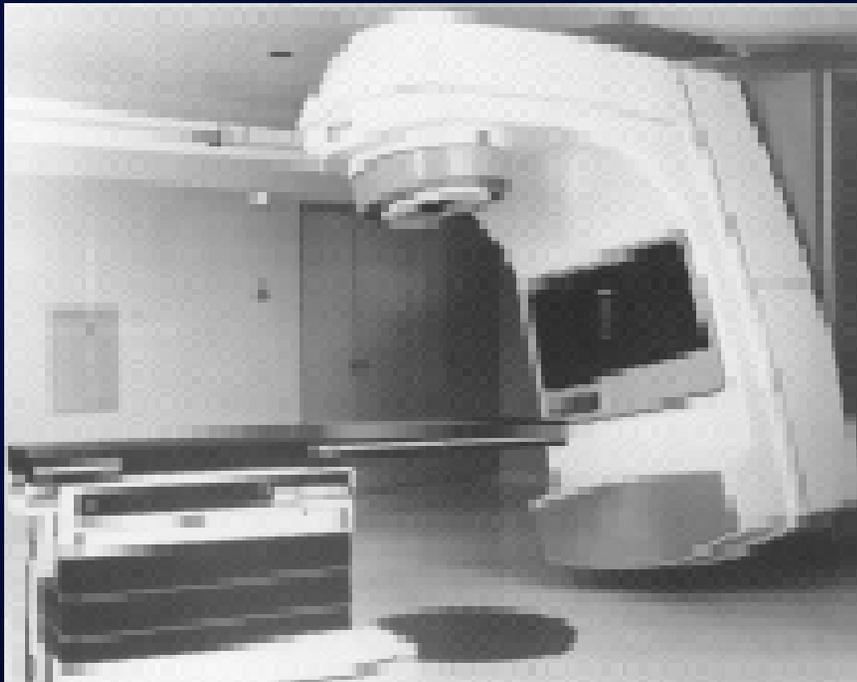
SRT MACHINES (2/2)

CYBERKNIFE:

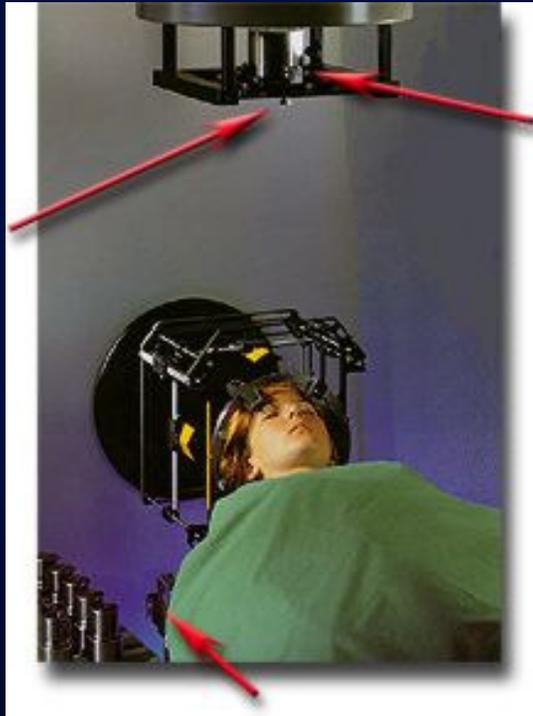
TOMOTHERAPY

**la Radioterapia
Stereotassica
con acceleratore lineare**

Terapia stereotassica realizzata con acceleratori lineari
irradiazione con più campi ad arco con diversi angoli di pendolazione e
diversi angoli di rotazione della pedana del lettino.



Per il trattamento si utilizza un collimatore aggiuntivo che vincolato alla testata definisce un campo a sezione circolare.



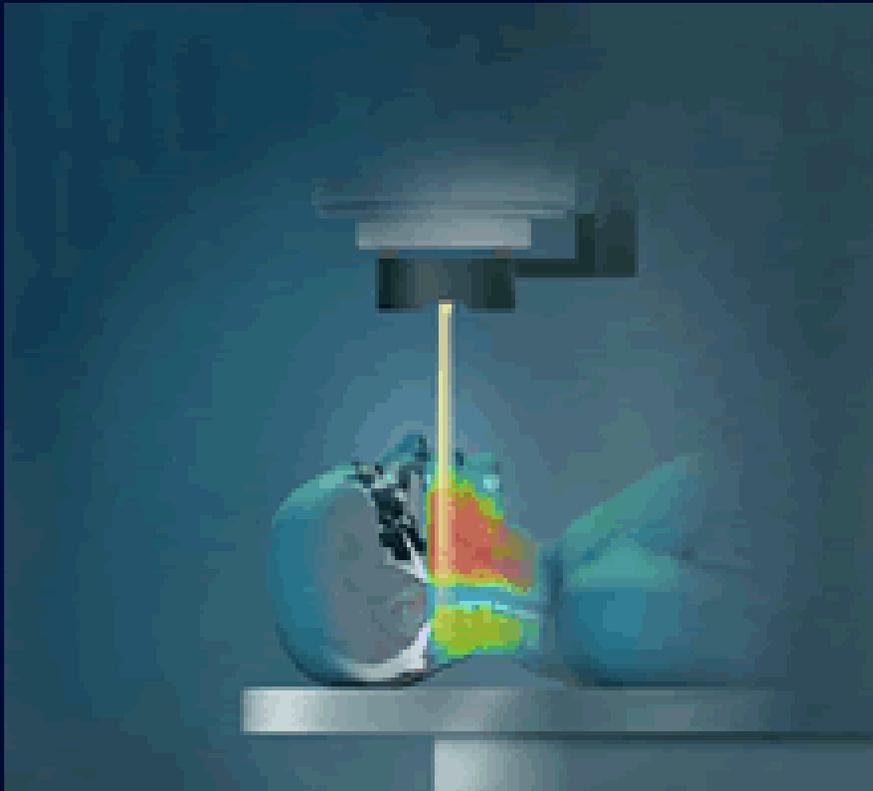
IMMOBILIZZAZIONE CON CASCO STEREOTASSICO

Tomoterapia

IMAT (Intensity Modulated Arc Therapy)

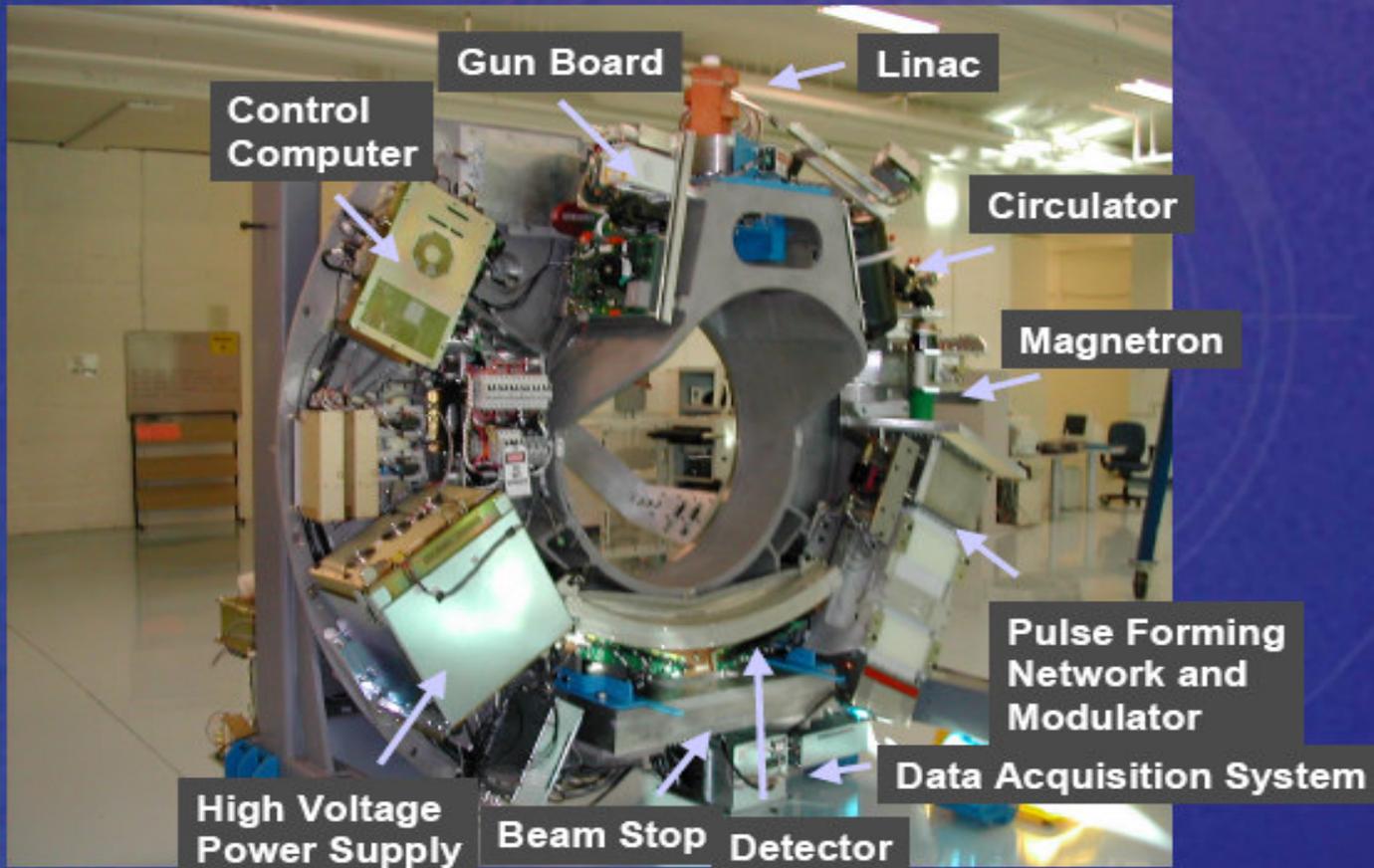
- Terapia rotazionale ; estensione della terapia step-shoot
- Per ogni angolo del gantry il campo modulato è suddiviso in una serie di segmenti che vengono erogati successivamente e sequenzialmente ad ogni rotazione successiva del gantry

Tomoterapia seriale: Sistema Peacock

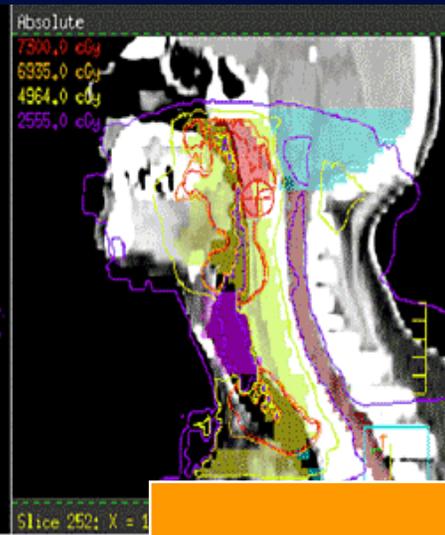
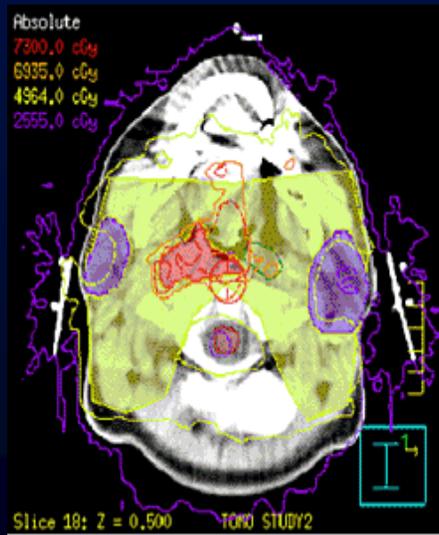


- Un fascio sottile (fan beam) irradia una “fetta” per volta il volume di trattamento.
- Dopo l’irradiazione di una “fetta” il lettino si muove a fascio spento e segue l’irradiazione della fetta successiva.....

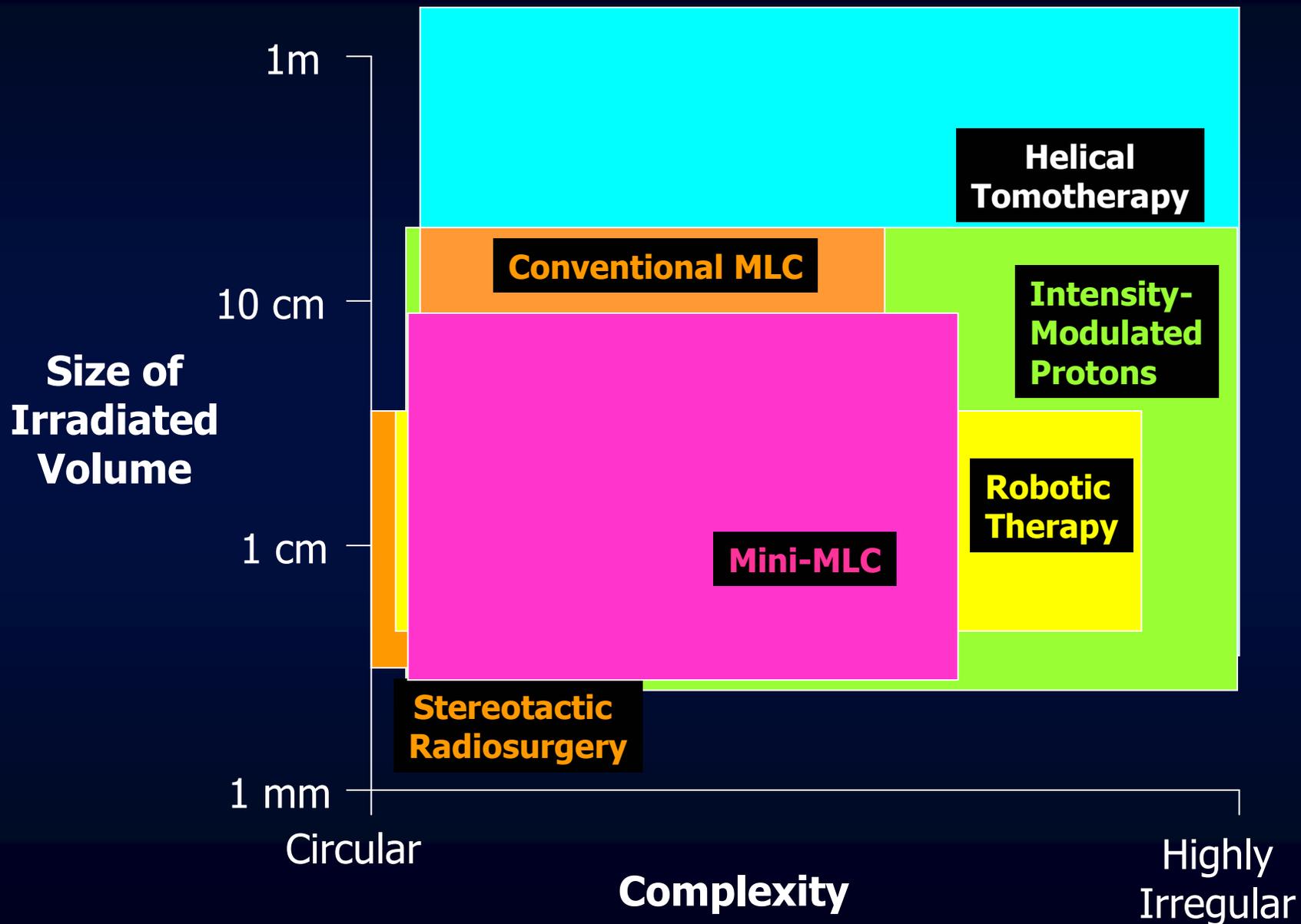
Helical Tomotherapy Unit



Tomoterapia elicale

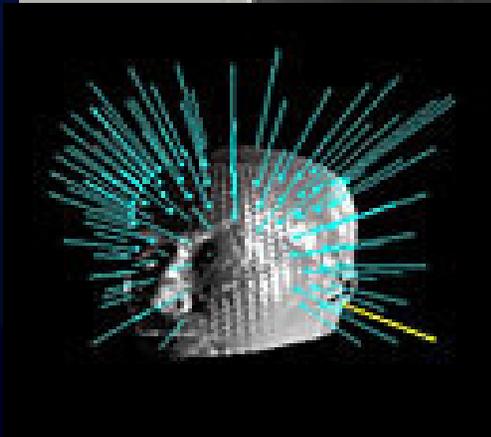


IL CASCO STEREOTASSICO NON È PIÙ NECESSARIO, CI SI BASA SUI REPERI OSSEI



Cyberknife

Cyberknife



- Acceleratore lineare montato su un braccio robotico con 6 gradi di libertà
- Collimatori circolari: diametro da 5mm a 60 mm
- Erogazione di fascetti di diversa fluenza a differenti direzioni
- Accoppiamento di un sistema fluoroscopico che permette di monitorare continuamente la posizione del paziente ed il relativo movimento d'organo

IL CASCO STEREOTASSICO NON è Più NECESSARIO, CI SI BASA SUI REPERI OSSEI

Favorable Outcomes using CyberKnife in Intra-Cranial (Brain) Tumors have been Reported

Pituitary adenomas

Kajiwara (2005)

Schwannomas

Ishihara (2004)

Gliomas

Yoshikawa (2006)

Brain Metastases

Shimamoto (2002)

Trigeminal Neuralgia

Romanelli (2003)

Peri-optic nerve tumors

Mehta (2002)

CyberKnife

Spinal Tumor Outcome Studies

<u>Author</u>	<u>n</u>	<u>Histology</u>	<u>Median Dose (Gy)</u>	<u>Outcome</u>
Dodd	51	Benign	19.6/1-5 fx	100% control 1 late spinal injury
Ryu	16	Various	11-25/1-5 fx	100% control No sequelae
Sinclair	15	AVM	20.5/2-5 fx	86% ↓volume No sequelae
Gerszten	18	Sacral tumors 94% malignant	15/1 fx	100% control No sequelae
Gerszten	26	Metastases	18/1fx	92% improved No sequelae
Gerszten	115	86% malignant	14/1 fx	94% improved No sequelae
Bhatnagar	35	Benign	16/1 fx	96% control No sequelae

Novalis

Novalis Brainlab

- Treatment planning (Brainscan 5.3.1)
- MLC (3 mm leaves)
- 6 degree freedom couch
- ExacTrac for set-up control :
accuracy for spinal SRS of 1 mm*

*Jin JY, Ryu S et al. Med Phys 2008;35: 1087-1093

- Treatment planning (iPLan Net)
- HD120 MLC (2.5 mm leaves)
- 6 degree robotic couch
- set-up control: ExacTrac + cone beam CT
- faster treatment thanks to ARC THERAPY
- adaptive gating
- high dose rate (1000 MU/min, 8 Gy/min)



“ . Dedicated stereotactic radiosurgery system featuring latest Trilogy linear accelerator

. Fine beam-resolution via Varian HD120 multi-leaf collimator—with 2.5 mm high-definition leaves

. Frameless Radiosurgery (greater patient comfort and greater flexibility for the clinician without compromising accuracy).

. High-precision target definition and delivery through BrainLAB iPlan and ExacTrac technologies

. Quick setup times and enhanced patient comfort via Robotic Treatment Couch

. Adaptive Gating—precise treatment of targets subject to respiration-related movement.

.Short treatment times—up to 50% faster than other systems”

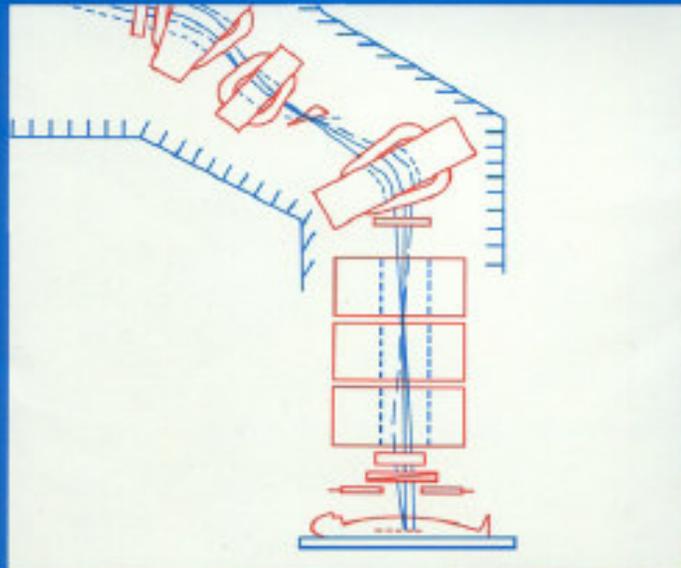
**IMPIEGO DEI PROTONI IN
RADIOTERAPIA E
RADIOTERAPIA A
MODULAZIONE DI INTENSITA'
PROTONICA**

Protons and Heavy (“Light”) Ions

Medical Physics Handbooks 8

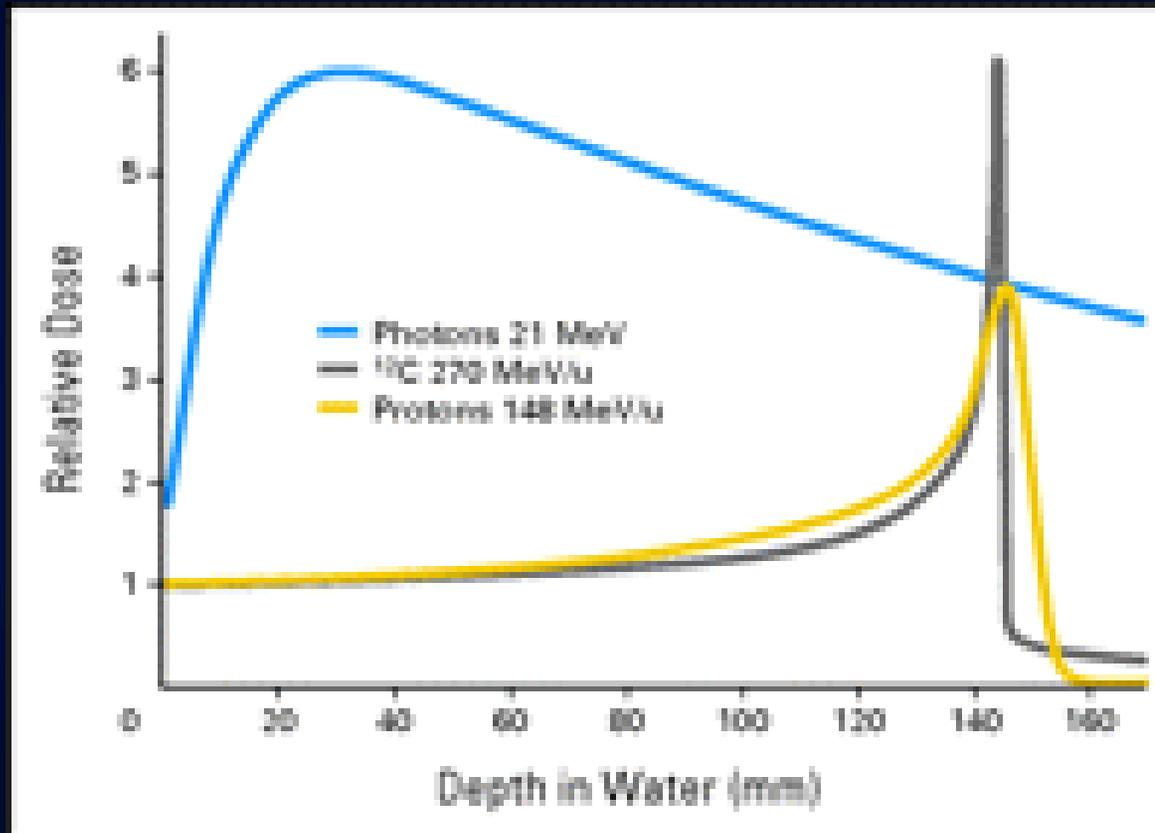
NUCLEAR PARTICLES IN CANCER TREATMENT

J F FOWLER

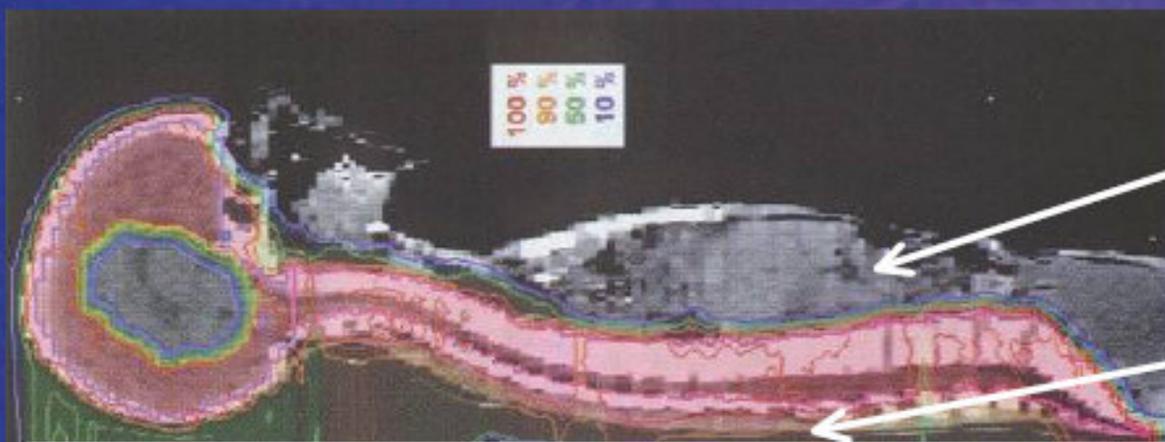


PSI Switzerland

IL PICCO DI BRAGG...



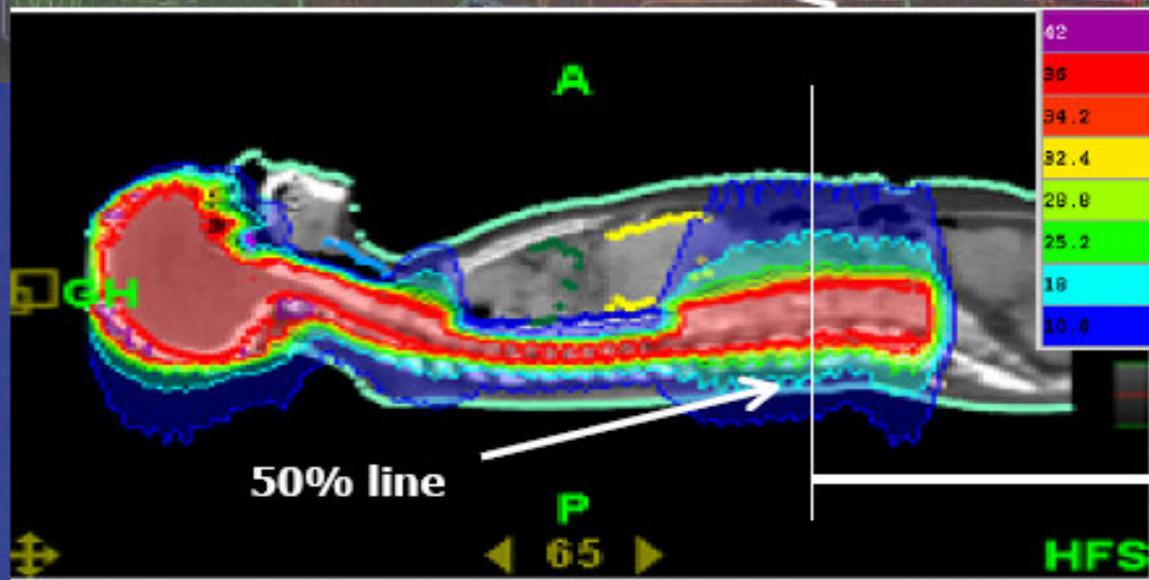
Dose Distribution Comparison



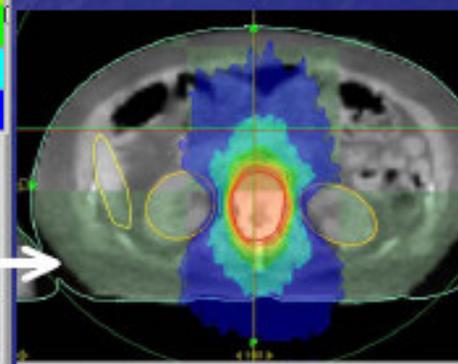
Protons

Low integral Dose.

90% line



Photons
(Tomotherapy)



TECHNIQUES COMPARISON

	Tecniche a confronto	Pt/Lesioni	Planificazione	Parametri di valutazione	Conclusioni
Nakamura et al 2003	Gamma vs IMRT	10 pts con lesioni benigne e maligne base cranio	- GTV=PTV - Is. di prescr.: 50% per Gamma e 75% per IMRT	- Copertura % - Indice di conformità - Indice di conformità 50% - Tempi di trattamento	- IC migliore per IMRT per isodosi di prescrizione; IC migliore per Gamma per isodosi più basse - Risparmio OAR simile - Tempi trattamento < per IMRT
Penagaricano 2006	Tomoterapia vs Gamma	5 pts con singola metastasi	- GTV=PTV - Stessa dose periferica di prescrizione 50% - Creazione ad hoc di disomogeneità con piani Tomo nel PTV	- DVH per dose da 5 a 40 Gy - Copertura - Indice di conformità - Tempi trattamento	- Copertura ed indice di conformità comparabili - Con Gamma si hanno volumi più grandi di alta dose e volumi più piccoli di dose bassa (vantaggi biologici superiori con Gamma)
Yartsev, 2005	Tomo vs 3DCRT, IMRT, archi stereotassici, protoni a spot scanning e scatterin gpassivo	12 pazienti lesioni benigne (meningiomi, neurinomi, adenomi)	- Dosi convenzionali (2 Gy/Fr) - Copertura ICRU (95% della dose al 95% del volume) - Normalizzazione piani alla dose media	- Parametri statistici di dose (media, Dmax, DVH, SD...) - Tempi trattamento	- Omogeneità distribuzione superiore in Tomo - Eccellente copertura per Tomo (V90 E V95) - Risparmio OAR: comparabile tra Tomo e altre tecniche con fotoni; migliore con protoni
Cozzi, 2006	Archi stereotassici, IMRT, AMOA, Tomo, Cyberknife	12 pazienti lesioni benigne	-IMRT: tecnica Step Shoot - Dosi convenzionali (2 Gy/fr) - Normalizzazione piani alla dose media - Copertura ICRU: V95>95%; Dmin>90%; Dmax<107%	- Parametri statistici dose - Indice di conformità (sia isodose del 95% e del 90%) - Dose integrale per tessuti sani - EUD PTV	- Copertura e omogeneità PTV: risultati migliori con Tomo seguito poi da IMRT e AMOA. Risultati peggiori con CyberKnife e archi - Indice di conformità: superiore per Tomo e Cyberknife - Risparmio OAR: constraints dose massima soddisfatti per tutte le tecniche. Migliore risparmio per dosi medio-basse con CyberKnife e archi - Dose integrale: risultati migliori per CyberKnife e Tomoterapia vs IMRT, AMOA, archi. - EUD: leggermente superiore per Tomo

	Tecniche a confronto	Pt/Lesioni	Pianificazione	Parametri di valutazione	Conclusioni
Chunhui, 2006	Tomoterapia vs IMRT	16 pazienti (11 con un solo target e 5 con due target)	<ul style="list-style-type: none"> - Espansione CTV - IMRT step shoot: ottimizzate sia con campi coplanari che non - Tomo: 1cm (Jaw), 0.1(pitch), 2.5(MF) 	<ul style="list-style-type: none"> - Indice di conformità - Indice di omogeneità - Indice di gradiente - Tempi trattamento 	<ul style="list-style-type: none"> - Conformità: migliore per piani Tom vs piani IMRT sia con campi coplanari che non. - Omogeneità: no differenza significativa fra le tecniche; omogeneità leggermente inferiore con Tomo vs IMRT con campi no coplanari - Gradiente migliore con Tomo - OAR: dosi medie superiori con Tomo - Tempi trattamento: superiori in Tomo
Soisson, 2006	Tomoterapia vs 3DCRT, archi no coplanari, IMRT con campi coplanari e no	10 pazienti	<ul style="list-style-type: none"> - PTV=CTV+2mm - Dosi con frazionamenti convenzionali - Dose di prescrizione impartita al 98% del volume 	<ul style="list-style-type: none"> - Indice di conformità - Indice di omogeneità - EUD - NTDmean per OAR - Stima volumi a bassa dose 	<ul style="list-style-type: none"> - Conformità: risultati peggiori con Tomo vs sia campi coplanari che non. - Omogeneità: migliore omogeneità con piani Tomo vs campi no coplanari; non grandi differenze vs campi coplanari - Basse dosi: valori più elevati con Tomo - EUD: risultati comparabili - NTDmean: risultati dipendenti da paziente e dall'OAR considerato

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...

I PAZIENTI.

GRAZIE

PER

L'ATTENZIONE