Radiotherapy in Neurospecialties

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SAFETY

ALARA (As Low As Reasonably Achievable): Time, Distance, and Shielding

PATHOPHYSIOLOGY

Mitotically active cells are most prone to radiation injury!

- tumor cells are often deficient in *repair mechanisms* (vs. normal cells); ***fractionation*** (daily small doses of radiation) allows normal cells to repair while tumor cells are unable to do so.
- *poorly oxygenated cells* (make up significant proportion of many solid tumors) are 2-3 times less sensitive to radiation than well-oxygenated cells (*oxygen is most powerful radiation sensitizer*); unsuccessful attempts to address this problem:
    a) hyperbaric oxygen
    b) hypoxic cell sensitizers (e.g. METRONIDAZOLE, MISONIDAZOLE)
    c) use of neutrons (less dependence on oxygen)
- other radiosensitizers (also not useful) – IODODEOXYURIDINE, BROMODEOXYURIDINE – incorporated into DNA of dividing cells (instead of thymidine) – cells become > 3 times more radiosensitive.

Tumor growth is controlled by 2 main mechanisms:

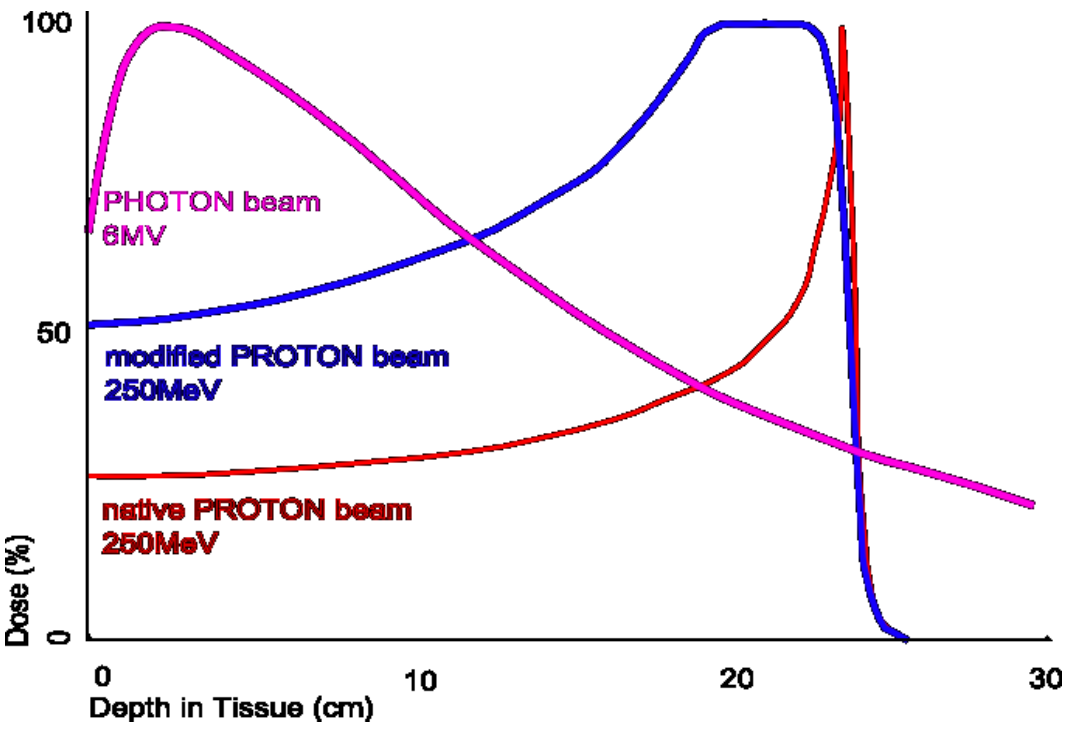
In higher-dose CENTRAL REGION - **direct cellular injury** (necrosis).

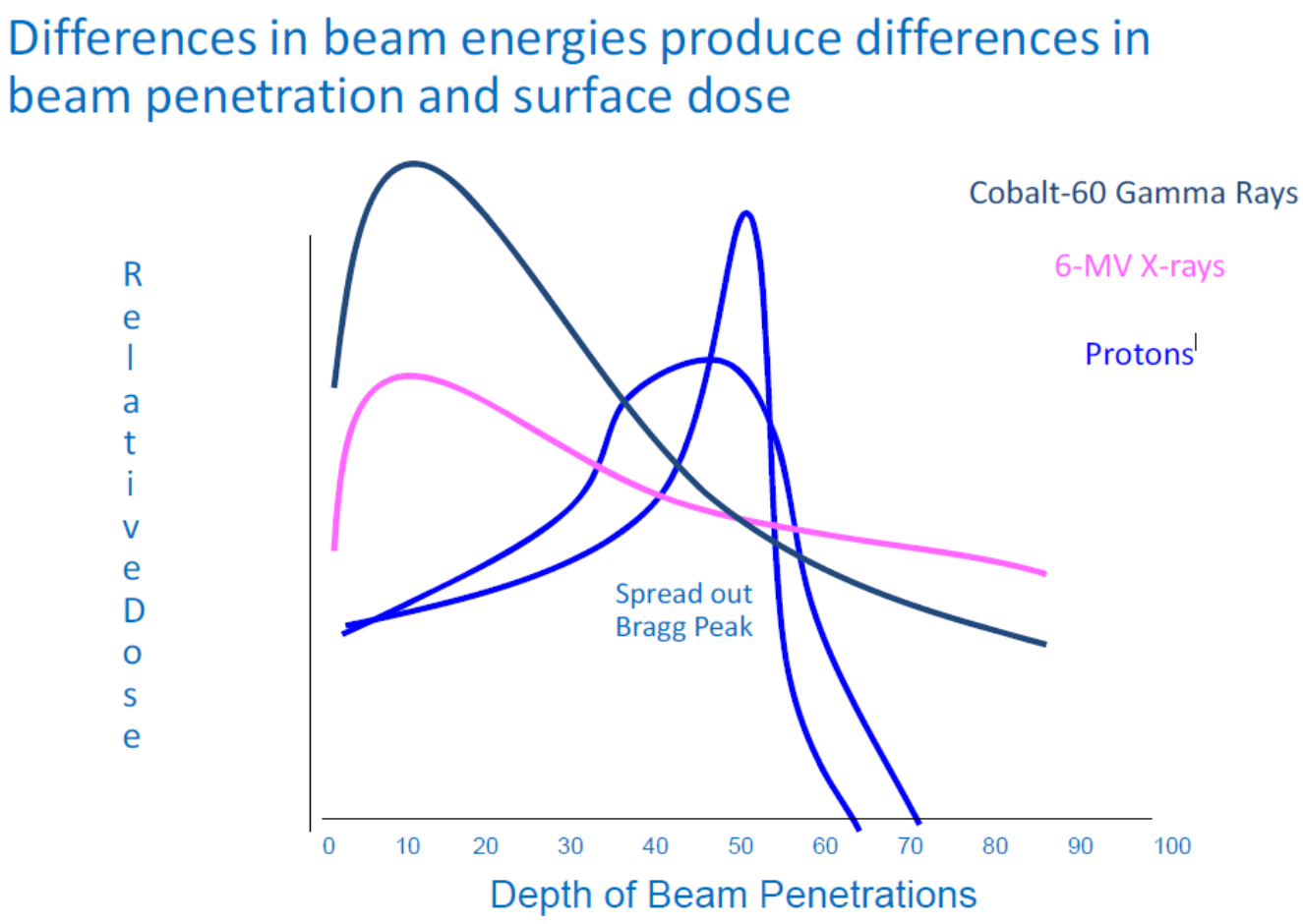
In lower-dose PERIPHERAL REGION - **vascular occlusion** → fibrosis.

- no extent of surgery can change tumor biology – important for local control – radiation matters!

EFFECTS OF DIFFERENT BEAMS

Bragg's Peak:





N.B. with proton beams higher doses can be achieved (vs. conventional photon irradiation) at the target because protons loose charge very quickly and there is no exiting beam that could damage nearby structures (like brainstem); skin sparing – energy is absorbed deeper.

TISSUE TOLERANCE

- depends on:
  1) fraction dose
  2) total dose
  3) volume of brain irradiated
  4) age (children < 3 years are more susceptible than adults).
- risk of injury may be amplified by some *chemotherapeutic agents*.
  e.g. high-dose **methotrexate** with radiotherapy, whether synchronously or at separate times → *necrotizing leukoencephalopathy* (focal areas of coagulative necrosis within white matter).
- *vasculopathies* (e.g. **diabetes mellitus**) increase risk of injury.

MAXIMUM RECOMMENDED SAFE SINGLE DOSE TO DIFFERENT STRUCTURES

Lateral wall of cavernous sinus:

N.B. CN 2 and CN 8 are very sensitive – safe doses < 8 Gy.
N.B. CN 3, 4, 6 are rather resistant – safe doses < 16 Gy (studies found no relationship of dose to cavernous sinus and neuropathy in CN III-VI – dose range 10-40 Gy)

Lens (eyes)

- shield eyes (tissue at risk) when doing functional/benign cases to allow blocking beams transiting lenses.

Anterior visual pathway (optic nerve, optic chiasm)

≤ 10 Gy (to ≤ 1% of optic nerve) - 0-2% risk of optic neuropathy; risk rises quickly at doses > 10 Gy.
≤ 8 Gy – if had previous XRT.

- risk of permanent optic neuropathy is < 2% for doses as high as 12 Gy delivered with the Gamma Knife®, as long as the patient has not received prior radiotherapy.
- optic apparatus may be more vulnerable because of previous compression and prior surgery.
- if the goal is close to zero percent risk of permanent optic neuropathy, consider 8 Gy to be a safe dose.
- when is appropriate to deliver higher doses to the optic apparatus? - *secretory pituitary macroadenomas* - higher tumor doses are required to normalize endocrine function (small risk of optic neuropathy is measured against the need for tumor control or hormonal normalization and these differential risks are shared and discussed with the patient pre-operatively).
- with current technique a 1–5 mm distance between the tumor and the optic chiasm is enough to safely and effectively perform Gamma Knife® SRS.
- sparing techniques:
  - if necessary, ***block selected radiation sources*** can be to reduce dose fall off to the optic apparatus.
  - ***fractionated schedules*** for larger lesions or impinging on the optic apparatus.
  - initial first stage microsurgery to ***reduce the subsequent tumor volume*** and create space between the tumor and the optic apparatus, thus allowing safe delivery of the highest dose of SRS possible.

Optic Nerve Radiation Tolerance:
Tishler (1996) 8 Gy
Duma (1993) 9 Gy
Leber (1998) 10 Gy
Stafford (2003) 12 Gy

- optic neuropathy develops 7- 30 months post SRS.
- abrupt change in vision - clinically anterior visual pathway involvement, typically decreased VA or homonymous hemianopia.
- MRI may show swelling and enhancement.
- occasional partial improvement with systemic steroids.

Pituitary
safe dose to gland is < 15 Gy, to stalk < 17 Gy
hypothalamus ≤ 15 Gy
limiting mean dose to the hypophysis for gonadotropic and thyrotropic functions - 15 Gy.
limiting mean dose to the hypophysis for adrenocorticotropic function - 18 Gy

Brainstem
≤ 8-10 Gy

Pyramidal (corticospinal) tract
≤ 20 Gy

Cochlea
≤ 4 Gy

Major arteries (e.g. carotid)
- no need to segment as "organ at risk" but keep hotspot < 25 Gy

Spinal cord
- 10 Gy to 10 % volume of spinal cord, defined as 6 mm above and below the target - 0% risk of myelopathy (14 Gy + less than 10% of cord with 10 Gy is safe in Cleveland Clinic).
- *cervical* and *thoracic* cords do not differ in radiosensitivity (formerly, was belief that cervical cord is more tolerant than thoracic cord).
- *fractionated:*
  - 45 Gy in 22 fractions over 5 weeks – safe (0.2% risk of myelopathy).
  - tolerance increases with *decreasing fraction size*.

BRAIN TOLERANCE

- threshold doses for brain injury: 35 Gy for 10 fractions, 60 Gy for 35 fractions, 76 Gy for 60 fractions.

DOSES TO LESIONS

Total dose depends on tumor histopathology and on CNS tolerance (depends on age):

1) *HIGH-GRADE GLIOMAS*: ≈ 54-60 Gy (fractionated). see p. Onc10 >>
   N.B. SRS is not recommended for newly diagnosed GBM! vs. recurrent GBM (SRS is an option)
2) *LOW-GRADE GLIOMAS*: 45-50.4 Gy. see p. Onc10 >>
3) *CNS LYMPHOMA*: 40-45 Gy (36 Gy to both eyes for ocular lymphoma). see p. Onc36 >>
4) *METASTASES*: 30 Gy whole-brain radiation (in 10 fractions) or 15-24 Gy (depending on tumor size) SRS. see p. Onc32 >>
5) *AVM*: 16-25 Gy (SRS). see p. Vas30 >>
6) *PITUITARY ADENOMA*: 12-16 Gy (SRS) for nonfunctioning, 30-35 Gy (SRS) for functioning. see p. Onc26 >>
7) *CRANIOPHARYNGIOMA*: 11-12 Gy (SRS).
8) *GLOMUS JUGULARE*: 14-16 Gy (SRS). see p. Onc64 >>
9) *VESTIBULAR SCHWANNOMA*: 13 (12-18) Gy (SRS). see p. Onc62 >>
10) *MENINGIOMA*: 13-16 Gy (SRS, at 50% isodose). see p. Onc38 >>
11) *PARKINSONISM, OCD TARGETS*: 130 Gy (SRS, at 100% isodose).
12) *TRIGEMINAL NEURALGIA*: 43 Gy (SRS, at 50% isodose). see p. CN5 >>

Total dose and dose-fractionation in **children** (single daily fractions of 1.8 Gy 5 days per week):

Age	Local fields	Whole brain	Spinal axis
< 3 yrs*	50.4 Gy/28 fx/6 wk	39.6 Gy/22 fx/4.5 wk	30.4 Gy/19 fx/4 wk
≥ 3 yrs	54 Gy/30 fx/6 wk	45 Gy/25 fx/5 wk	36 Gy/20 fx/4 wk

*children < 3 yrs pose significant risk of injury - dose reductions of 20-25% are common (some advice chemotherapy, in attempt to delay radiation).

SIDE EFFECTS

Most patients tolerate radiotherapy remarkably well (worsening of neurologic status during treatment is unusual).

1) mild skin **erythema** may be seen in first week of treatment.
   - moist desquamation may occur in retroauricular region where skin sparing is lost.
   - ***topical steroid creams*** are adequate (if treatment is necessary).

2) temporary **alopecia** within radiotherapy fields is universal; women usually have return of hair growth after treatment; hair growth in men is more variable.
   - if skin dose is excessive (e.g. over frontal region, vertex, and occiput, where radiation beam enters tangentially and so loses skin-sparing properties of perpendicular beam), permanent alopecia may occur.

3) **otitis media / externa** - after radiotherapy to posterior fossa (eustachian tube is obstructed by swelling).

4) **fatigue** - occurs toward end of radiotherapy; can persist for several weeks.

5) some degree of **hematologic suppression** is seen with treatment to *whole CNS*.

COMPLICATIONS

- reported as infrequent (2-5% cases) - unrealistically low - reflect fact that most irradiated patients with tumor die before brain injury appears.

- mechanism of injury - ***peroxidation of lipids*** in myelin and neuronal membranes (DNA synthesis, primary target of radiation, occurs infrequently in neurons).
- severity depends on individual BRAIN TOLERANCE. *see above >>*

CORTICOSTEROIDS may improve neurologic symptoms associated with radiation injury (at least in ACUTE and EARLY-DELAYED reactions)

Optic neuropathy – see above >>

1. ACUTE REACTIONS

(occur during or shortly after irradiation up to 6 weeks) - caused by *radiation-induced edema* → **acute encephalopathy**;

- localized edema is more common with single-session SRS than with standard fractionation.
- most common after **large dose fractions** (3.0-6.0 Gy) delivered to large brain volume: within few hours after first fraction - headache, nausea, vomiting, somnolence, fever, and worsening neurologic symptoms (if ≥ 7.5 Gy are used, may culminate in death).
- with **conventional daily fractions** (1.8-2.0 Gy) - mild headache and nausea, becoming progressively *less severe with each succeeding fraction*.
- prophylaxis & treatment - start ***corticosteroids*** for at least 48-72 hours before radiotherapy (dose can usually be tapered relatively early, and often discontinued after 1-2 weeks).

N.B. SRS decreases peritumoral edema with brain mts but increases with meningiomas!

INCISION HEALING PROBLEMS

- consider placing incisional VAC for irradiated wounds.

2. EARLY-DELAYED REACTIONS

(appear within 1-6 months after irradiation) - *temporary demyelination* caused by:

a) radiation effect on ***oligodendroglial cells*** → demyelination.
b) radiation-induced changes in ***capillary permeability*** (i.e. transient disruption of BBB) → vasogenic edema → demyelination.

TRANSIENT RADIATION LEUKOENCEPHALOPATHY

- neurologic deterioration (e.g. reappearance of initial tumor's symptomatology), focal encephalopathy, **"somnolence syndrome"** in children (lethargy, anorexia, headache, ataxia - last ≈ 1-2 weeks).

- resolves within several weeks without specific sequelae.
- **CT** – hypodensity of white matter.
- **EEG** – diffuse slow-wave activity.
- prophylaxis & treatment - ***corticosteroids***

TRANSIENT RADIATION MYELOPATHY

- develops after latent period of 2-4 months → gradually resolves over ensuing 3-6 months without specific therapy!

- momentary, electrical shock-like paresthesias / numbness radiating from neck to extremities, precipitated by neck flexion (*Lhermitte's sign*).

3. LATE-DELAYED REACTIONS

(develop > 6 months after irradiation) – permanent damage:

SECONDARY NEOPLASIA

– meningiomas (!!!), soft tissue sarcomas, nerve sheath tumors, thyroid cancers (after treatment to spinal axis).

Definition of radioinduced tumors (**Cahan criteria** - Cahan et al., 1998):

1) tumor must occur in previously irradiated field
2) long interval (usually several years) from time of irradiation
3) tumor must be pathologically different from the primary tumor
4) tumor must be not present at the time of irradiation.
5) patient must not have genetic predisposition for tumor.

Risk
Gamma Knife: 0.001 % (0 % in 6200 GK procedures in Pittsburgh)
fractionated radiotherapy: 1-3 %

Radiosurgery-induced Neoplasia

Probably Yes	Probably No	Don't Know	Benign
Lancet 360:309 2002	J Neurosurg 95:518; 2001	J Neurosurg 89:653; 1998	J Neurosurg 105:325; 2006
Surg Neurol 60:60; 2003		IJROBP 62:32; 2005	Neurosurgery 52:1436; 2003
Lancet 356:1576; 2000		Am J Otol 21:364; 2000	
J Neurosurg 95:710; 2001		Neurol Med Chir 44:29; 2004	
J Neurosurg 94:816; 2001		J Neuro-Oncol 66:301; 2004	

- ***SRS has lower risk*** because: smaller irradiated volume, high single dose to target leads to cytotoxicity, not mutagenicity, extremely small volumes and doses along entrance and exit paths, smaller number of DNA injury/repair events.
- SRS does not seem to increase the risk of secondary neoplasia in patients with genetic syndromes (e.g. NF2).
- low dose of radiation, such as 1 Gy, has ***relative risk*** of 1.57-8.75 (increases to 18.4 for interval of time 20-25 years).
- 3 radiation-associated gliomas and 5 malignant vestibular schwannomas have been reported in literature ← all do not meet all Cahan criteria.

HYPOTHALAMIC-PITUITARY SUPPRESSION

- dose related (esp. *GROWTH HORMONE deficiency* - can occur after doses as low as 18 Gy; *TTH* is least sensitive).
  - yearly endocrine evaluations should be done for at least first 3 years after therapy.
  - early detection of deficiency permits appropriate hormonal replacement therapy before irreversible damage has occurred.
  - spinal radiotherapy may cause ***growth arrest*** in children.

WHITE MATTER INJURY

- most serious consequence of standard radiotherapy (single most dose-limiting factor) - idiosyncratic *white matter necrosis* caused by:
  a) VASCULAR HYPOTHESIS: vascular ***endothelial*** injury → hyalinized thickening of blood vessels → thrombosis & occlusion of capillaries and small arteries → neovascularization
  b) GLIAL HYPOTHESIS: direct effect on ***oligodendroglial*** cells.
  c) IMMUNOLOGIC HYPOTHESIS: irradiated glial cells release antigens that induce ***autoimmune*** reaction.
- develops with increasing frequency with increasing radiation doses (e.g. only < 1% patients treated with conventional dose-fractionation).
- onset 6 months ÷ 10 years after treatment.
- *asymptomatic ÷ potentially fatal*.

RADIATION NECROSIS

(after *localized therapy*; major late complication of SRS) - focal lesion at/near original tumor site.

Manifests 6-24 months after radiotherapy, lasts 18 months

- incidence with SRS is 7-10%.
- risk factors:
  1) dose
  2) treatment volume
  3) fraction size and treatment duration (i.e. more common with SRS than with fractionated treatment)
  4) dose homogeneity and conformality
  5) chemotherapy
  6) previous radiation
  7) male sex
- clinically - acts as expanding mass lesion: focal neurologic signs (re-emergence of initial tumor symptoms), seizures, increased ICP (can be fatal via herniation).
- imaging - contrast-enhancing mass (look for reticulate pattern) surrounded by vasogenic edema.

MRI signs suggesting necrosis (vs. tumor recurrence):
1) nonenhancing tumors prior to surgery.
2) lesion some distance from primary glioma but within radiation field.
3) lesion in periventricular white matter.
4) lesion has granular-reticular enhancement (soap-bubble or Swiss-cheese appearance) without much mass effect
5) no increase in FLAIR signal (vs. growing tumor – FLAIR↑)

Radiation necrosis induces **clinical** and **CT/MRI** changes indistinguishable from tumor progression – can be differentiated with **DYNAMIC TESTING**:

Radiation necrosis is hypometabolic with stagnant flow and leaky capillaries; **tumor** is hypermetabolic with brisk flow and leaky capillaries

1) **perfusion-weighted MRI** (optimum rCBV cutoff value is 2.1* - sensitivity is 100%, specificity is 95.2%) – most practical test!
   *< 2.1 – necrosis; > 2.1 – tumor recurrence
2) **TRAM (treatment response assessment map), s. delayed (60 min) postgadolinium MRI** – in tumors contrast gets washed out at 60 mins, in radiation necrosis contrast stays (gets "trapped" and even brighter at 60 mins) – very sensitive test (some say even better than pMRI).
   - TRAMs calculated from delayed-contrast MRI enable reliable (sensitivity/specificity > 70%) differentiation between tumor (blue in the TRAMs) and non-tumoral tissues (red).
   - TRAMs are calculated by subtracting 3D T1-MRIs acquired 5 min (early time point) post-contrast injection from those acquired 60-105 min (late point) later.
     - in tumor tissue, contrast gets washed out in 60 minutes
     - in nontumor tissue (such as radiation necrosis), contrast extravasates and stays for > 60 minutes

   N.B. novel immunotherapies induce inflammatory reactions and results are more difficult to interpret
3) **MRS** (probably sensitivity and specificity similar to PWI-MRI) see p. Onc1 >>
4) **PET** – controversial and imperfect:
   a) **^{18}fluoro-deoxyglucose** (FDG) (75% sensitivity and 81% specificity for malignant tumor vs. radiation necrosis); limitations of FDG: uptake by normal cortex, lack of uptake by low-grade gliomas, uptake by abscess, uptake by radiation necrosis.
   b) **amino-acid PET** - 3,4-dihydroxy-6[18F]fluoro-phenylalanine (FDOPA) (96% sensitivity and 100% specificity with ratio of tumor to normal striatum > 1.0), O-(2-[18F]fluoroethyl)-L-tyrosine (FET), carbon-11-methyl-methionine, 3-O-methyl-6-[18F]fluoro-L-DOPA (OMFD)
5) **SPECT** with Thallium-201: index < 3.0 = radiation injury; index > 5.0 = tumor recurrence; those in between received repeat scans once a month for 2 months until it fell within one of the above values; those that remained between 3 and 5 was diagnosed as radiation injury (sensitivity was 90% and specificity was 90.5%)
6) **ASL (arterial-spin labeling)** – the best! (↑perfusion – likely tumor recurrence)

N.B. because most patients have mixture of necrosis and tumor, **biopsy** may be required to confirm diagnosis! (also often ameliorates symptoms)
- biopsy sample must be only large enough to exclude tumor recurrence without causing clinically significant neurologic deficits.
- *histologic hallmark of radiation necrosis - demyelination and oligodendrocyte dropout*; necrotic tissue without predominance of malignant cells.

Treatment:
a) **observation** – for asymptomatic cases.
b) **steroids*** – symptomatic improvement.
c) **anticoagulation** (WARFARIN - alternative when surgery is not feasible; HEPARIN to aPTT↑ 1.5 times control) – because radiation necrosis pathophysiology involves vessel thrombosis and subsequent occlusion; lacks demonstration of real benefit.
d) **antiplatelets** (PENTOXIFYLLINE, ASPIRIN, and TICLOPIDINE); Cleveland Clinic uses Trental 1200 mg/d as a first choice drug for radiation necrosis.
e) VITAMIN E
f) **hyperbaric oxygen therapy** (2.0-2.5 atm. for 10-30 sessions 90-120 minutes each) – promotes perfusion and angiogenesis; efficacy is not well documented; according to Cleveland Clinic, prophylactic use cuts risk of radiation necrosis by 50%.

g) BEVACIZUMAB (AVASTIN®)* – very effective!; no surgery for 1 month after last dose; anecdotal reports of increased risk of SDH; decreases enhancement of any remaining tumor.

N.B. may cause *"overpruning" of blood vessels* → vascular insufficiency → *worsening necrosis*

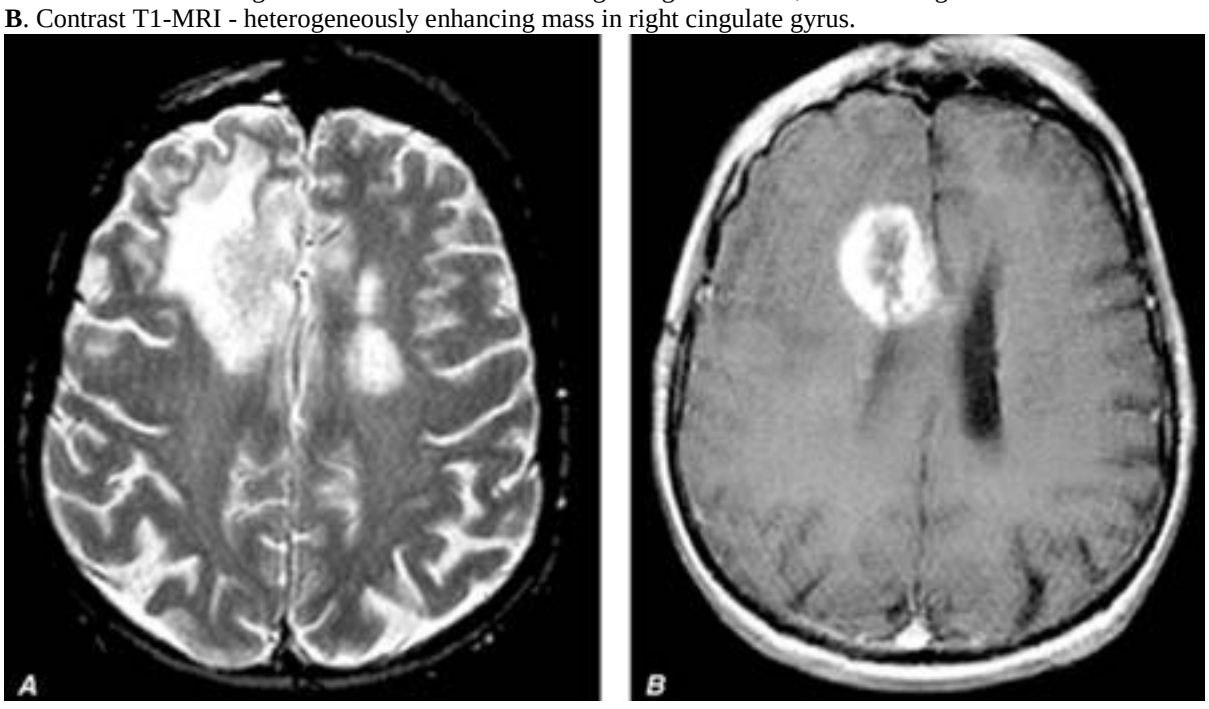
h) **LITT ablation** – mechanism unknown: converts apoptotic (radiation) necrosis into coagulative (thermal) necrosis, attracts inflammatory cells to clear necrosis, ablates VEGF-producing astrocytes?

i) **surgical debulking** – palliative measure for favorably situated symptomatic lesions.

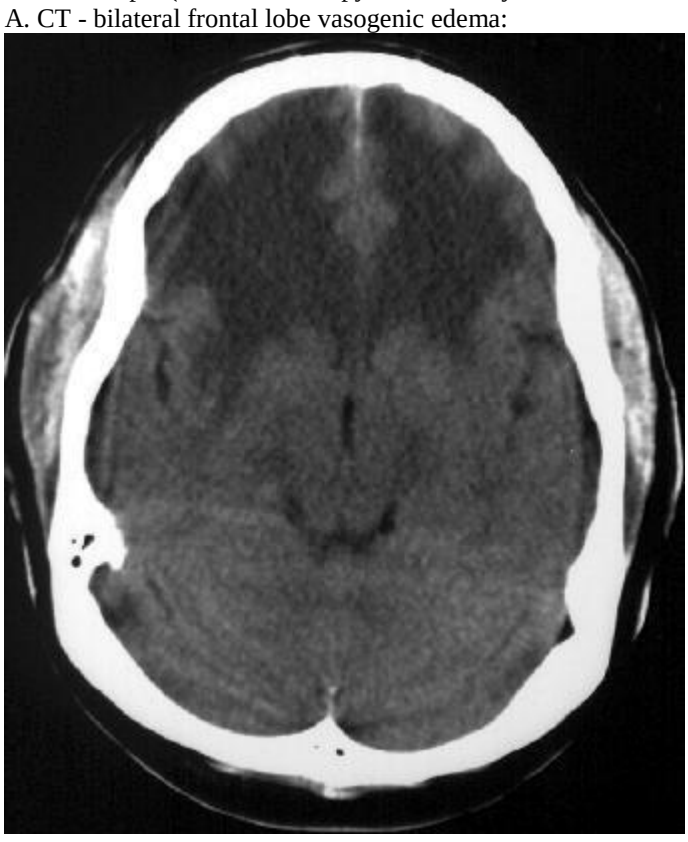
j) METHYLPHENIDATE, DONEPEZIL – for neurocognitive dysfunction, fatigue, quality of life improvement.

*only these medications are shown in trials to be effective

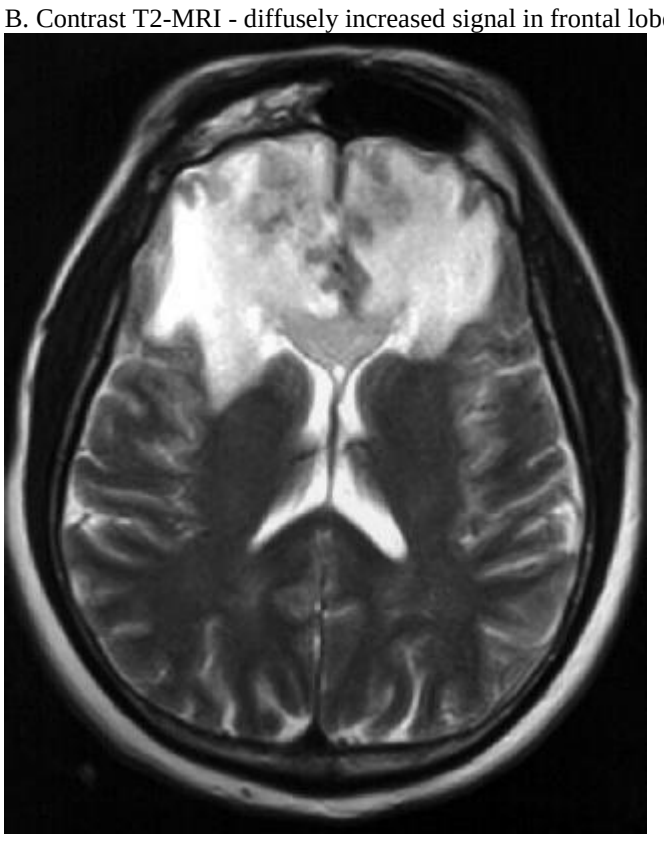
Focal radiation necrosis 3 years after radiotherapy (70 Gy) for nasopharynx carcinoma:
A. T2-MRI - mass in right frontal lobe with surrounding vasogenic edema; abnormal signal also on left.
B. Contrast T1-MRI - heterogeneously enhancing mass in right cingulate gyrus.



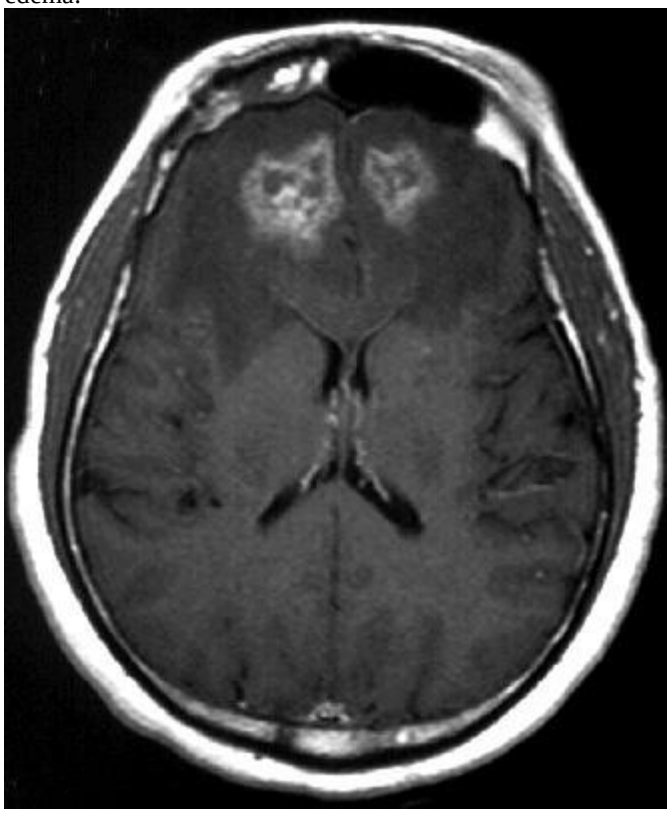
Other example (after radiotherapy for maxillary sinus carcinoma):
A. CT - bilateral frontal lobe vasogenic edema:

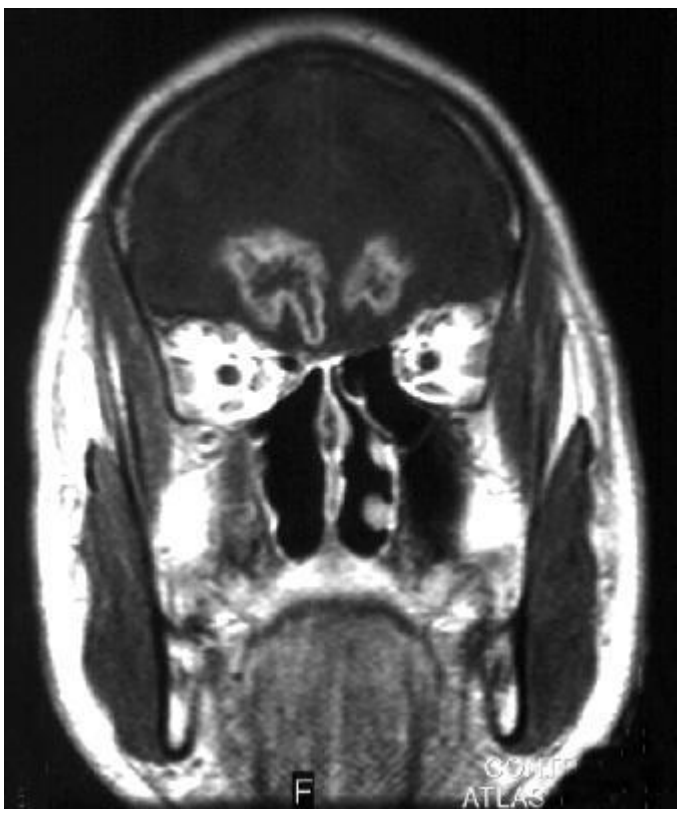


B. Contrast T2-MRI - diffusely increased signal in frontal lobes:



Contrast T1-MRI - two lesions in frontal lobes bilaterally; rim enhancement; decreased surrounding signal is edema:



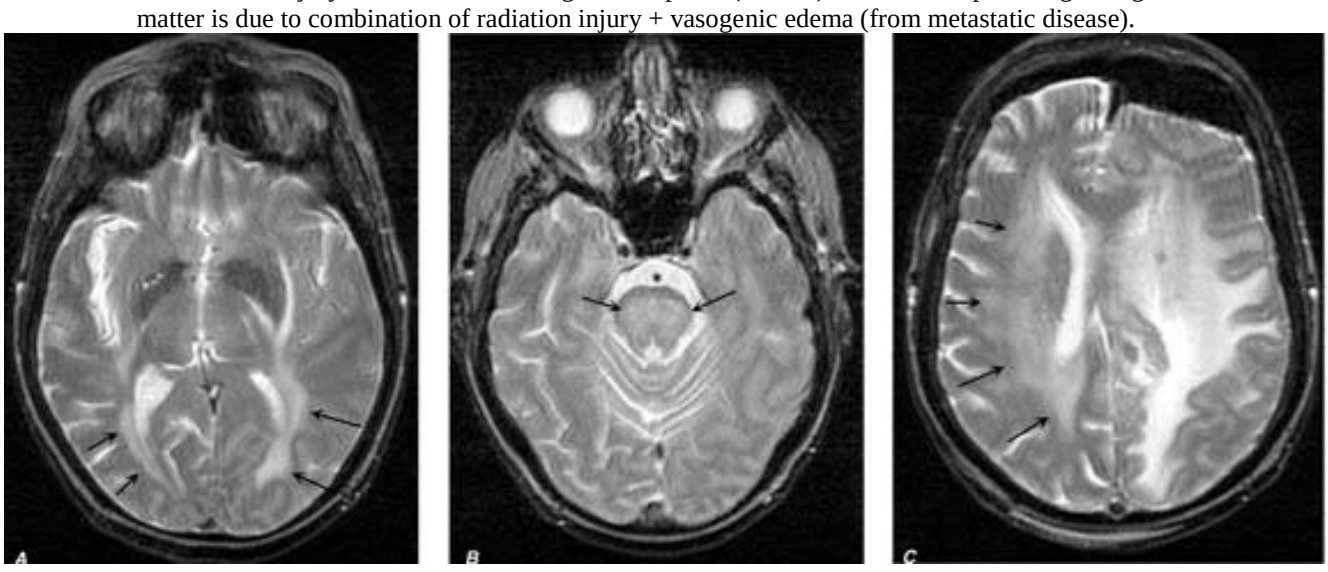


DIFFUSE WHITE MATTER INJURY

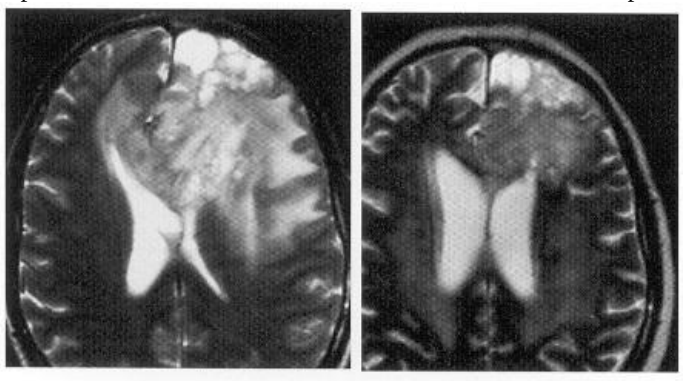
(after *whole-brain radiation*) - varying degrees of neuropsychological impairment (up to incapacitating dementia), gait apraxia.

- CT *diffuse white matter hypodensity* (atrophic dilatation of adjacent ventricle indicates demyelination rather than edema).
- MRI-T2 *diffuse nonenhancing periventricular white matter hyperintensity*.
  periventricular white matter is highly susceptible to radiation injury!
- ***diffuse cerebral cortical atrophy*** (late finding related to diffuse white matter injury) is observed in 17-39% patients.

T2-MRI of diffuse white matter injury 1 year following whole-brain radiation (55 Gy):
A. High signal in periventricular white matter (*arrows*).
B. Diffuse high signal in pontine white matter (*arrows*) - demyelination or small vessel ischemic injury.
C. Radiation injury to white matter of right hemisphere (*arrows*); in left hemisphere higher signal of white matter is due to combination of radiation injury + vasogenic edema (from metastatic disease).



Anaplastic astrocytoma (MRI-T2):
A. Before treatment - large mixed solid and cystic tumor in left frontal lobe which infiltrates across corpus callosum and causes considerable mass effect; vasogenic edema lateral to tumor.
B. After treatment - tumor has shrunk with regression of mass effect and edema; subtle diffuse high signal separate from tumor in white matter of both cerebral hemispheres (radiation-induced leukoencephalopathy).



Source of picture: Ronald G. Grainger, David J. Allison "Grainger & Allison's Diagnostic Radiology: A Textbook of Medical Imaging", 4th ed. (2001); Churchill Livingstone, Inc.; ISBN: 978-0443064326 >>

DEMENTIA (COGNITIVE DECLINE)

(≥ 50% patients who survive whole-brain radiation for 5 years).

- becomes fully developed after several years.
- most pronounced in patients who have had whole-brain irradiation + chemotherapy.
- local field (vs. whole-brain) radiation has reduced incidence of dementia.
- special problem in children - irradiated children have IQ decrements and behavioral disturbances; even radiation fields limited to posterior fossa have been associated with intellectual declines! - yearly psychologic evaluations should be done for at least first 3 years after therapy.
- **MRI / CT** - cerebral atrophy.
- prophylaxis:
  1) hippocampus-sparing regimens (esp. for young patients)
  2) MEMANTINE (off-label based on results from RTOG 0614; start 5 mg daily → slowly titrate it up to 10 mg BID, to complete a 6-month course).

Neural progenitor cell (NPC) niches

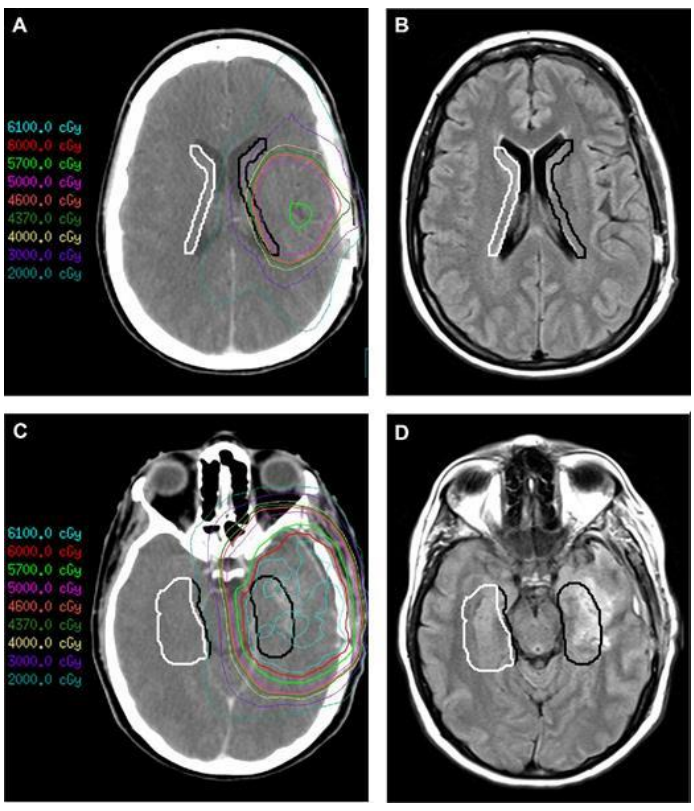
- found in the subventricular zones (SVZ) of the lateral ventricles and the hippocampal dentate gyri,
- produce new neurons and glia through adulthood - may aid in repair after injury.
- irradiating the NPC niches leads to death of proliferating cellsjavascript:; and neurocognitive decline in rodents; NPC may also be involved in the development of glioblastoma.
  - several studies suggest that increased dose to the SVZ may improve survival or tumor control in patients with glioblastoma

NPC niches-sparing radiotherapy without compromising coverage of the target volume (GBM)

A Prospective Cohort Study of Neural Progenitor Cell-Sparing Radiation Therapy Plus Temozolomide for Newly Diagnosed Patients With Glioblastoma. Chengcheng Gui et al. Neurosurgery, Volume 87, Issue 1, July 2020, Pages E31–E40

- OS and PFS were comparable to a historical control.
- GBM recurrence in the spared NPC niches was not observed.
- lower radiation doses to the NPC niches were associated with less severe deterioration of verbal memory, preserving cognition.

Sample treatment plan with NPC niches delineated:



RADIATION MYELOPATHY

– irreversible! - one of most feared complications in clinical radiotherapy!

- pathophysiology – as in radiation necrosis of brain (i.e. spinal cord infarction with necrosis, hemorrhage, and demyelination).
- bimodal distribution - first peak at 12-14 months after irradiation and second at 24-28 months.
- incidence for conventionally fractionated irradiation (1.8-2 Gy per fraction, 5 fractions per week): 57-61 Gy - incidence 5%; 68-73 Gy - incidence 50%.
- clinical features:
  - insidious onset: painless progressive paresthesias, UMN & LMN weakness that may progress (over several months) to complete paraplegia.
  - rarely, abrupt onset – due to infarction.
- diagnosis - no confirmatory imaging / laboratory studies (diagnosis of exclusion); **MRI / myelography** - to rule out compressive lesion.
  T2-MRI – slightly swollen cord with signal↑ regions → myelomalacia.
  T1-MRI – vertebral marrow replacement with fatty tissue (homogeneously bright vertebrae).
- no known treatment (steroids may improve symptoms transiently).
- ≈ 50% patients die from secondary complications.

RADIATION-INDUCED VASCULOPATHY

- latent period can be up to 23 years.
- typically affects extra- or intracranial portions of *INTERNAL CAROTID ARTERIES*.
- ***accelerated atherosclerosis***, localized stenosis, irregular vessel contour, even complete occlusion of portion of artery in radiation portal.
- ***moyamoya pattern*** may develop.
- ***telangiectatic vessels*** (may hemorrhage) occasionally form; up to ***pseudoaneurysm*** formation.
- ***mineralizing microangiopathy*** with dystrophic calcification - punctate calcifications in basal ganglia, cortex and brain stem; asymptomatic.
- clinically: TIA, ischemic stroke.

RADIATION OPTIC NEUROPATHY

- develops within 3 yrs after treatment directed to orbit, sinuses, pituitary, or intracranial tumors.
- painless visual loss (usually monocular), papilledema in most (→ optic atrophy later), hemorrhagic exudates.
- 50% patients improve, some become blind.
- T2-MRI - high signal in intracranial portion of optic nerve.
- **steroids** are ineffective.
- prophylaxis - **shield optic nerve** from radiation portals.

RADIATION-INDUCED NEUROPATHY

(incl. radiculopathies, plexopathies)

- *skull base tumors* often lie in close proximity to cranial nerves;
- sensory nerves, including special sensory nerves such CN2 and CN8, are more susceptible to injury than motor nerves

EXTERNAL BEAM RADIATION THERAPY (EBRT)

a) **γ-photons** emitted from ^{60}Co sources
b) **X-rays** generated from linear accelerators
c) particulate radiation (such as **neutrons**) generated from cyclotrons - no therapeutic advantage over X-rays; particles deposit all energy in tissue and have no exit dose.

- all forms act similarly - produce fast-moving electrons and free radicals in biologic tissue that *interrupt chemical bonds between DNA base pairs*.
- disadvantages of traditional EBRT:
  1) loss of function of adjacent healthy tissues.
  2) radioresistant tumors (because of dose limitations of surrounding tissues), e.g. *MENINGIOMAS*, *ACOUSTIC NEUROMAS*.

VOLUMES

Gross tumor volume (GTV) - all known disease, including adjacent nodes, visible on CT / MRI.

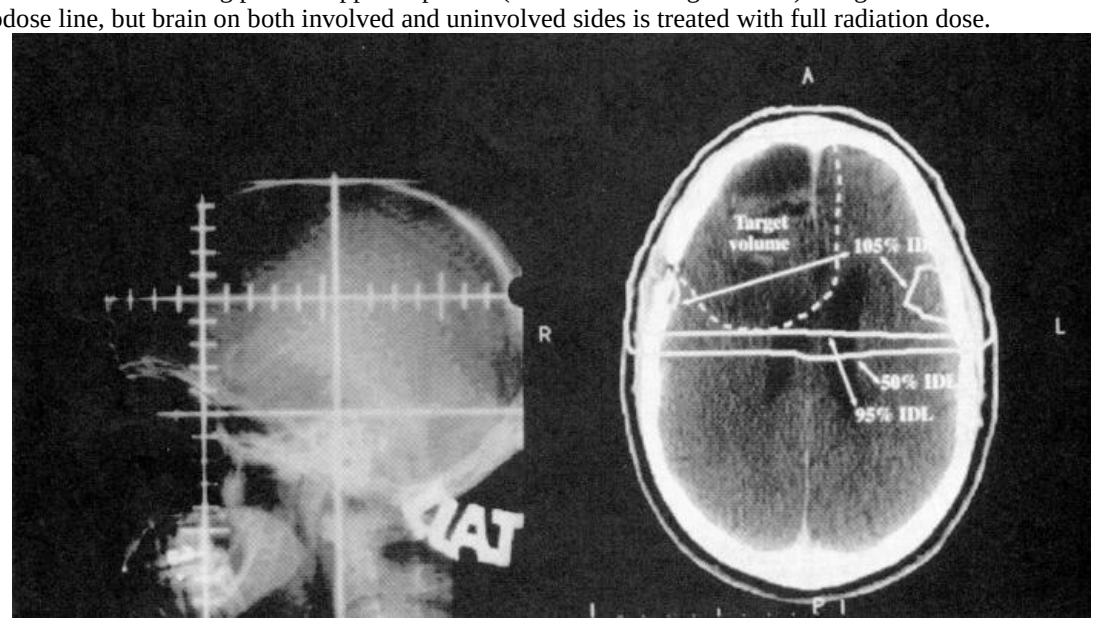
Clinical tumor volume (CTV) - GTV plus surrounding tissue that presumably harbors microscopic disease; CTV size depends on tumor histology. see p. Onc3 >>

Planning target volume (PTV) - provides margin around CTV to allow for movement and treatment setup variation.

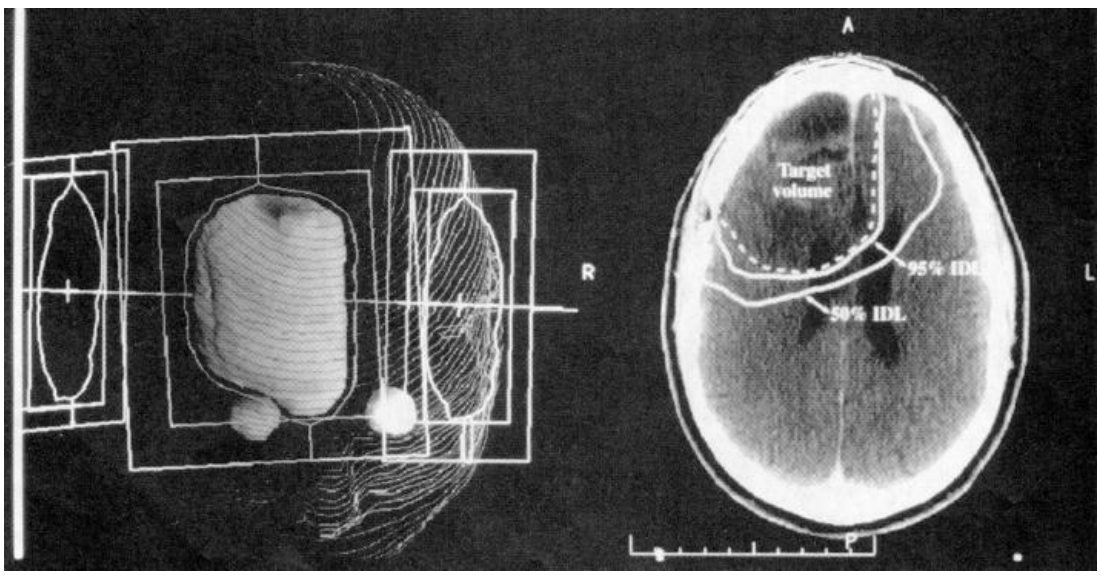
- beam is delivered through **COLLIMATOR**, which shapes beam (i.e. field or treatment area is defined by size and shape of collimator); usually 2-3 portals or fields are used.

- variation in beam intensity, location, angle, shielding can be used to protect surrounding tissue, but, in general, ***entire field receives treatment dose*** (because healthy tissues are more resistant to effects of radiation, tumor cells are killed while surrounding tissue eventually recovers).
- for target volumes less than whole brain, use technique sparing surrounding uninvolved normal tissues:
    a) lateral opposed fields
    b) wedged pairs
    c) three or four field arrangements
    d) arcs or full 360° rotations
    e) "conformal therapy" - multiple beams with individual beam shaping and intensity.
- treatment mandates *precision in daily setups* - patients are treated ***prone, in immobilization cast***; sedation or anesthesia is usually necessary only for youngest children (< 3 yrs).
    – immobilization is especially important in *whole CNS irradiation* - to maintain fixed relationship at junction between lateral opposed fields (used to treat brain) and posterior field (used to treat spinal axis).

Standard partial brain field for frontal lobe glioma;
left - simulator film: hatched lines represent 1-cm scale; center of this 11 × 10-cm field is located where hatched lines meet.
right - dose distribution using parallel opposed portals (left lateral and right lateral) - target volume is well encompassed by 95% isodose line, but brain on both involved and uninvolved sides is treated with full radiation dose.



Conformal radiotherapy of same frontal lobe glioma;
left - beam's-eye view of vertex field that is shaped to treat target while avoiding most of normal brain; two smaller round structures inferior to target volume are eyes of patient.
right - dose distribution now conforms much more closely to shape of target volume; normal brain is receiving only 50% of dose.



DOSAGE

- **total dose** depends on *tumor histopathology* and on *CNS tolerance*. see p. Onc3 >>

Standard for gliomas – 60 Gy

FRACTIONATION

Support for Fractionation:

1. Allows for repair of normal tissue
2. Allows for reassortment of tumor cells (to sensitive cell cycle phase) and improve overall cell kill
3. Allows for reoxygenation of cells that may be hypoxic in the center by reducing overall tumor burden
4. Allows for repopulation of normal cells (also tumor cells)

- small daily fractions are safer and more effective than larger fractions over shorter periods.
- alternative methods (not more effective clinically):

HYPERFRACTIONATION* (≥ 2 small doses during day) - if sufficient time is allowed between fractions (6-8 hours) for repair of sublethal radiation damage in normal tissues, it is theoretically possible to increase total radiation dose by 25-30% (in the same overall treatment time) without increasing risk of normal tissue injury.

*does not seem to be worthwhile.

ACCELERATED FRACTIONATION (≥ 2 conventional doses during day - shortened overall treatment time) - reduced opportunity for tumor repopulation (e.g. rapidly proliferating *GLIOBLASTOMA MULTIFORME*).

IMRT

Newer fractioned radiotherapy techniques such as intensity modulated radiotherapy (IMRT) can minimize the amount of normal brain exposed to radiation compared with conventional or standard 3-D conformal techniques.

WHOLE-BRAIN RADIATION THERAPY (WBRT)

Disadvantages of WBRT:

1. WBRT takes time to deliver (typically 2-3 weeks vs. SRS – 1 days), thereby delaying systemic therapy (systemic and radiation therapy are not delivered concurrently).
2. WBRT results in loss of hair, which can impact quality of life.
3. WBRT may negatively impact ability to optimally treat new local disease should WBRT fail.
4. Increased risk of neurocognitive decline (*hippocampus-sparing WBRT* – expensive technique)

STEREOTACTIC RADIATION

- delivery of precise dose of high-energy radiation through stereotactically directed multiple, well-collimated beams converging on small lesion.

- in past, stereotactic radiation could only be delivered in single dose; today, because of **noninvasive fixation devices**, single-treatment delivery is no longer mandatory.

> **RADIOSURGERY** – term is used if number of sessions is ≤ 5 and only for cranial or spinal targets

- sophisticated imaging devices and 3D treatment-planning computers allow ***much more specific targeting of lesion*** - significantly less radiation to surrounding healthy tissues.
- RADIATION THERAPY PLANNING currently takes 2 forms:

I. **BEAM FIRST (S. FORWARD) PLANNING** - *target volume* of radiation is determined first, and then surrounding tissue volume is planned; works extremely well in tumors with regular or spherical shape.

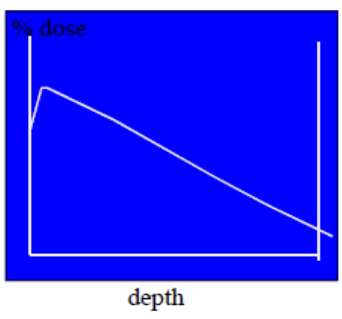
II. **DOSE-FIRST (S. INVERSE) PLANNING, S. PEACOCK TOMOTHERAPY** - determines safe *dose for surrounding healthy tissues* first, and then computer workstation determines required beam intensity and shape for each portion of field; works very well for irregularly shaped lesions.

The Principles of Skull Base Radiosurgery:
http://www.medscape.com/viewarticle/574708?src=mp&spon=26&uac=121060BZ

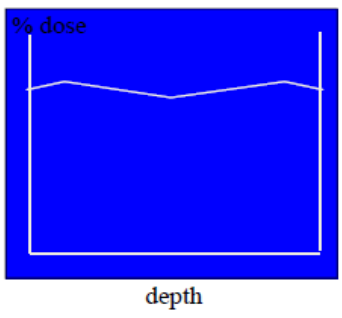
HOW BEAMS COMBINE

How beams combine

- Single-beam %depth-dose curve

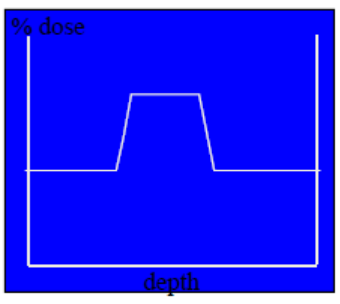


- Parallel-opposed beams %depth-dose curve

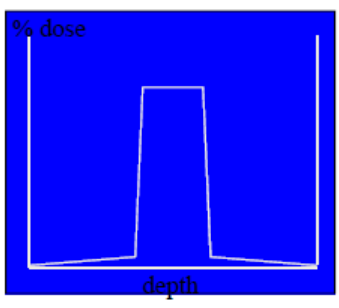


How beams combine

- Four-beam (AP, PA, LT, RT) %depth-dose curve along one axis



- Many beams %depth-dose curve



INDICATIONS

- lesions < 3-4 cm:

Brain tumors:
1) metastases
2) meningiomas see p. Onc38 >>
3) acoustic or trigeminal neuromas
4) recurrent pituitary adenomas
5) solid residuals of craniopharyngiomas
6) hemangioblastomas
7) malignant sharply localized tumors
8) selected gliomas (thalamus or brainstem); gliomas, when malignant, are always poor indication for radiosurgery because of their diffuse mode of invasion (except pilocytic astrocytomas - excellent indication for radiosurgery when they are small, well circumscribed, deeply seated, and difficult to excise safely).

Skull lesions - hard for GK due to chances of collision (less risk with Icon).

Certain pain syndromes: glossopharyngeal neuralgia, trigeminal neuralgia see p. CN5 >>

Certain epilepsy cases

Certain psychiatric disorders: OCD (anterior cingulotomy, anterior capsulotomy) see p. Psy25 >>

TYPES – SRS (STEREOTACTIC RADIOSURGERY)

- highly focal, closed skull (noninvasive!) external irradiation that uses stereotactic device for precise target localization (high radiation dose* to intracranial target in 1-5 sessions** without delivering significant radiation to adjacent normal tissues - intersection of multiple beams of radiation at isocenter with steep dose gradient).

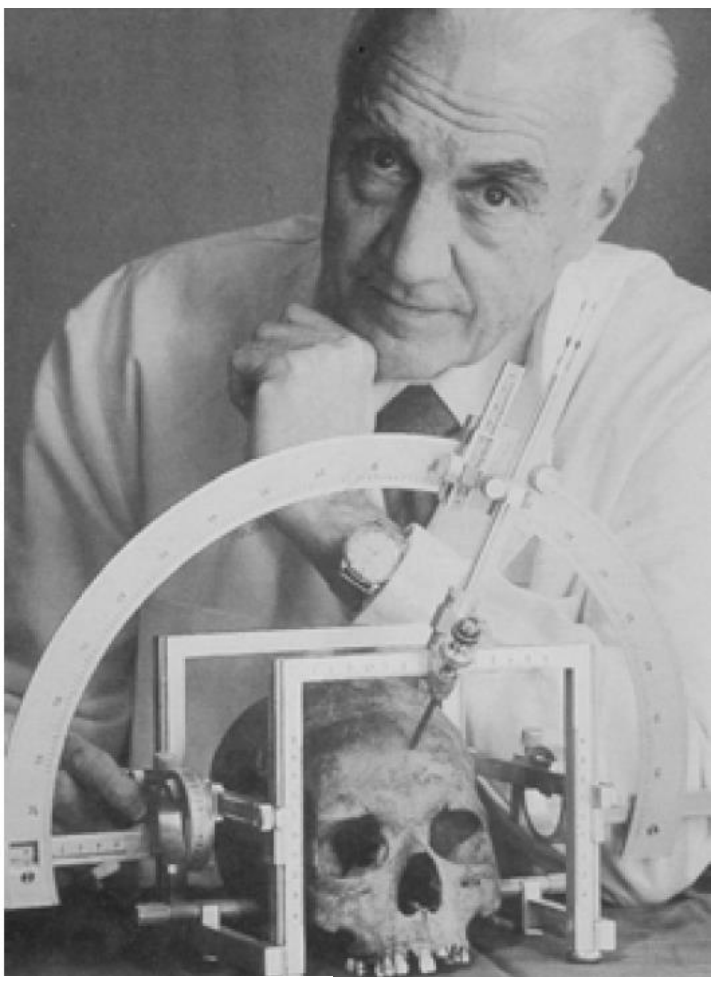
> Can achieve tumor ablation without craniotomy!

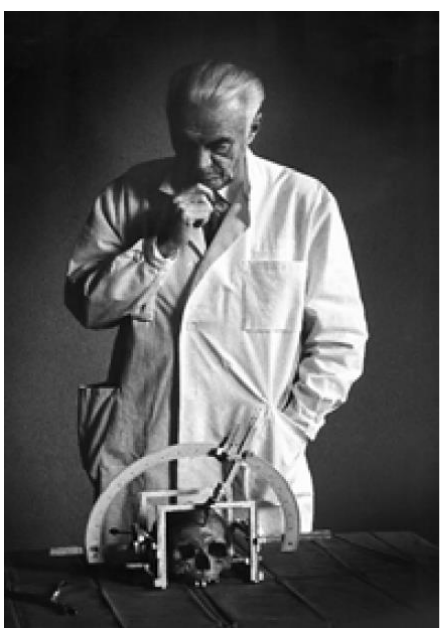
*even radioresistant tumors can be treated - challenged traditional radiobiological concepts
1-5 treatments per target – treatments are called ***sessions* (vs. ***fractions*** in fractionated conformal radiotherapy).

> AANS/CNS/ASTRO Definition of Radiosurgery *Barnett et al, J Neurosurg 106, 1-5, 2007*
> Stereotactic Radiosurgery is a distinct discipline that utilizes externally generated ionizing radiation in certain cases to inactivate or eradicate (a) defined target(s) in the head or spine without the need to make an incision. The target is defined by high-resolution stereotactic imaging. To assure quality of patient care the procedure involves a multidisciplinary team consisting of a neurosurgeon, radiation oncologist, and medical physicist.

Stereotactic Radiosurgery (SRS) typically is performed in a single session, using a rigidly attached stereotactic guiding device, other immobilization technology and/or a stereotactic image-guidance system, but can be performed in a limited number of sessions, up to a maximum of five. Technologies that are used to perform SRS include linear accelerators, particle beam accelerators and multisource Cobalt 60 units. In order to enhance precision, various devices may incorporate robotics and real time imaging.

- term formulated by Lars Leksell, MD in 1951:





- used either as boost to conventional, fractionated radiation or as single treatment.
- radiation beams intersect at one point (called ISOCENTER).
- first step in single-dose procedure is to attach patient's head to ***stereotactic head frame*** (has coordinate system for target determination); for multisession treatment – use custom ***mask*** or ***refixation frame*** (e.g. Extend – for Gamma Knife Icon).
- next, ***series of images*** are taken with head ring in place (CT, MRI, SPECT, or PET).
- images are transferred with underlying coordinate system to **computer workstation**.
- physician prescribes *individual treatment plan* by outlining lesion to be treated.
- final verification is performed with TARGET POSITIONER (i.e. trial run is performed on positioner before treating patient).
- because dose that can be safely administered in single session is limited by volume irradiated, radiosurgery is restricted to ≤ 4 cm lesions (e.g. AVMs, pituitary adenomas, vestibular schwannomas, meningiomas, small gliomas, small brain metastases).
  in > 4 cm, radiation dose to surrounding structures becomes too great – use fractionation!
  - gliomas, with no well-defined margin, are not ideally treated with radiosurgery.
  - tumor may appear to grow immediately after treatment.
  - treatment can worsen peritumoral edema (H: prolonged course of high-dose steroid).
- may also be used to create anatomical highly-delineated lesions for functional (pain, movement) disorders.
- ***several lesions*** can theoretically be treated on single clinic visit (as number of lesions increase, overlapping of fields exceeds tolerance of healthy brain to radiation injury!).

INDICATIONS FOR MULTISESSION SRS

(e.g. using Extend mask on GK):

A) benign tumor > 10 cc in volume
B) tumor abutting the optic pathway
C) vestibular schwannoma with the intent of hearing preservation
D) tumor previously irradiated with single-fraction SRS.

TYPES - SBRT (STEREOTACTIC BODY RADIOTHERAPY)

= SRS for extra-cranial sites and can be performed in one to five sessions (fractions).

- gamma-ray photons, X-ray photons, protons, helium ions, and neutrons have all been used for SBRT and SRS.

PLATFORMS – A. GAMMA RAYS

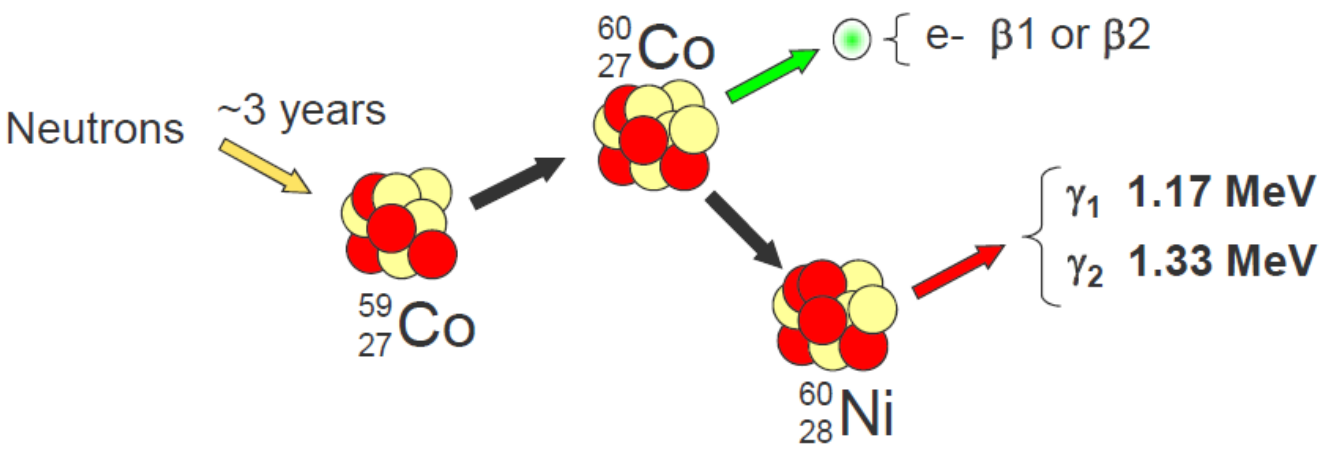
- multiple highly collimated ^{60}Co beams

COBALT SPECIFICS

- 27 protons
- naturally occurring form (100%) is **Co59** (not radioactive)
- **Co59** can be transformed to **Co60** by the addition of a neutron (in a nuclear reactor)
- **Co60** undergoes beta decay* with T1/2 = 5.2714 years** – produces **Ni60** which immediately emits 1 or 2 gamma rays (average energy 1.25 MeV).

*i.e. emits beta particle

**treatment times get longer as Co60 sources decay (twice as long at the end of 5 years)



GAMMA-RAY PHOTONS VS. X-RAY PHOTONS

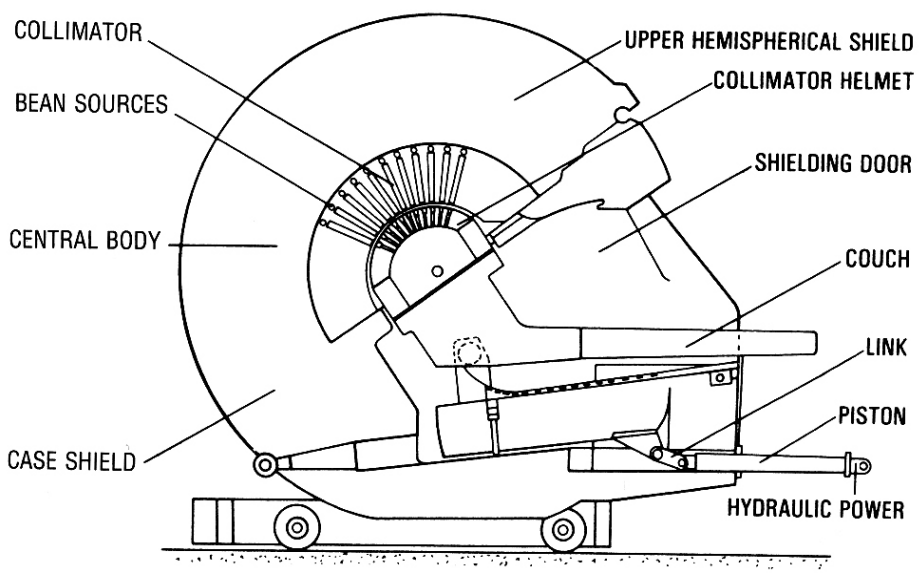
- Gamma-ray photons and x-ray photons are physically alike, but differ in point of origin:
  A) Gamma-ray photons - originate from an atom's nucleus
  B) X-ray photons - originate from an atom's electron shell
- photon energy usually stated in MeV
- Gamma-rays are usually narrow spectrum (isotope dependent); X-rays are usually broad spectrum.

MODELS

1) Gamma Knife (Elekta AB)
2) RapidArc (Varian Medical Systems)

- very precise.
- machine contains 20 grams of cobalt and 20 tons of protective shield.
- cobalt needs replacement every 5 years (cost approx. 1 mln USD)
- cobalt activity at loading - 6000 Curie or 222 TBq.
- dose-rate at focal point > 3 Gy/min.

Cross-section of Gamma Knife, model U showing cobalt 60 sources in central body aligned with primary collimators and collimator helmet.



GAMMA KNIFE MODELS

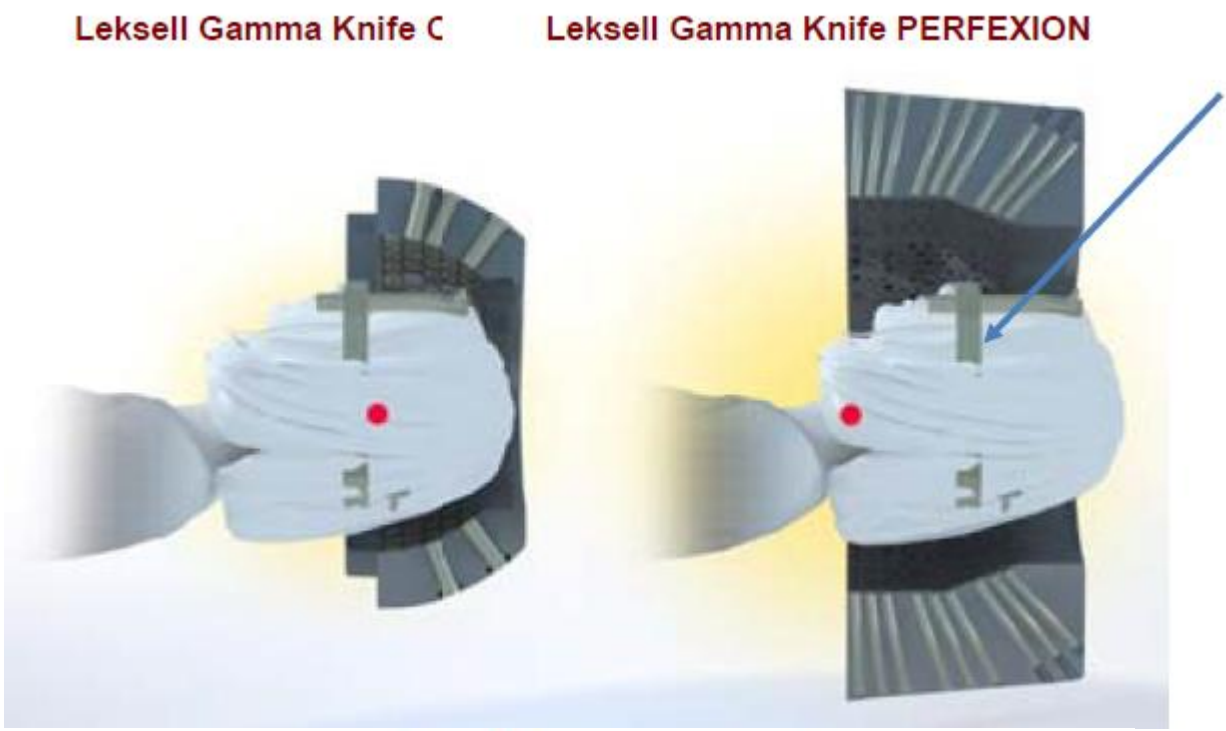
Model A
Model B
Model C
Perfexion (192 cobalt sources) - fully automated (except gamma angle change)
Icon ("Perfexion Plus") – Perfexion designed for multisession treatment (has onboard cone-beam CT and mask adaptor), frameless high def patient motion management - detects any movement > 0.15mm in 3D.

Perfexion:

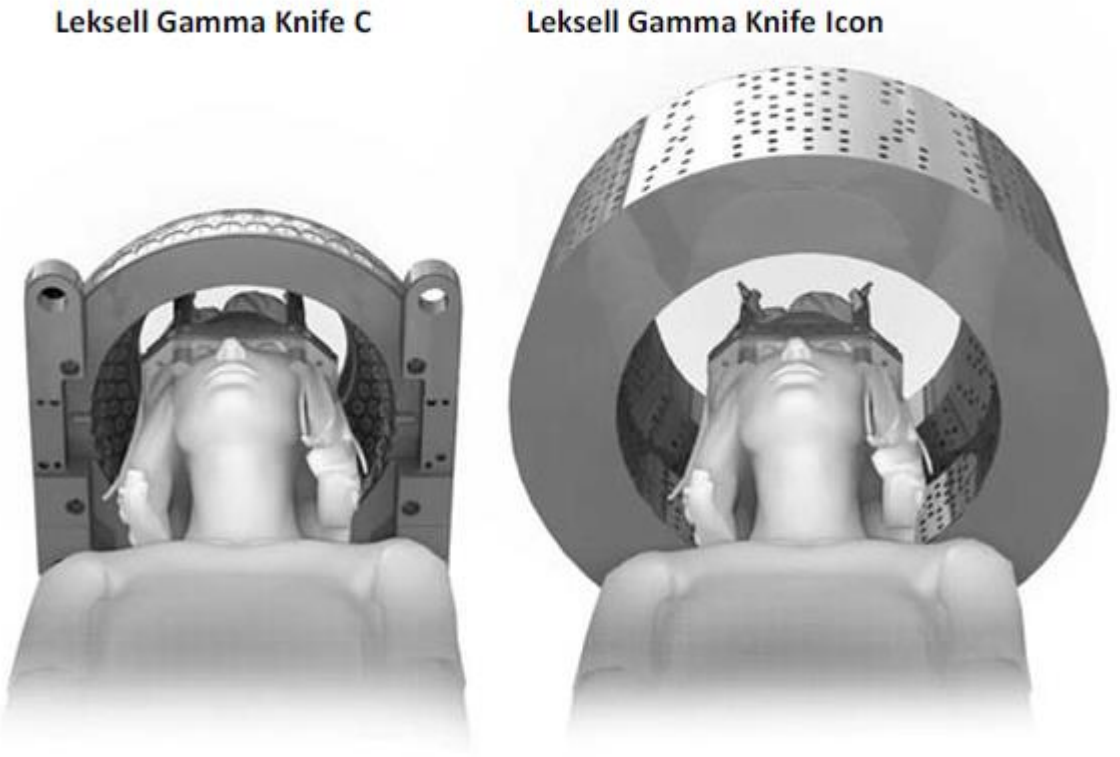
Icon ("Perfexion Plus"):

Perfexion vs. Model C:

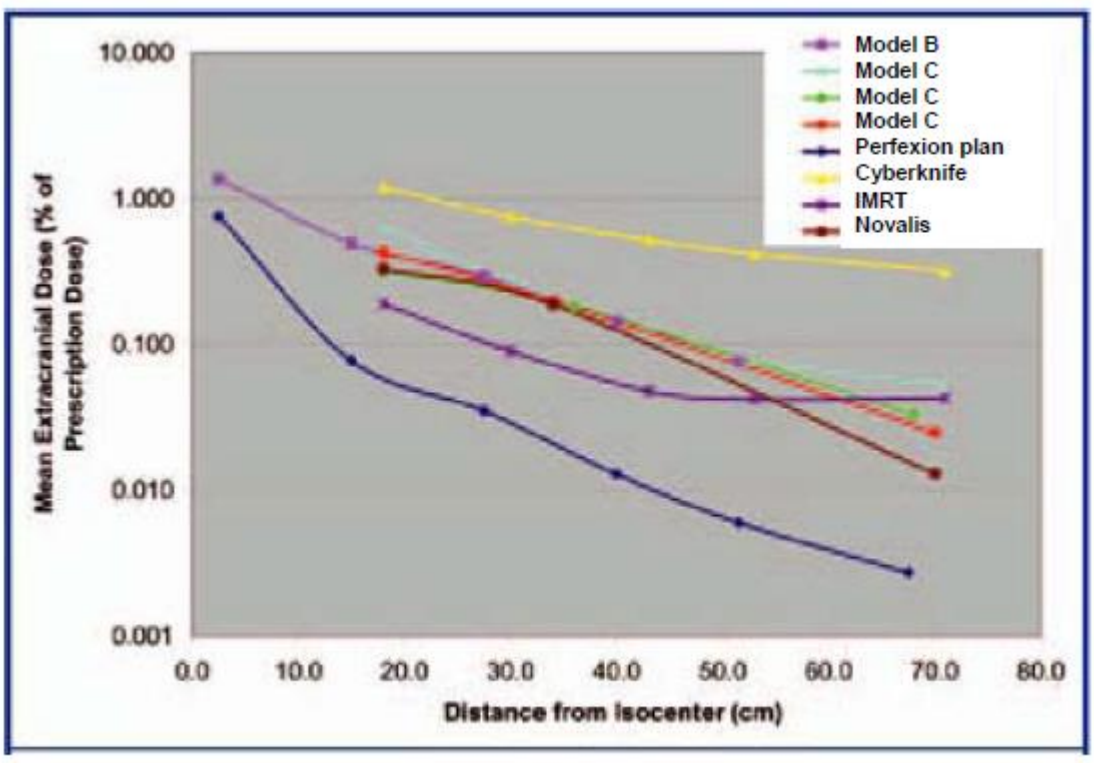
- automated collimation.
- automatic plugging by sectors (no more manual plugging); sector *off* during patient positioning, sector *home* during system idle.
- the whole patient moves between shots (Model C – head moves, but body remains immobile – problems with neck).
- increased treatable volume by more than 300%
- increased volume has eliminated problem with X-axis (lateral)
- improved Focus Access; human heads are longer front-to-back than wide – still occasional problem with extreme back > front targets (due to pins/posts)



Collimator size

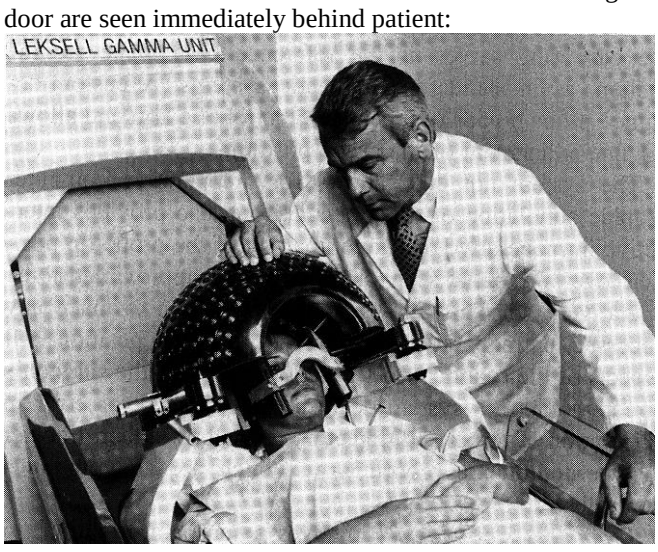


Best safety profile among SRS systems:



Lindquist C, et al. Neurosurgery 61:ONS-130, 2007

Patient is fixed in stereotactic frame with intracranial target centered at isocenter of collimator helmet; shield and shielding door are seen immediately behind patient:



FRAME

All GK models use Leksell Model G frame
Icon may also use Extend frame for multisession treatment – need special training as reapplications must be within 1 mm of precision.
Accuracy – 0.4 mm for frame, 0.7 mm for mask.

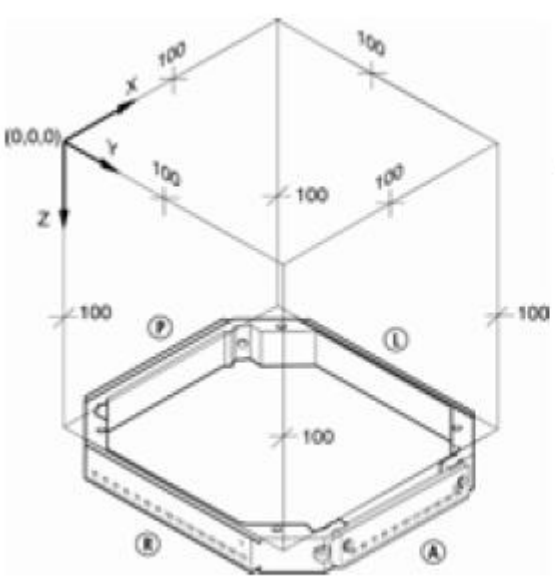
- Components
- base frame
- mouth piece
- support posts
- pins
- ear pieces

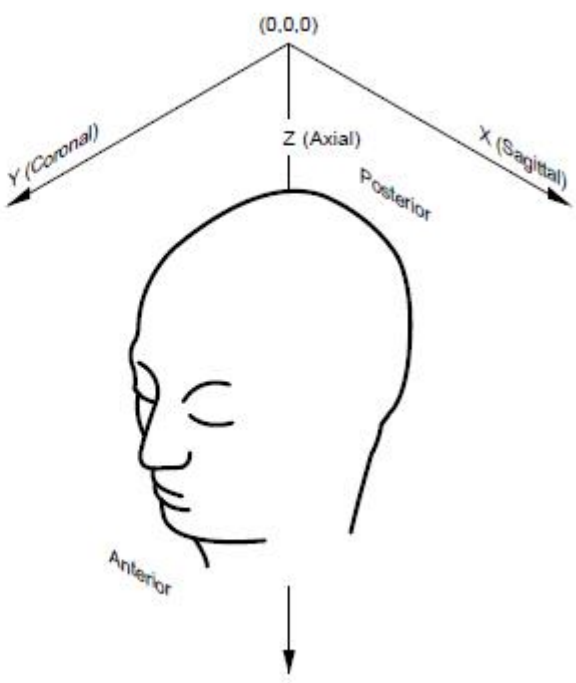
Refixation Device – Extend frame Perfexion only

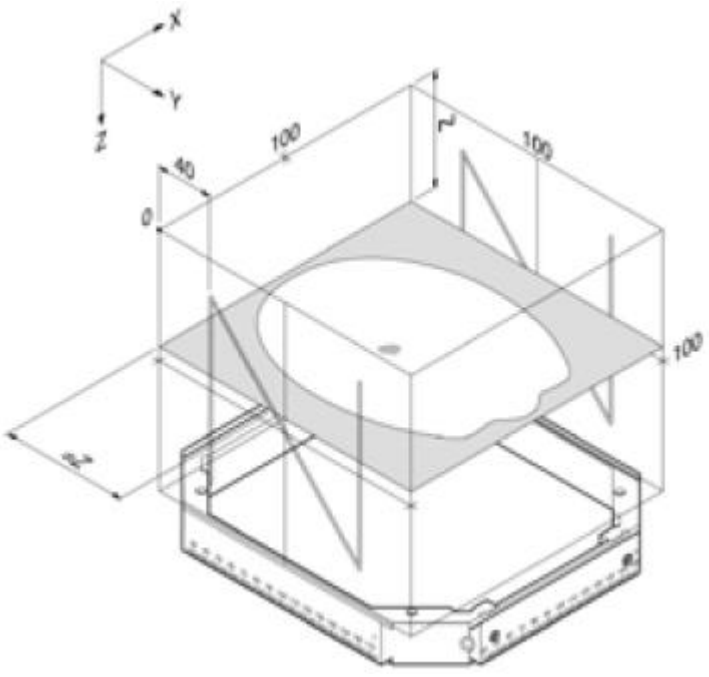
- Multi-session radiosurgery
- Vacuum secured/monitored custom mouthpiece
- Molded occiput cushion
- Not Icon compatible

BASE FRAME

- anodized aluminum (special cleaning)
- part of localization system - Cartesian coordinate system; zero point (0,0,0) - above, behind and to the right of patient; ***all coordinates positive***; X is left-right, Y is anterior-posterior, Z is inferior-superior; 100 is middle of frame.

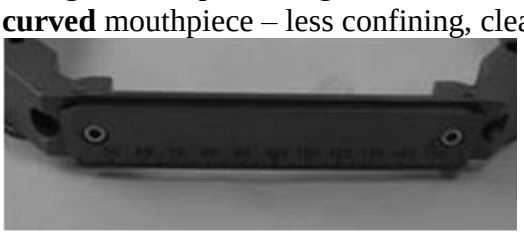






MOUTHPIECES

straight mouthpiece – rigid
curved mouthpiece – less confining, clears the nose, use of straw, ?intubation



slotted mouthpiece – three posts only for previous craniotomy see below >>

POSTS

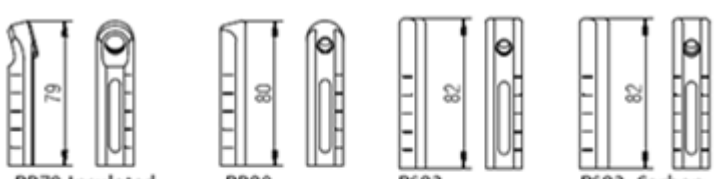
Long angled (routine for front) – pins face down:

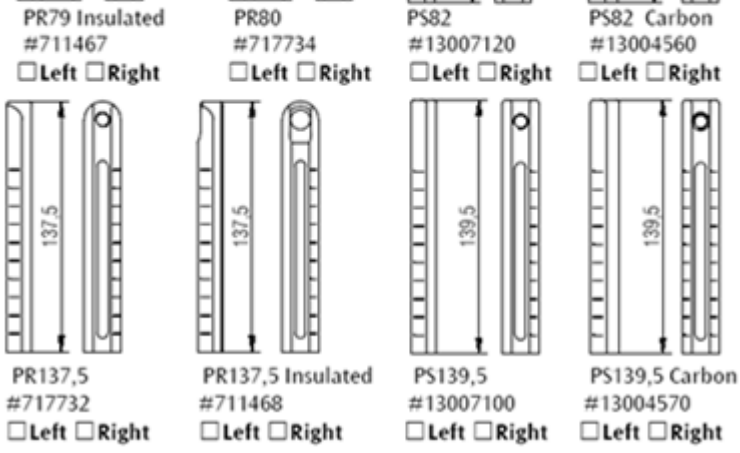
Long curved – pins face down:

Long straight – pins perpendicular:

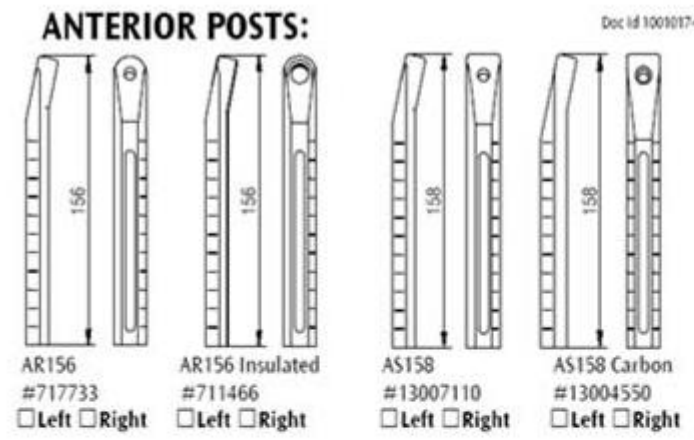
Short straight (routine for posterior)– pins face up:

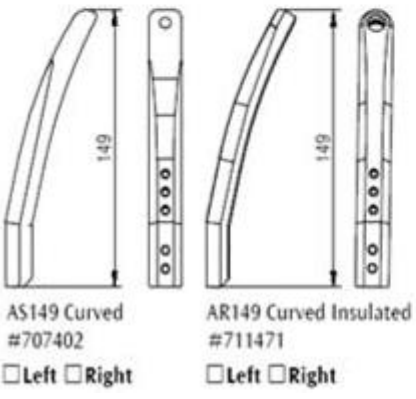
POSTERIOR POSTS:





ANTERIOR POSTS:





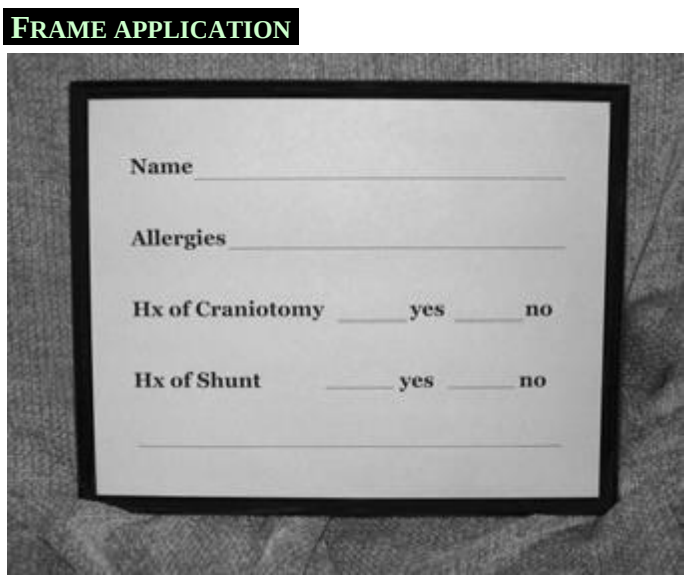
- standard pins are MR compatible, but produce CT artifact (aluminum pins available).
  BrainLab pins are made of carbon fiber and have white ceramic tips – maximum 100 resterilizations
- avoid imaging conflict (CT), or get pre-frame high-resolution CT, too.

N.B. for MRI use only insulated posts (pins are insulated from posts) – prevent induction of currents!

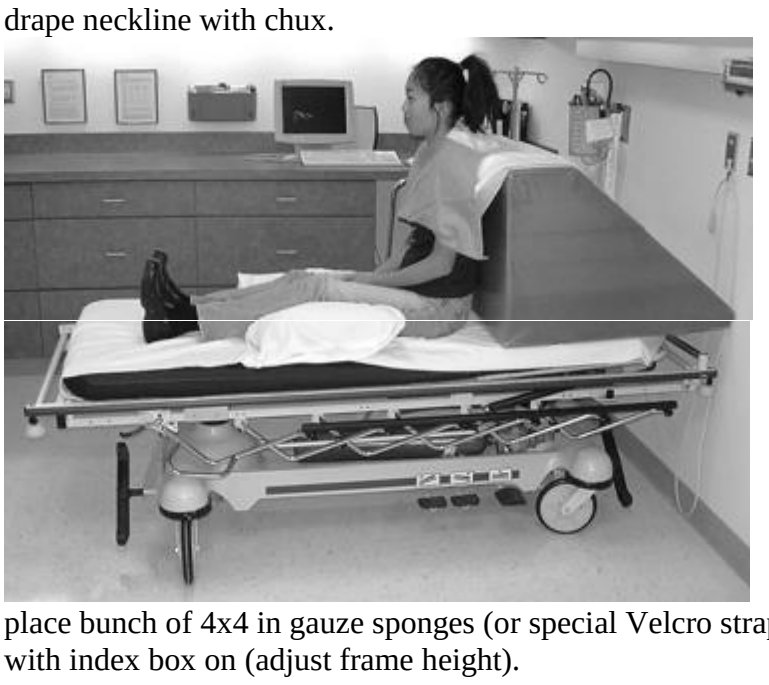
EAR PIECES

- used for functional procedures with old software where rotation is undesirable.
- used for "solo" placement of frame (not recommended).
- precludes simultaneous use of index box

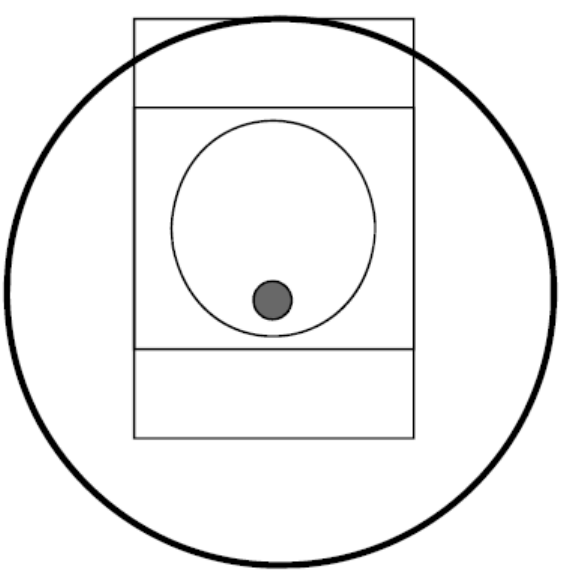
FRAME APPLICATION



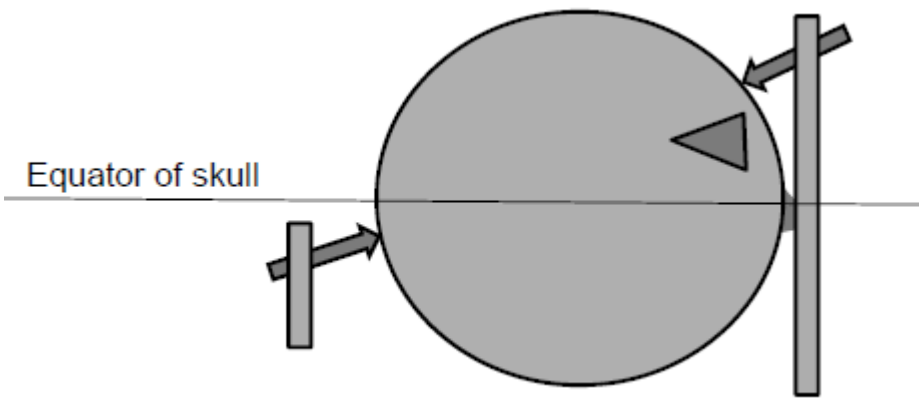
- patient sitting upright against blue triangle cushion behind back, sitting at 80-90 degree angle.
- drape neckline with chux.



- place bunch of 4x4 in gauze sponges (or special Velcro strap) on top of head to help support frame with index box on (adjust frame height).
- make sure frame base sits parallel to the floor – when attached to the table it will keep patient's head in neutral position.
- no need for sedation; use only **anxiolytic** (e.g. 0.5-2 mg of MIDAZOLAM + MORPHINE) to blunt bradycardia (as *diving reflex* due to pressure on V1).
- inject 1% LIDOCAINE (up to 20 mL) trough post hole with 25G ***spinal needle***;
  - if using addition of 10% BICARBONATE to blunt pain, risk of severe delayed periorbital edema (Cleveland Clinic does not use bicarb).
  - May inject 1 mL at each target area and later inject full volume (numbed skin is less sensitive to large volume stretch pain).
  - when hitting the bone, measure needle length – will know the length of pins (add 4-5 mm for exposed thread) – need to keep pins as short as possible to minimize the chance of collision; (therefore pins have female hex socket)
- use smallest **index box**.
- tighten **pins** only 3 finger tight using driver (Brain Lab recommends torque wrench set at 30 N.m) - posts should begin to flex; pin threads ideally not exposed at the end of tightening (minimize collision risk).
- remove index box.
- ***target must be above frame base*** (cannot target below it), i.e. place frame low as the lowest treatment point – top of frame base (in Perfexion can treat up to C1 level).
- avoid pins in the plane of target (pin artefacts on imaging).
- apply frame centered left-to-right.
- *if target is in posterior skull, move frame posteriorly* (so target moves towards the center of frame base) – only adjustment needed for frame (otherwise, collisions with GK Perfexion are very rare).



- **posts**:



- use shortest pins possible to avoid helmet collision.
- typically, start with pair of angled long posts in front, then short straight in rear.
- front posts above supraorbital ridge, avoid temporal fossa (problem for lateral placement).
- posterior pins typically as high as possible below skull equator.

FRAME CAP

- to check for collisions:

- after frame placed, place Frame Cap - does Frame Cap fit? (to ease clearance check)
- check for frame warpage (also bubble helmet).
    - if fits, then just perform skull measurements (and / or get whole-head CT)
    - if not, then also measure posts (above & below, type) and pin length.
- may final tighten pins (don't over/under-tighten).

POOR PLACEMENT – UNACHIEVABLE TARGET

Move offending pin/post, reimage, co-register and finalize plan - almost always manageable without having to reapply frame!

PREVIOUS CRANIOTOMY

- for patients with <u>previous frontal craniotomy</u> use:
    a) post into *infraorbital rim* (well tolerated) - use long straight post (issue regarding post identification).
    b) ***slotted mouthpiece*** and only 3 posts:

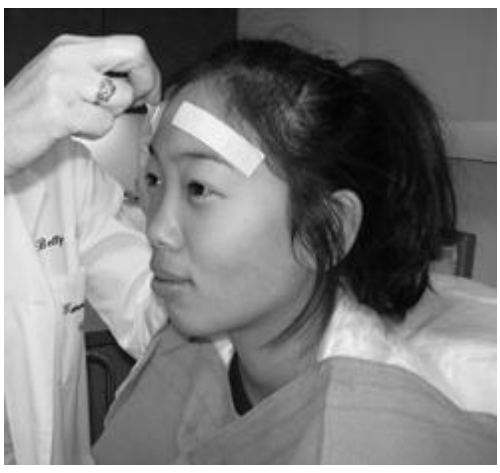
Do not use standard corner locations with only three posts!

- shunts with craniotomy may require ***rotated placement***; software allows reformatting to AC-PC line but can't draw objects in reformatted images.

FRAME REMOVAL

(after treatment)
Drape for frame removal
Secure frame utilizing black Velcro strap:

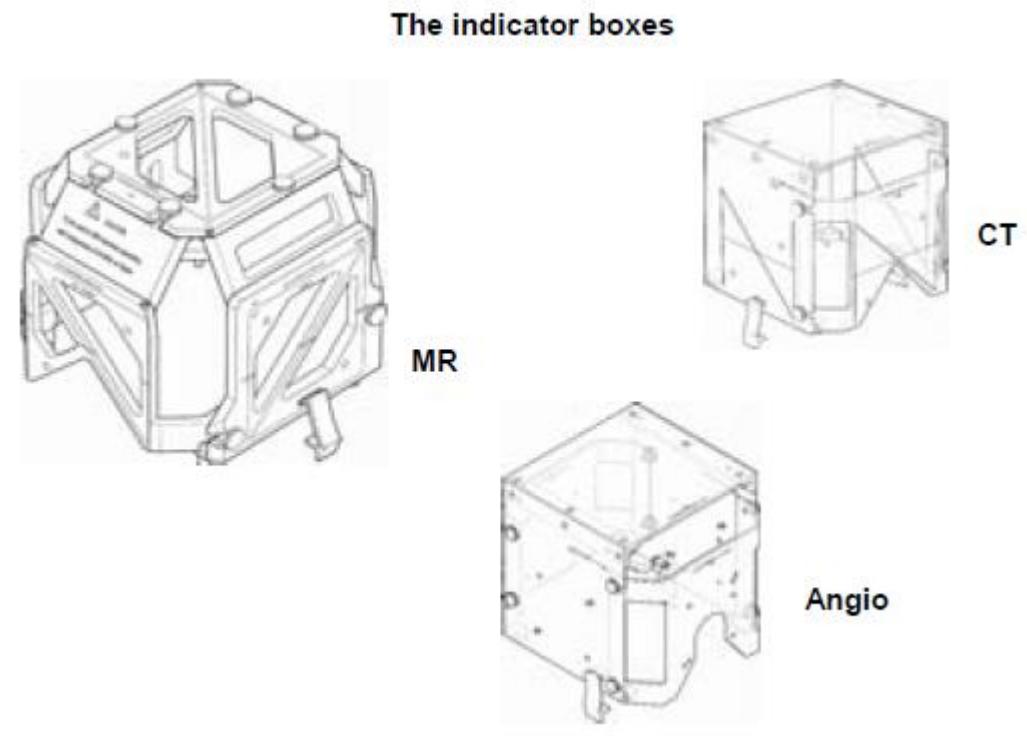
Assess pin sites:
Clean sites with H2O2
Apply antibiotic ointment
Apply Band-Aids



IMAGING

- day prior to procedure - use volumetric **MRI** for targeting; use axial images to minimize distortions (especially if using frame on); do preplanning.
- on the day of procedure, use **CT with frame on** for stereotactic localization.
- only transverse MRI images should be used because of fiducial distortion near frame.
- ideally, portion of slab used for definition should contain target but probably better to avoid using slices near base of frame.
- include eyes when doing functional/benign cases to allow blocking beams transiting lenses.

INDEX BOX



- "N" shaped Index Box
- uses "best fit" to shape
- does not require perfect orientation in scanner
- does require no movement during scan
- gantry tilt of zero in CT
- only need two side faces of box; if thin slab (< 4 cm) use third face
- beware poor "docking"
- beware air bubbles in MRI fiducials

POSTPROCEDURAL IMAGING

- maximum lesion volumes appear at 6-9 months.
- maximum T2-MRI volumes may persist at maximum volume 3 years or more after treatment.

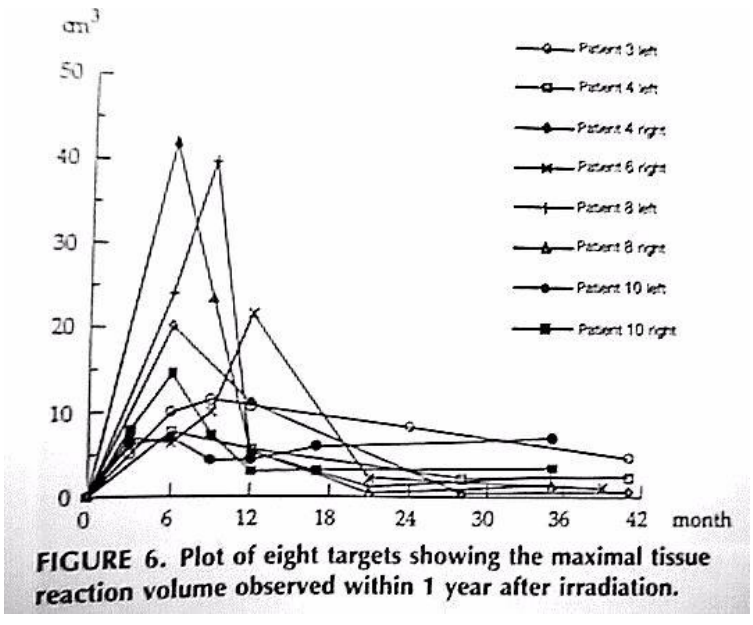
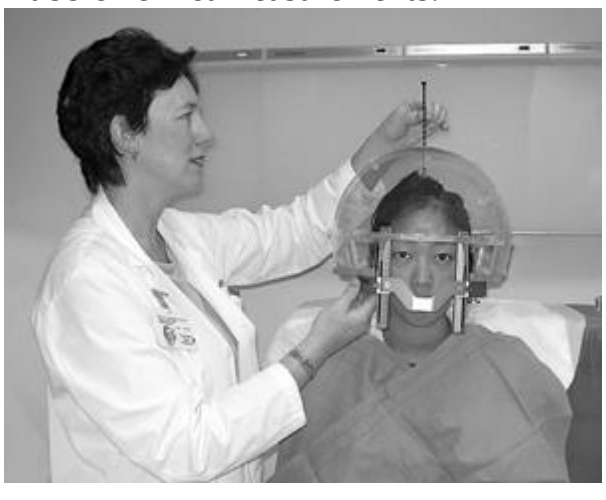


FIGURE 6. Plot of eight targets showing the maximal tissue reaction volume observed within 1 year after irradiation.

SKULL MEASUREMENT

- latest generation of PFX software allows for skull contouring using CT data
- requires acquisition from below the base frame to above the head.
- preemptively manage skull defects – bolus or CT scanning through head and frame.

Bubble helmet measurements:



Bubble helmet

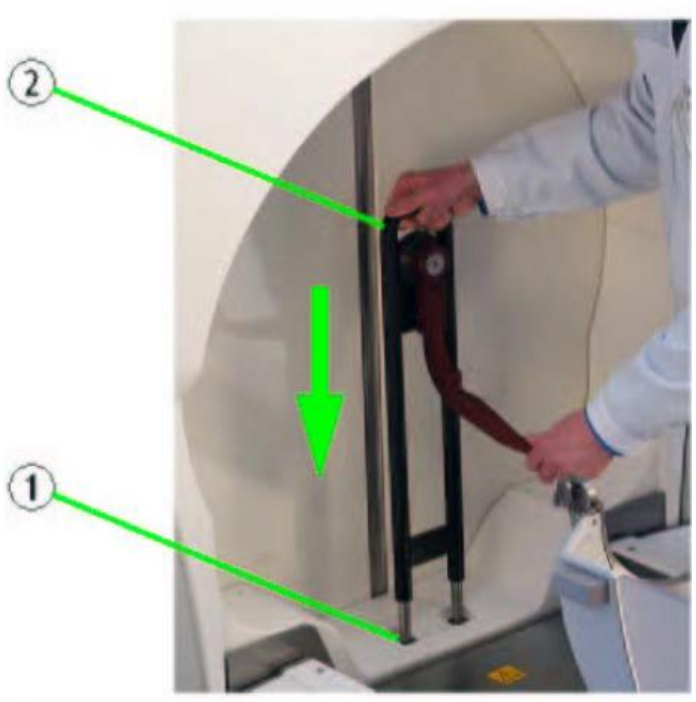
- Too few data points!
- Poor representation of shape of the head.
- Easily mislead by concavities
- Depth differences, **therefore dose differences**
- Better if the "system" would get head shape from CT and do voxel-based 3D dose calculation
  - but would require whole-head CT
  - would take a long time to calculate

CLEARANCE TOOL

- required when clearance to post, frame or screw < 13 mm
- required when clearance to patient's head < 20 mm
- can not override a clearance check
- all clearance checks must be done before treatment
- rule of thumb – try to keep, at least 4 mm for the closest collision
- be careful when "accept or reject" a position

Enter the treatment room. Make sure you can clearly read the instructions on the treatment room monitor when standing alongside the head end of the patient couch.

From the tool cabinet, take out the clearance check tool. Mount the tool at the head end of the patient couch by inserting the two bars into the corresponding holes ① in the cover just below and outside the shielding doors. Hold and lower the clearance check tool by using the handle ②.



WARNING 7.3 **Before mounting the clearance check tool, check that the contact surfaces near the end of the two bars are clean (see Section 9.3 on page 139). Any dirt between the tool and the mounting point may affect the precision of the clearance check and lead to contact with the collimator cap during treatment.**

7 Make sure the tool is inserted all the way into the holes. The following message is then displayed in the **Information** field:
`Clearance tool mounted.`

7.6.3 Docking and verifying the patient

8 On the treatment room monitor, verify the gamma angle of the selected run.

9 Dock the patient according to Section 7.3.3 on page 98.

WARNING 7.4 **When docking the patient during clearance check, make sure to keep the arm of the clearance check tool clear of the patient's head. Otherwise injury to the patient may result.**

10 Check the **System's checklist** area on the treatment room monitor. Verify that the gamma angle interlock specifies the correct gamma angle, and that all of the other physical interlocks are set, except for the treatment room door interlock:

Before the first clearance check run can be started, the ID of the patient must be verified. The following message is displayed:
`Confirm patient ID.`

11 Verify that the static patient information is identical with the actual patient.

12 On the manual control, press the **Accept** button to confirm the patient ID.

Note: *All buttons on the manual control require a dead man's switch to be activated, i.e. to simultaneously press a button on the underside of the manual control.*

After patient verification, the following message is displayed:
System ready for clearance check.

Aborting the clearance check run

Up to this point, it is possible to click **Cancel**, which returns to the Select Run page and allows you to select another run. Once the clearance check run has been started, the run can be aborted in the following way:

- To abort the clearance check run, press and hold down the **Reject** button on the manual control for 3 seconds. The following message is displayed:
  Clearance check aborted.
- To confirm the abortion, press the **Accept** button. When the couch has returned to the home position, the Select Run page is displayed.
  To cancel the abortion and return to the previous action during the run, press the **Reject** button.

When the abortion is confirmed, all clearance check positions already accepted or rejected will keep their status.

7.6.5 Executing the clearance check run

The clearance check run can now be started.

WARNING 7.5
During all movement of the couch during clearance check, make sure to keep the arm of the clearance check tool clear of the patient's head. Otherwise injury to the patient may result.

13 Press and hold down the **Continue** button on the manual control. The couch starts moving to the clearance check position and the following message is displayed:
Moving to clearance position.

When the position has been reached, a signal is heard and the following message is displayed:
Clearance position reached.

14 Release the **Continue** button.

If the **Continue** button is released before the position has been reached, the positioning is halted. To continue the positioning, press and hold down the **Continue** button again. It is also possible to abort the run.

The clearance check position should now be verified by using the clearance check tool.

15 Using one hand, carefully rotate the arm of the tool around the patient's head and the coordinate frame. Verify that the arm passes completely clear of the head and the coordinate frame during one complete revolution of the arm. If the arm comes into contact with any part during the revolution, the clearance check position must be rejected. Note that a rejected position means that the treatment cannot be started.

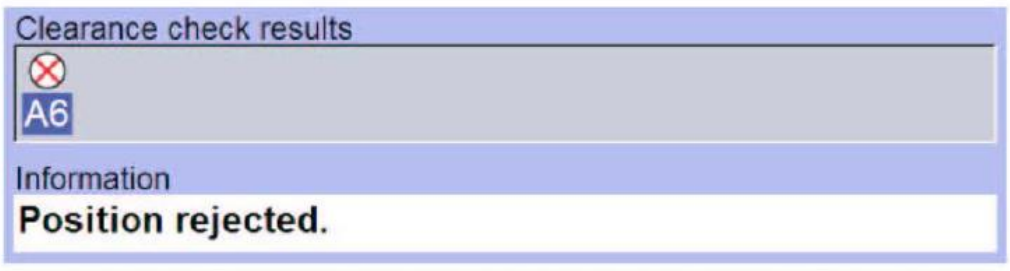
16 On the manual control, press the **Accept** or **Reject** button.

17 If the position was accepted, the shot identification is added to the clearance check results list with a pending (blinking) acceptance icon, and a message is displayed:

- To confirm the acceptance, press and hold down the **Continue** button. The couch moves to the next clearance check position in the run and the procedure is repeated from step 13. If there are no more positions in the run, continue with step 19.
- To cancel the acceptance, press the **Reject** button. The position can now be verified again.

WARNING 7.6
To accept a clearance check position without performing the verification procedure, or if the verification failed, may lead to contact with the collimator cap during treatment.

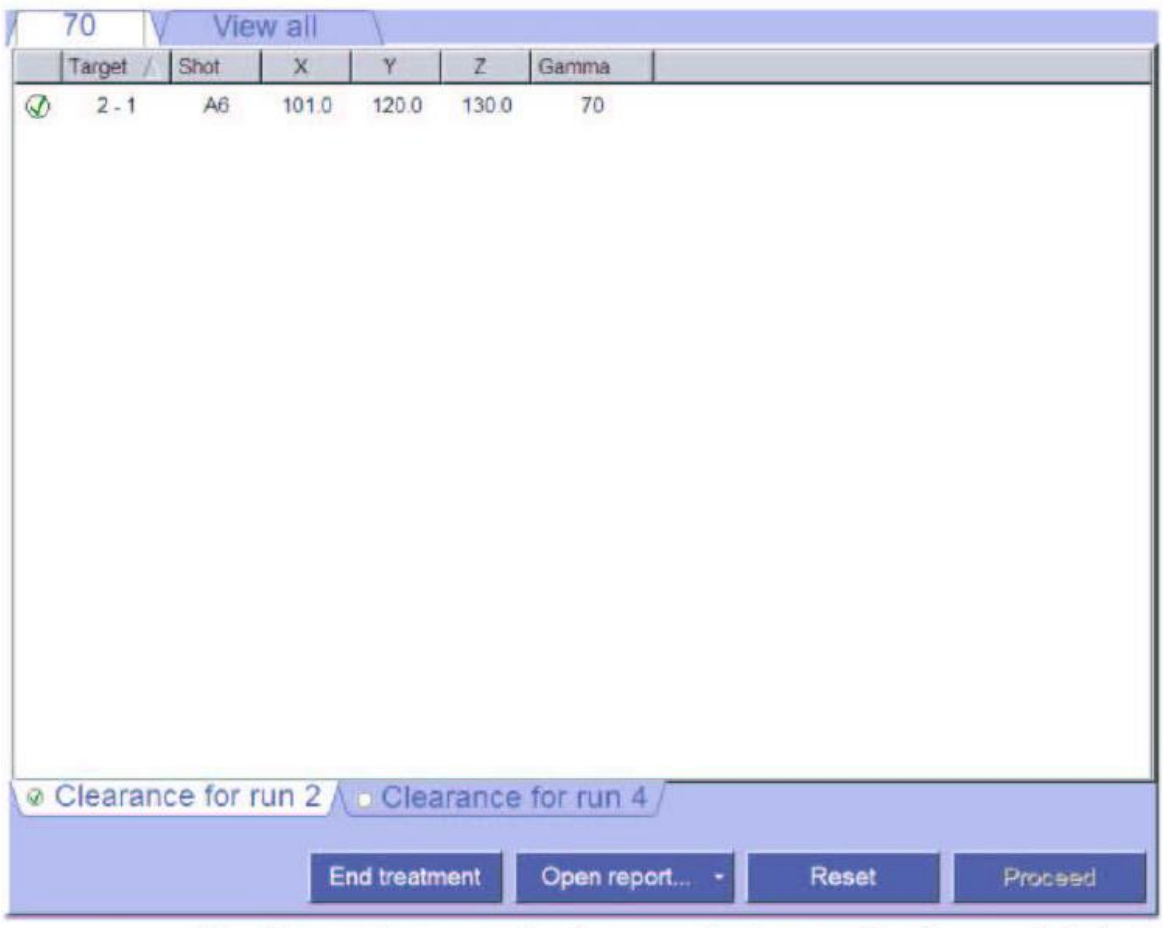
18 If the position was rejected, the shot identification is added to the clearance check results list with a pending (blinking) rejection icon, and a message is displayed:



- To confirm the rejection, press the **Accept** button. If there are more clearance check positions in the run, the procedure is repeated from step 13. If there are no more positions in the run, continue with step 19. Note that a rejected position means that the treatment cannot be started.
- To cancel the rejection, press the **Reject** button. The position can now be verified again.

19 When all clearance check positions in the run have been accepted or rejected, the couch is ready to move to the home position. Press and hold down the **Continue** button. The following message is displayed:
Moving to home position.

20 When the couch has reached the home position, the Select Run page is displayed again. The status of the clearance check verification is indicated in the list of shots, and in the tab title for the executed run.



21 If you wish to reset the clearance check status for **all** runs, click the **Reset** button on the Select Run page. A warning message is displayed, requesting you to confirm or cancel the status reset for all runs.

Note: *Resetting the status cannot be undone and will force you to redo all the clearance check runs that have been executed.*

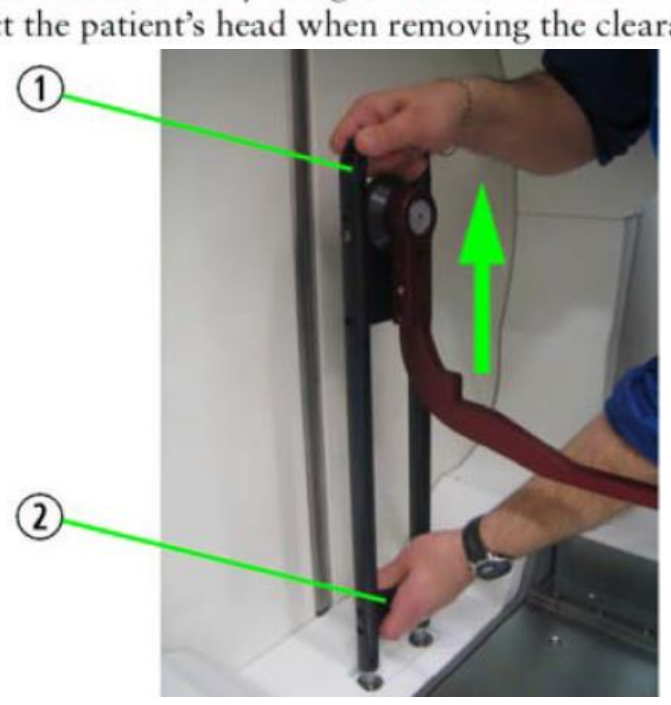
Completing the clearance checks

The clearance checks may call for several runs in more than one gamma angle. To complete the clearance checks, all runs must be executed:

22 Execute any remaining clearance check runs for the current gamma angle. On the Select Run page, check the lower row of tabs to see if there are any more runs that have not been completed for the current gamma angle. If so, select a new run and repeat the clearance check procedure from Section 7.6.5 on page 109.

23 Execute the clearance check runs for any remaining gamma angles. On the Select Run page, check the upper row of tabs to see if there are any more gamma angles that contain runs to be executed. If so, select a new gamma angle and dock the patient according to Section 7.6.7 below, and then repeat the procedure from Section 7.6.5 on page 109.

24 When all clearance check runs have been executed, carefully remove the clearance check tool from the head end of the patient couch. Hold and lift the clearance check tool by using the handle ① and the crossbar ②. Make sure to protect the patient's head when removing the clearance check tool.



25 Place the clearance check tool back in the tool cabinet.

26 If all clearance check positions were accepted, the treatment runs can now be executed. Select the **Treatment** tab and continue with the instructions in Section 7.7 on page 114.

Docking the patient in a new gamma angle

When changing gamma angles during a clearance check session, the patient needs to be undocked from the previous gamma angle and then docked in the new gamma angle. The patient may remain laying down on the couch during the redocking procedure.

1 On the Select Run page in the **Clearance** tab, select the tab for the new gamma angle you wish to execute the runs for.

2 In the lower row of tabs, click on the tab for the run you wish to perform next.

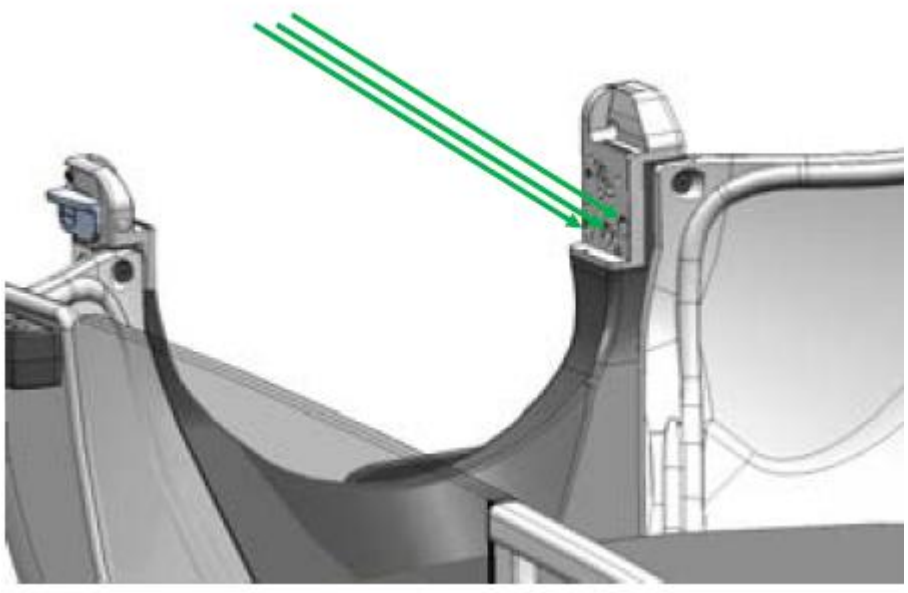
3 Click on the **Proceed** button.

You can perform the runs for a gamma angle in any order.

TRUNION (FRAME ADAPTER), GAMMA ANGLE

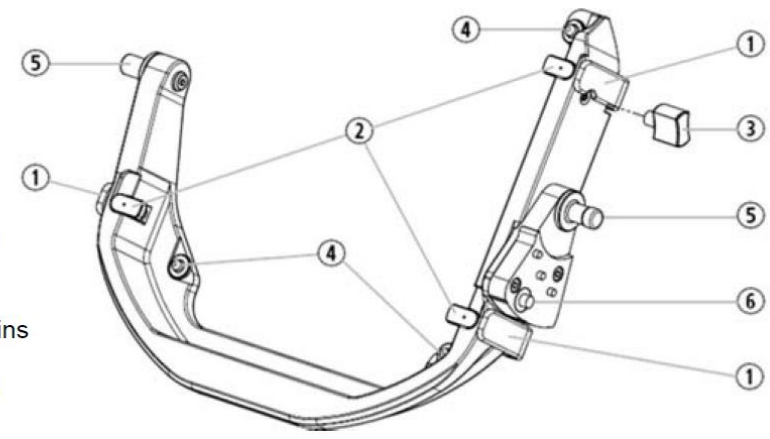
- **trunion** – frame adapter to table; it can engage frame in three positions (**gamma angles**):
  a) **90** degrees – default, neutral
  b) **70** degrees – only for (para)sellar tumors to protect optic apparatus
  c) **110** degrees – only if need to avoid collision

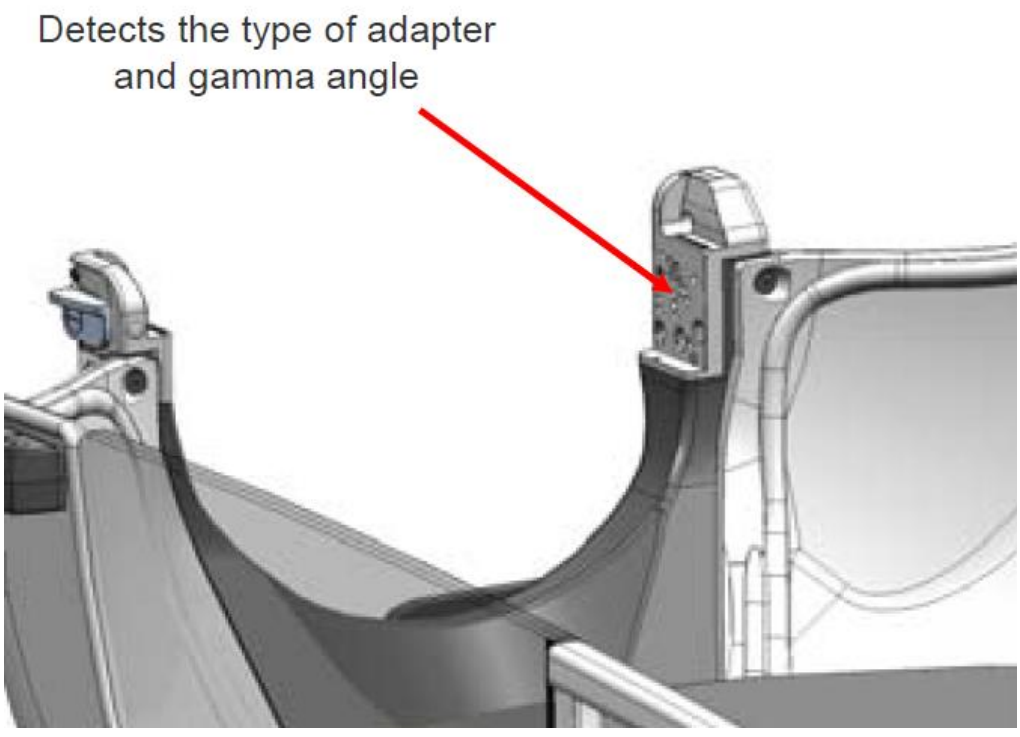
  N.B. gamma angles must be changed manually (adds 5 minutes)

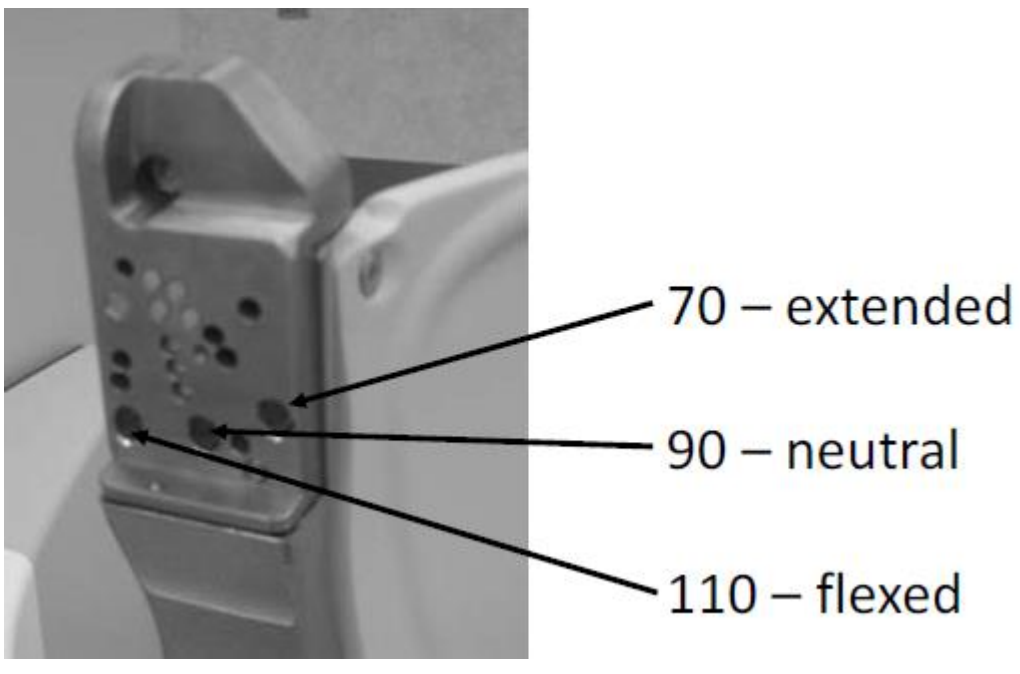


Frame adapter

The frame adapter is attached to the coordinate frame positioned on the patient's head. The frame adapter with patient is then docked to the docking device of the patient positioning system.







Locking Down Frame Adapter


EMERGENCY PROCEDURES

Priority – to extract the patient ASAP!

Control room has two buttons:
Pause – safely pauses the run, so patient can have a break.
Freeze (red button) – freezes everything and moves sources to home.

Activating the emergency stop

Use the **Emergency Stop** button whenever there is an urgent risk of injury to patient or operator, and the movement of the couch and shielding doors must be stopped immediately.

1 Press the **Emergency Stop** button ① on the control panel, or the optional emergency stop button in the treatment room.

Resetting an emergency stop

Resetting the emergency stop will initiate the Emergency Exit sequence (see Section 8.2.4 on page 129). Since this will start the movement of the couch and shielding doors again, make sure these movements are safe before resetting the emergency stop.

1 Reset the **Emergency Stop** button by turning it counter-clockwise as indicated by the arrows on the button.

2 The Emergency Exit sequence is initiated (see Section 8.2.4 on page 129).

When walking into room – notice colors of radiation warning lamp (not much can do about it, but will dictate the speed you move):
Green – shield door is closed (red – door is open)
White – sources in home position (if not, can move sources manually to home position from the back of machine)

Radiation warning lamp

A wall-mounted radiation warning lamp in the treatment room indicates the status of radiation and sectors.

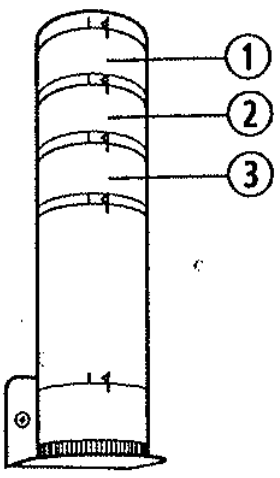


Figure 3.12 Radiation warning lamp

The three colored lamps indicate the following:

- Red ①: Radiation, that is, whenever the Beam off state is not reached (radiation beams activated). For more information, see the **Radiation** indicator on page 31.
- White ②: All sectors are locked in the sector home position.
- Green ③: Beam off (the same as the **Beam off** indicator on the control panel).
- The **Beam off** indicator ⑭ lits green when the shielding doors are closed and the radiation sectors are locked in sector home position (radiation beams deactivated). No direct radiation comes out in the treatment cavity.
- The **Radiation** indicator ⑮ lits or blinks yellow whenever the **Beam off** state is not reached (radiation beams activated). The indicator is continuously lit when the **Beam on** state is reached. The indicator blinks during transition between **Beam on** and **Beam off**, that is, during positioning, when the shielding doors are opening or closing, and when the radiation sectors are moving.

X lock (on the left side of patient table) – use only if patient is not centered left-to-right.
Z lock (at the end of patient table) – use to extract the patient.

Manual pull-out of the couch

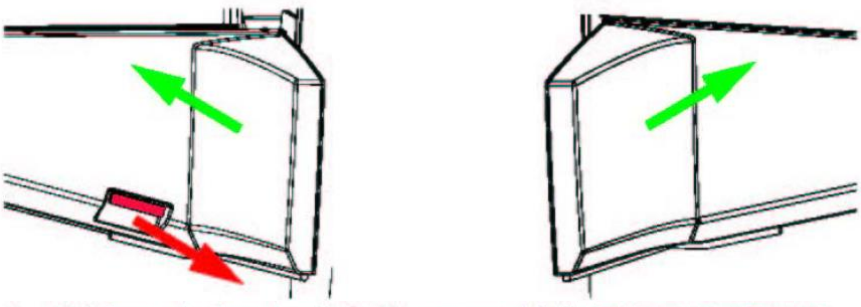
If the couch has not returned from the treatment position, or contact with the collimator cap has occurred, the patient must be withdrawn from the radiation unit as soon as possible by pulling out the couch by hand:

1 Enter the treatment room.

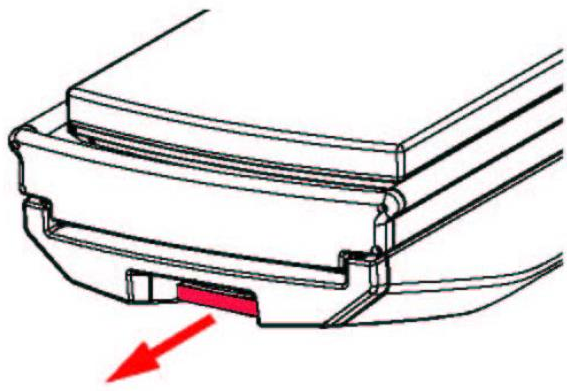
2 If contact with the collimator cap has occurred:

(a) On the left side of the couch, pull the couch release handle for X movement, labelled **EMERGENCY X-RELEASE**.

(b) Pull or push the couch slightly in the X direction towards the center position, so that any contact with the collimator cap is eliminated. Either pull the couch using the release handle, or push the couch by applying force to the lower part of the couch as indicated by the green arrows:



3 Pull the couch release handle for Z movement, labelled **EMERGENCY Z-RELEASE**.



4 Pull the couch out to the fully withdrawn position.

5 Release the patient from the couch.

6 Leave the treatment room together with the patient.

7 Push back the couch release handles into locking position (clutch engaged).

8 In the control room, acknowledge the error message. Let the system reset and execute the initialization sequence described in Section 5.2 on page 66.

9 If the shielding doors did not close during the initialization sequence, manually close the shielding doors as described in Section 8.6 on page 133.

10 Check if the radiation sectors have returned to the sector home position. This is the case if the white lamp on the wall-mounted radiation warning lamp is lit. If not, close the sectors manually as described in Section 8.7 on page 134.

If the couch cannot be pulled out by hand, follow the instructions in the next section.

Emergency undocking

If the couch cannot be pulled out manually, the patient must be undocked from the treatment position without withdrawal of the couch:

1 Go close to the right shielding door.

2 Unlock the frame adapter and release the patient from the docking position.

If the patient is positioned too far to the right, it may not be possible to unlock the frame adapter, since the lever on the docking device cannot be moved properly. In that case, do the following and try again:

(a) On the left side of the couch, pull the couch release handle for X movement, labelled **EMERGENCY X-RELEASE**.

(b) Pull or push the couch to the left, so that it becomes possible to unlock the frame adapter. Either pull the couch using the release handle, or push the couch by applying force to the lower part of the right side of the couch as indicated by the green arrow:

3 Release the patient from the couch.

4 Leave the treatment room together with the patient.

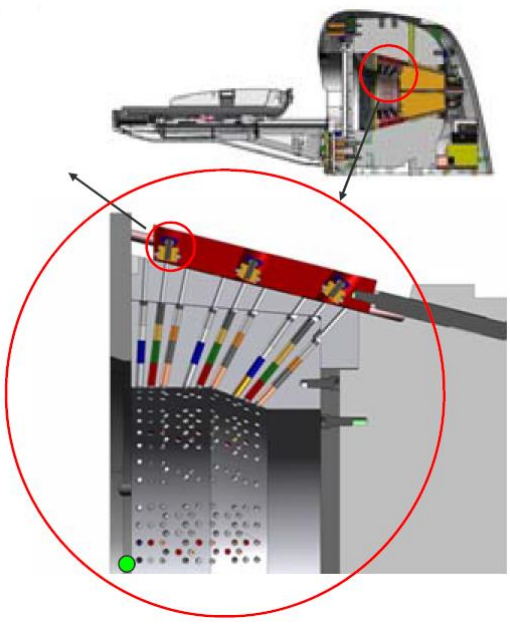
5 Check if the radiation sectors have returned to the sector home position. This is the case if the white lamp on the wall-mounted radiation warning lamp is lit. If not, close the sectors manually as described in Section 8.7 on page 134.

Safe State

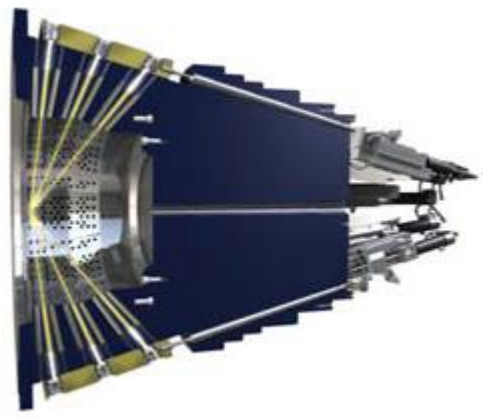
- there is no longer risk for the patient or personnel to become injured from the machine ***despite a non-working system***:
    - sectors are brought to Home position, the shielding doors are closed, i.e. the machine is at 'beam off' and it is safe to be in the room.
    - patient is taken out of the radiation unit and the bed is brought to the Out position.
- if the normal control system does not work, there is a fully electronically controlled safety system that takes over and that puts the system and patient to a safe state.
- if the safety system fails to operate as intended the operator shall go in to the treatment room and manually take the patient and system to a safe state.

COLLIMATORS, SECTORS (PERFEXION)

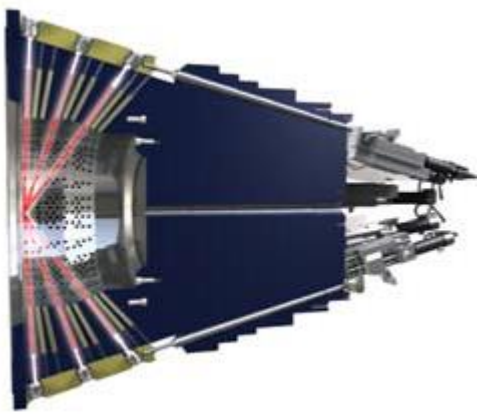
- collimator body made of tungsten.
- 8 independent sectors (24 collimators with 24 Co60 sources per sector).
- three sizes of collimators – 16 (green), 8 (red), 4 (yellow) mm
- by moving a sector, the corresponding set of sources is aligned with a specific size of collimator, thus achieving Beam On.
- beams focus on at point on central axis.
- ~1 second to change beam configuration.
- 5 different sector positions (listed from back to front)
    a) Home (back most)
    b) 8 mm
    c) Sector Off (BLOCKED)
    d) 4 mm
    e) 16 mm (front most)



Sectors and sources are aligned with the 4 mm collimators, resulting in a 4 mm shot:



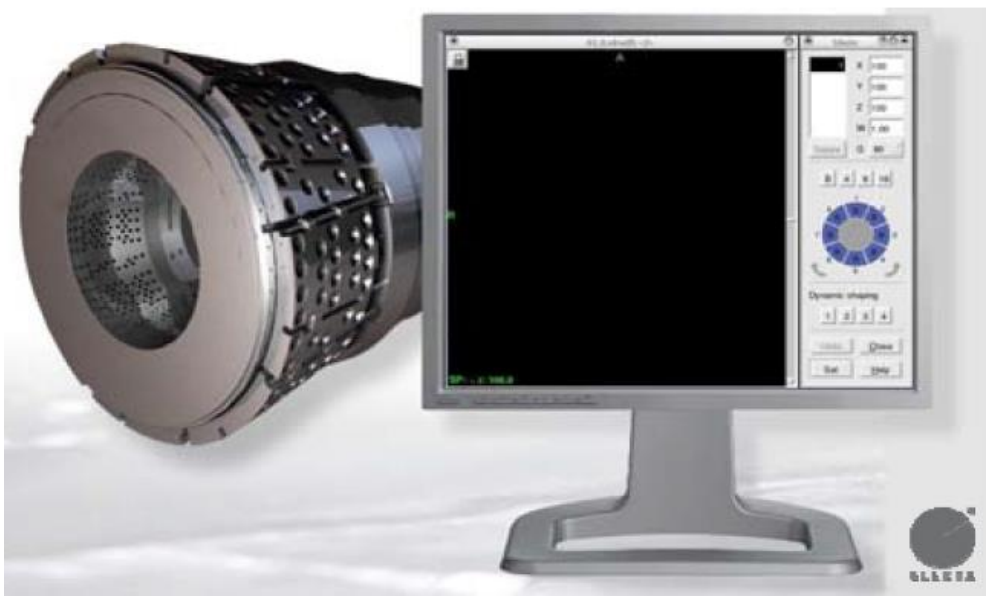
Sources aligned with the 16 mm collimators:



DOSING

- one ***beam on*** time with one isocenter is called **shot**
    - shots with all collimators of same size are called **classic** shots; shots combining different collimators are called **composite** shots; some collimators can be completely blocked to increase conformality but sector blocking increases treatment time (less source is available to deliver the dose).
    - unlimited number of shots – excellent conformality.
    - **run** – all shots with same gamma angle (so theoretically maximum 3 runs per patient).

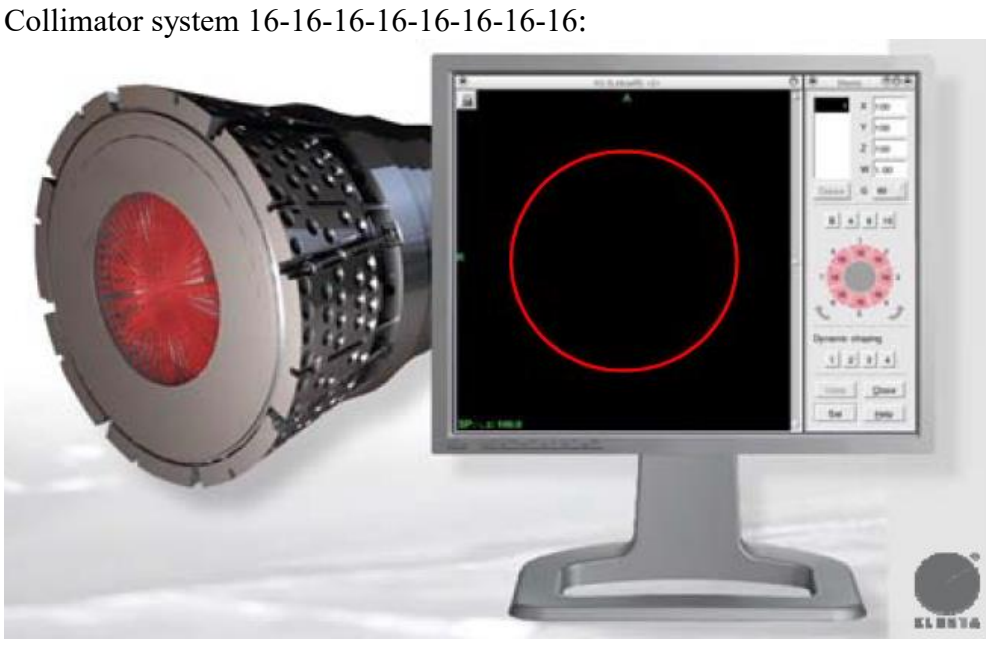
Collimator system 0-0-0-0-0-0-0-0:



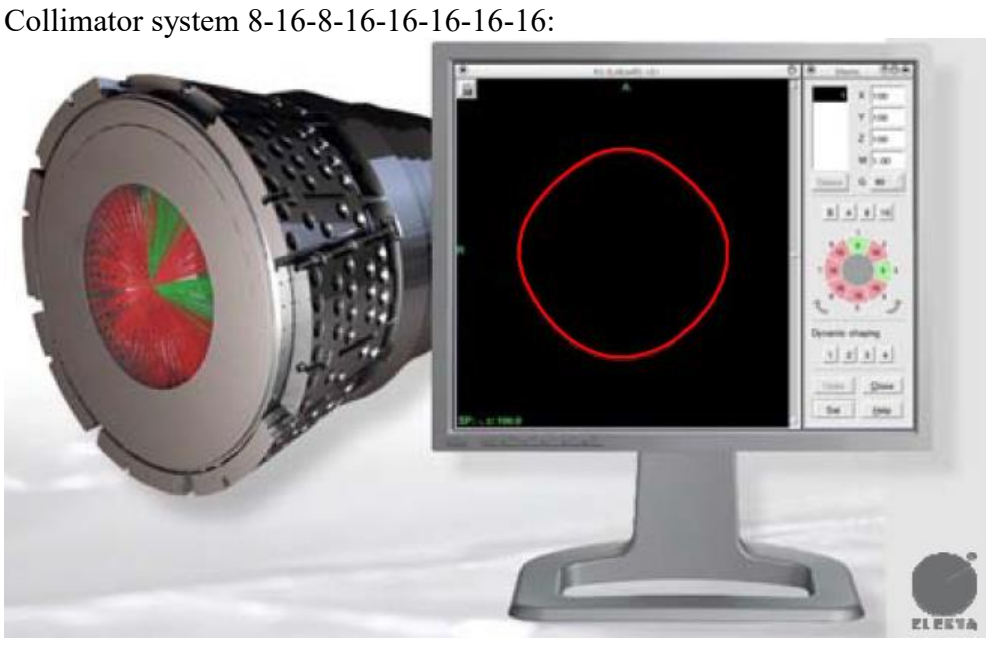
Collimator system 4-4-4-4-4-4-4-4:

Collimator system 8-8-8-8-8-8-8-8:

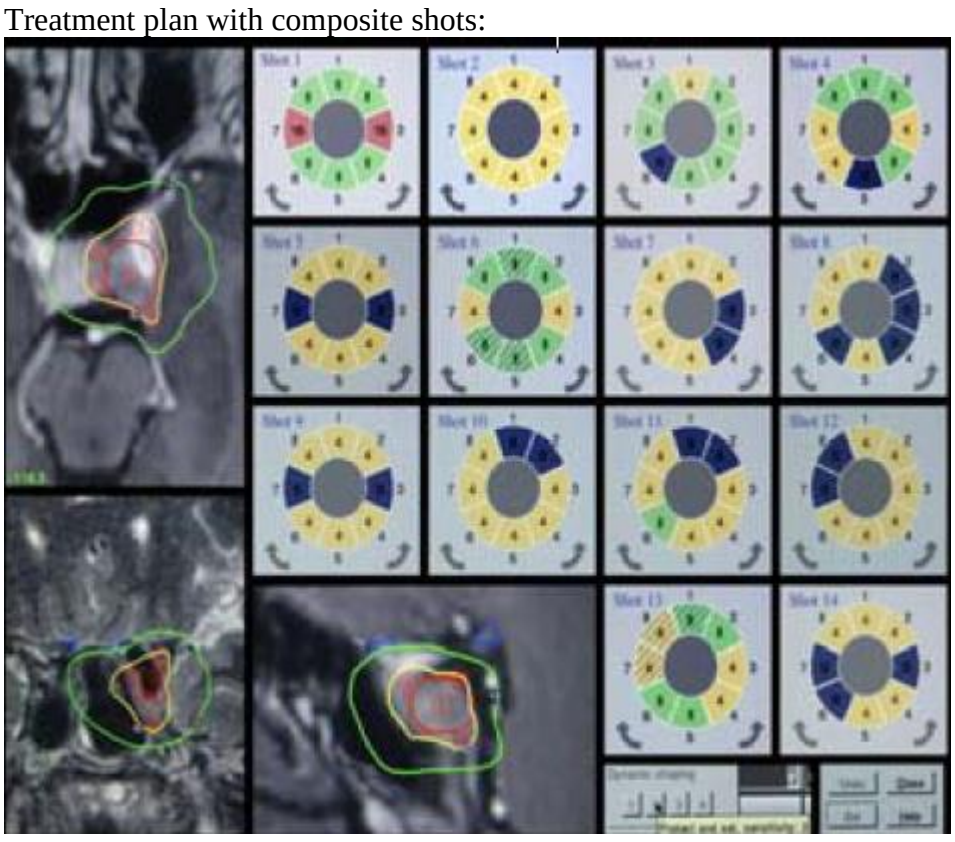
Collimator system 16-16-16-16-16-16-16-16:



Collimator system 8-16-8-16-16-16-16-16:



Treatment plan with composite shots:



DYNAMIC SHAPING

– method to preserve critical structures (first have to segment such structure on imaging)

- five levels from 0 (no dynamic shaping) to 4 (maximum dynamic shaping).
  - choosing level 0 undoes dynamic shaping for shots that are selected
- how to preserve target coverage:
  - limit level of dynamic shaping
  - apply to only some of shots
  - limit size of risk structure – create virtual 'shield'

LEKSELL GAMMAPLAN® PFX™

PLAN QUALITY METRICS

- coverage of the target – 99-100% (lower quality plan – coverage ≥ 95%).
- GTV = CTV = PTV (usually no or very small margins) about volumes – *see above* >>

Conformality ratio (ability to conform dose to the target) =
= entire volume getting the prescribed dose / target volume getting the prescribed dose

Has to be ≤ 2 (except for very small targets); for perfect plan, ≤ 1.5

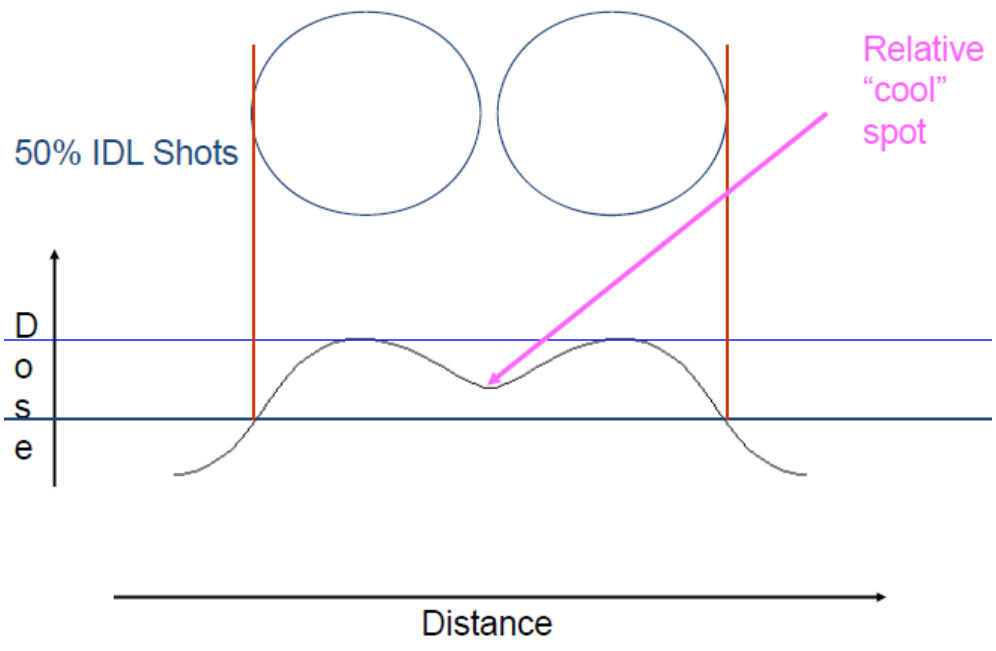
Inhomogeneity ratio IR = maximum dose MD / the prescribed dose PD

Dose Homogeneity – the consistency of dose within the treated volume

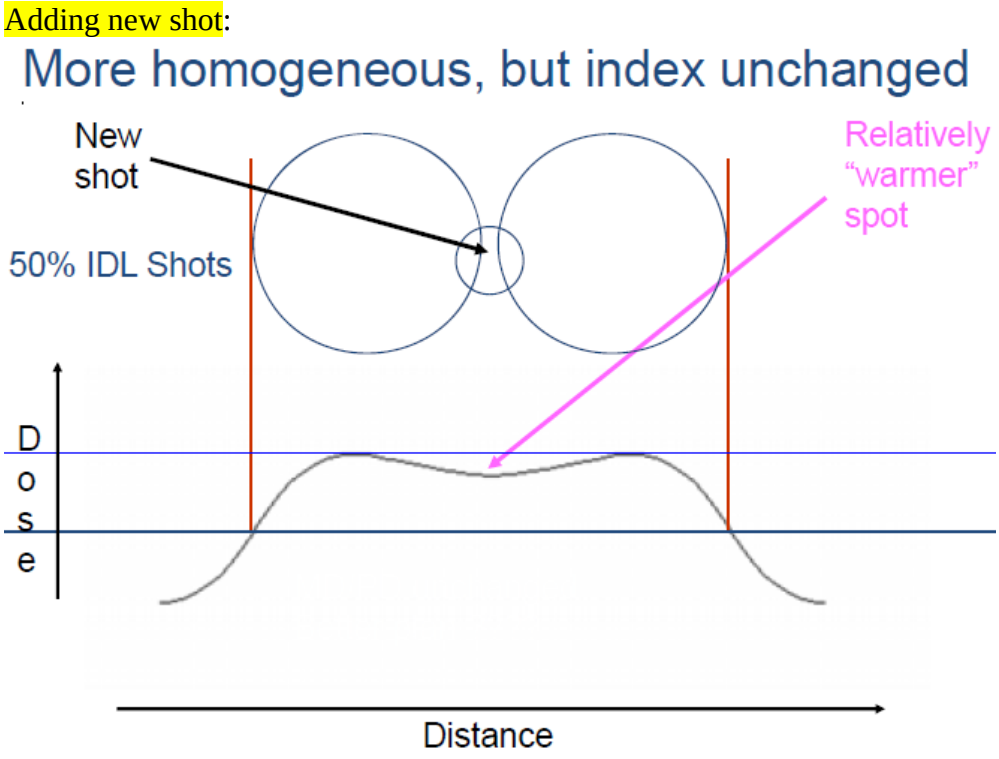
- IR has to be ≤ 2
- MD/PD = 100% IDL / 50% IDL = 2.0 ← don't prescribe to < 50% IDL

How to Achieve Conformal Therapy – match size, shape, location of dose to target:

1) multiple isocenters (shots)
2) multiple locations
3) various sizes
4) various intensities (weighting)
5) various shapes (composite shot)
6) various tilts (gammas)



Adding new shot:



Hot Spot

- if treating to 50% IDL there will be a hot spot receiving twice that dose - where to put it? (risk of necrosis, risk of injury to vital structure)

Keep it in the target – not in normal brain!

- avoid cranial nerves: internal auditory canal, surface (esp. medial) of vestibular schwannoma, lateral wall of cavernous sinus.
- avoid arteries: carotid in cavernous sinus.

Gradient (Paddick) index = prescription isodose volume / half of prescription isodose volume
Keep ≤ 3.0 (difficult for small targets, or when using high isodose lines)

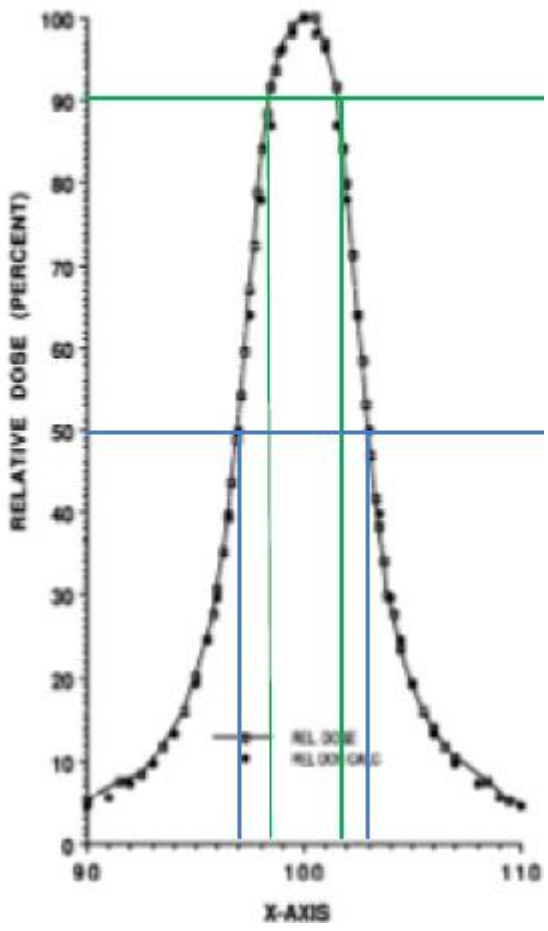
- rationale – which volume is more responsible for the late complications – prescription isodose volume or half of the prescription isodose volume which partially covers healthy tissue?
- it's a simple measure of the individual plan dose gradient.

HOW TO INCREASE EFFICIENCY

1. Fewest Gamma Angles
2. Limit blank sectors (every sector blocking increases treatment [beam on] time by 1/8)
3. Treat to higher isodose lines

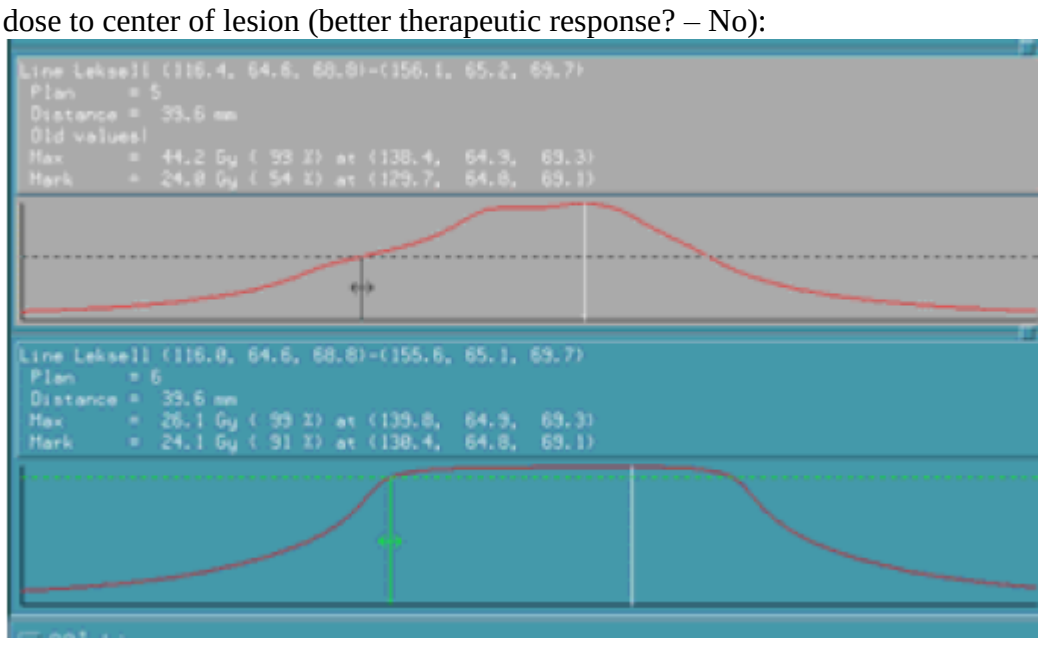
SHOT STRATEGY

- maximize size of shot – see *INVERSE PLANNING* >>
  - treatment plan with many small shots will have better conformity but will result in a long beam-on time, compared to a plan with few large shots.
- do not prescribe to < 50% IDL (increases risk of adverse radiation event)
- prescribe to 50-60% isodose line:
  - steep dose falloff:



— higher dose to center of lesion (better therapeutic response? – No):

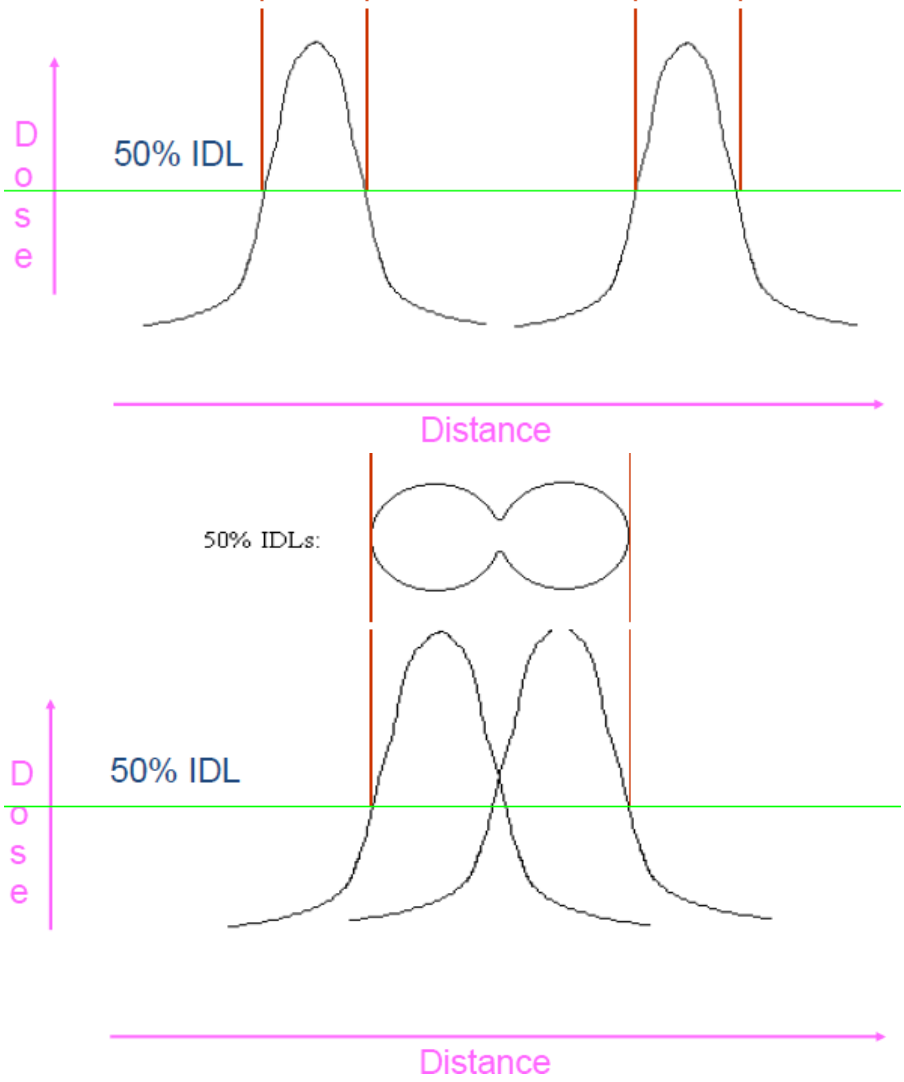
52%



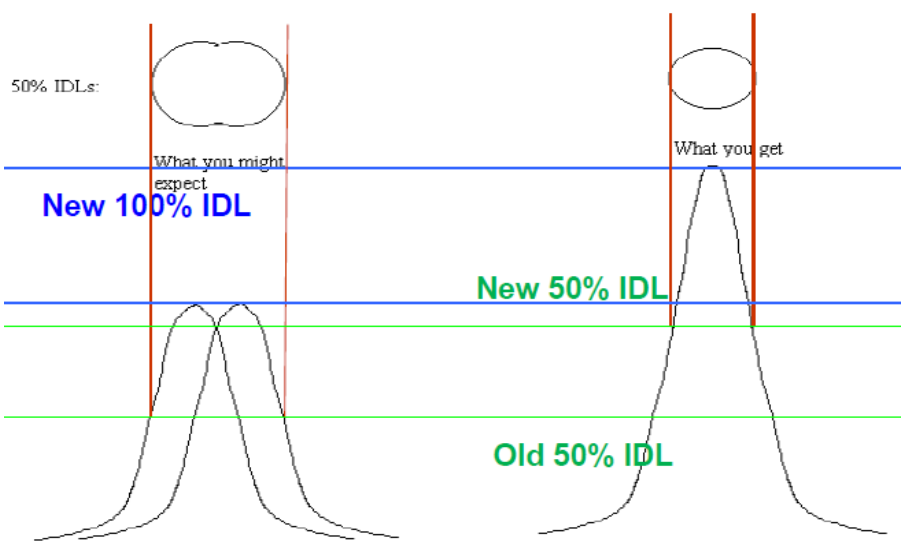
91%

— almost double the time to treat.

<u>Effects of Normalization on multiple shots</u>



Normalized to 100% IDL



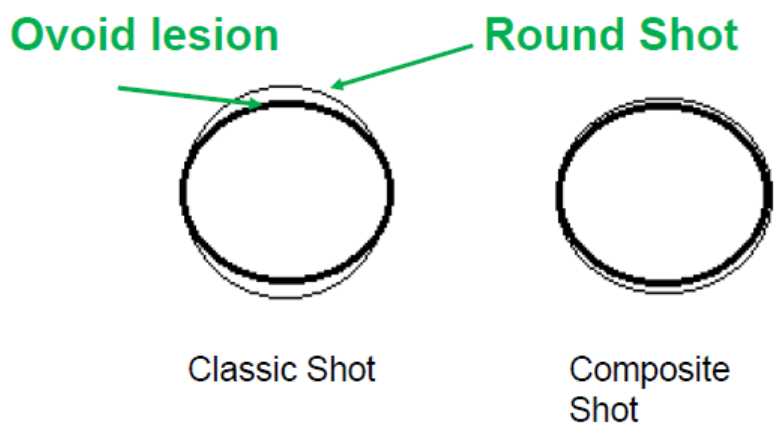
Multiple shots do not "add" together, but interact due to renormalization!

How to minimize this?:

1) ***add new shots at low weight*** and gradually increase until satisfactory coverage, or overall treatment IDL starts to shrink
2) ***monitor a high IDL*** (e.g. 90% IDL)

SHOT SHAPING STRATEGIES

Shaping with composite shots



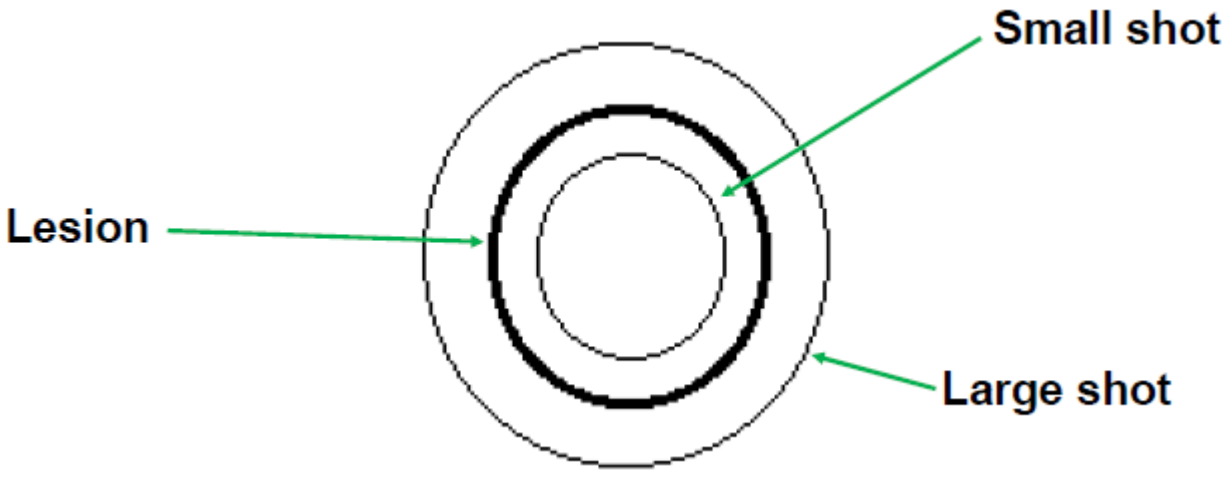
- principal effect of composite shot is in transverse plane!
- composite shots may improve conformality, but may extend treatment time – especially if blank sectors.
- use smaller shots near critical structures – steeper falloff.

Using Blank Sectors

- reshape IDL to better match target.
- protect vital structures (limit beams passing through, tighten IDLs near it).
- shaping effects most pronounced on lower IDLs or large shots.
- decreases overall drop-off.
- extends treatment time.

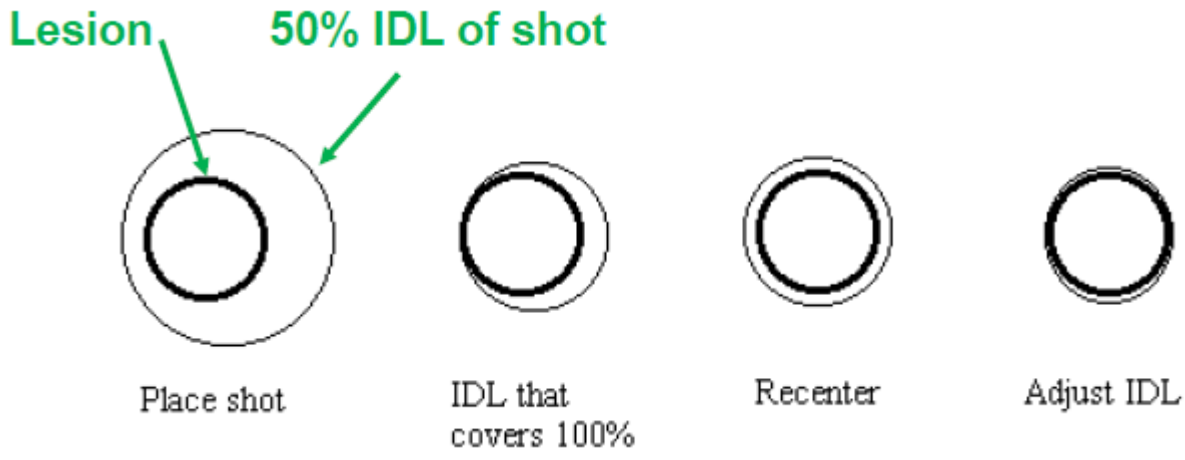
Small [< 16 mm] spherical lesions

Traditional Approach:

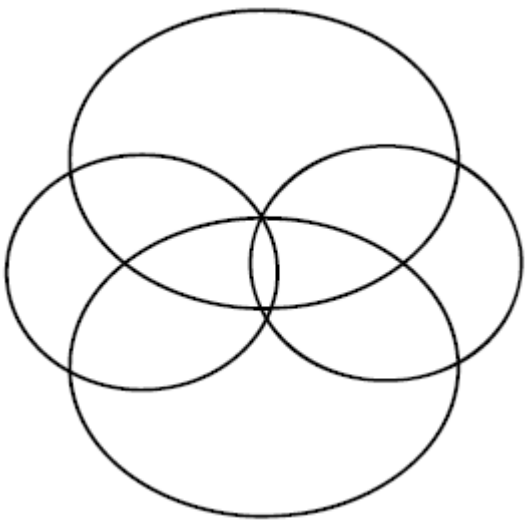


Adjust relative weighting so that 50-60% IDL just covers target

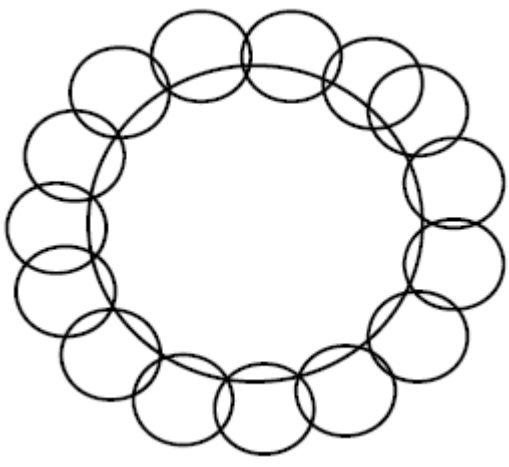
Contemporary approach:



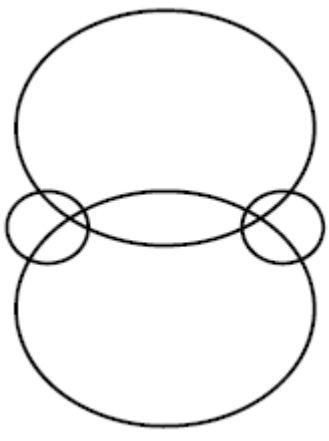
Large [> 16 mm] spherical lesions



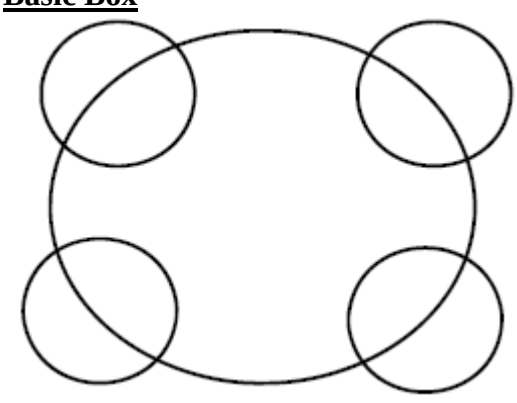
Poor way to make large sphere:



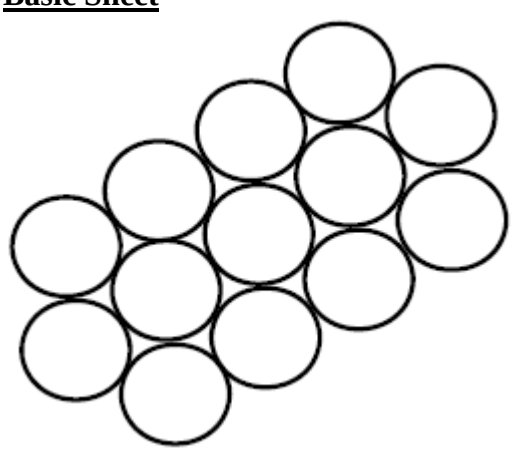
Basic cylinder



Basic Box

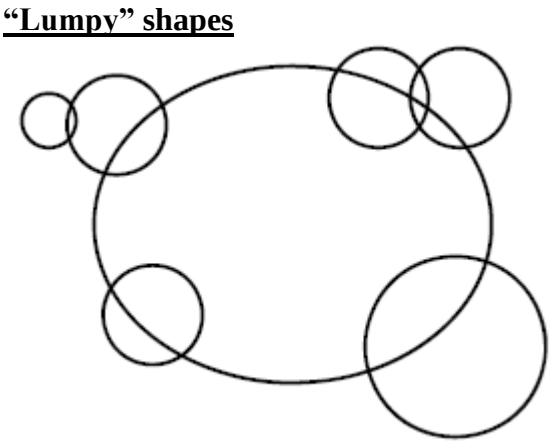


Basic Sheet

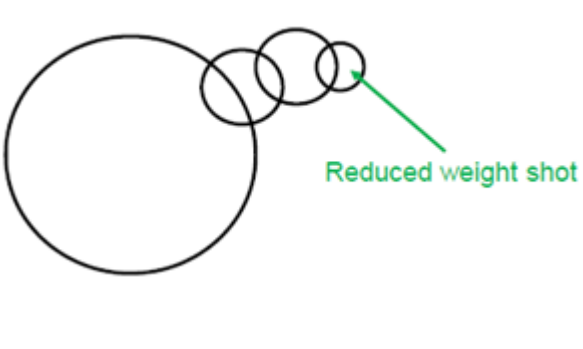


N.B. may be able to craft sheet with composite shot (six sectors blank - takes much longer to treat)!

"Lumpy" shapes



Acoustic neuroma



Cystic lesions (e.g. large cystic metastatic brain tumors) - use "donut's shape" dose planning with coverage of the contrast-enhancing tumor capsule by multiple small-sized isocenters.

WORKFLOW

I. Create patient file: **Patient** → **Patient Management** → **New** → Fill in demographic data selecting **Treatment** as type

II. Import images: **Patient** → **Import DICOM** → **Select pt name** → **Select date / time of study** → **Select series** → **Import**

III. Define images: Click on image icon with ? → **Define** → Place red markers on fiducials → **Define** → **Accept** definition result → **Accept** original view, coronal view, sagittal view → Open images → **Workspace** → **Standard**

IV. Outline tumor / structures (Optional. Can be done any time forward of here)

- Center target in window using crosshairs
- If necessary, magnify images depressing and dragging right mouse button

Tools → **Volumes** → **New:** Enter name

Draw

a) Manual
b) Semi-automatic: re-select workspace, click semiautomatic checkbox, use slider to select tumor in red, click and drag in image

Edit

- Select Volume Type **Target**
- Select Color

V. Enter frame data: **Plan** → **Frame definition** → Select **Frame cap fits** (PFX only / if it does fit) → Select **Use measurements** (optional for PFX) - enter measurements

VI. Enter skull data: **Plan** → **Skull definition**

Images or **Measurements**

Images (only if you have a whole head CT): **Select "**whole head CT study" → **Run** → **Approve**

Measurements: Enter bubble data → **Plot** → **Accept**

VII. Set up plan: **Plan** → **New Plan, c**omplete dialogue box selections → **Ok**

VIII. Set up a target: **Plan** → **Target** → **New**

If volume drawn and type target selected: **Enclose volume** → Select target volume
If volume not drawn and labelled as target: Enter name → Click on target to center grid → Use grid size slide bar to size grid

IX. Place shots: **Plan** → **Shot:** Place and adjust shots → **Close**

X. Check Clearance: **Tools** → **Clearance** → **Close**

XI. Prescribe dose: **Plan** → **Target** → **Set Dose:** Enter prescription → **OK**

XII. Check histograms / dose measurements: Select 1/1 or Sum → **Tools:**

Measure: Select 1/1 or sum
Histogram: Select object / target → Scroll on graph to desired margin or dose

XIII. Approve plan: **Plan** → **Approve** → Enter Treatment Date → **Approve**

XIV. Print: **Patient** → **Print** → **Print** → **Close**

XV. Export: **Patient** → **Export protocol** → **Export** → **OK**

COREGISTRATION MODULE

I Select coregistration from image icon menu
II Select dataset to be used as reference from drop down menu
III Manually adjust images
    Use control key and left mouse button to move orthogonally
    Use control key and right mouse button to rotate in any view
IV Automatically match mutual points
    Select Run
V Check match between datasets
    Select display "XX" inside lens
    Enlarge lens using right mouse key inside of lens
    Examine images in all planes and at multiple levels
VI Accept the coregistration results
    Select Verify
    Accept each orientation

RETREATMENT MODULE

Pre-planning

I. Create patient file: **Patient** → **Patient Management** → **New:** Fill in demographic data selecting Pre-planning as type → **OK**

II. Import images: **Patient** → **Import Images** → **Select pt name** → **Select date / time of study** → **Select series** → **Import**: answer all dialogue boxes → **Close**

III. Apply virtual frame: Click and hold over image icon with ? → **Pre-plan Reference**

IV. Accept virtual skull: **Plan** → **Skull** → **Plot** → **Accept** → Open Images
- **Workspace**
- **Standard**

V. Outline tumor / structures (Optional. Can be done any time forward of here): **Tools** → **Volumes** → **New:** Enter name → **OK**
Draw
    Manual
    Semi-automatic: re-select workspace, click semiautomatic checkbox, use slider to select tumor in red, click and drag in image
Close

VI. Set up a target: **Plan** → **Target** → **New:** Enter a name, Position the grid, Adjust grid size → **OK**

VII. Place shots: **Plan** → **Shot**: place and adjust shots → **Close**

IX. Prescribe dose: **Plan** → **Target** → **Set Dose:** Enter prescription → **OK**

X. Check histograms / dose measurements: Select 1/1 or sum → **Tools** → **Measure** → **Histogram** → Select object / target → **Close**

XI. Exit patient file until ready to treat

XII. Select patient file: **Patient** → **Patient Management** → Click on patient name in database → **New** → **New Examination for selected patient:** verify demographic data, selecting **Treatment** as type and identify operator → **OK**

XIII. Import images as described in step II

XIV. Define images as described in step III

XV. Enter skull data as described in step V

XVI. Enter frame data as described in step VI

XVII. Import pre-plan: **Patient** → **Import Examination:** select appropriate examination from list → **OK**
Perform co-registration:
- Automatic: select **RUN**
- Manual: use **CTRL** and left or right mouse to adjust position of selected study in relation to reference study then **RUN**
- Examine studies using lens: **Lens – xx inside** → Drag lens around images

Verify → **Accept** each orientation → **OK**

Retreatment

XVIII. Select patient file: **Patient** → **Patient Management:** Click on patient name in database → **New** → **New Examination for selected patient:** Verify demographic data, selecting **Treatment** as type and identify operator → **OK**

XIX. Import images as described in step II

XX Define images as described in step III

XXI. Enter skull data as described in step V

XXII. Enter frame data as described in step VI

XXIII. Import previous treatment plan: **Patient** → **Import Examination:** Select appropriate examination from list → **OK**
Perform co-registration
- Automatic: select **RUN**
- Manual: use **CTRL** and left or middle mouse to adjust position of selected study in relation to reference study then **RUN**

Examine studies using lens → **Verify** → **Accept** each orientation.

XXIV. View previous treatment margins: View images - Treatment margins from previous treatment will be displayed as volumes shown as thick blue lines.

XXV. Proceed with planning as usual.

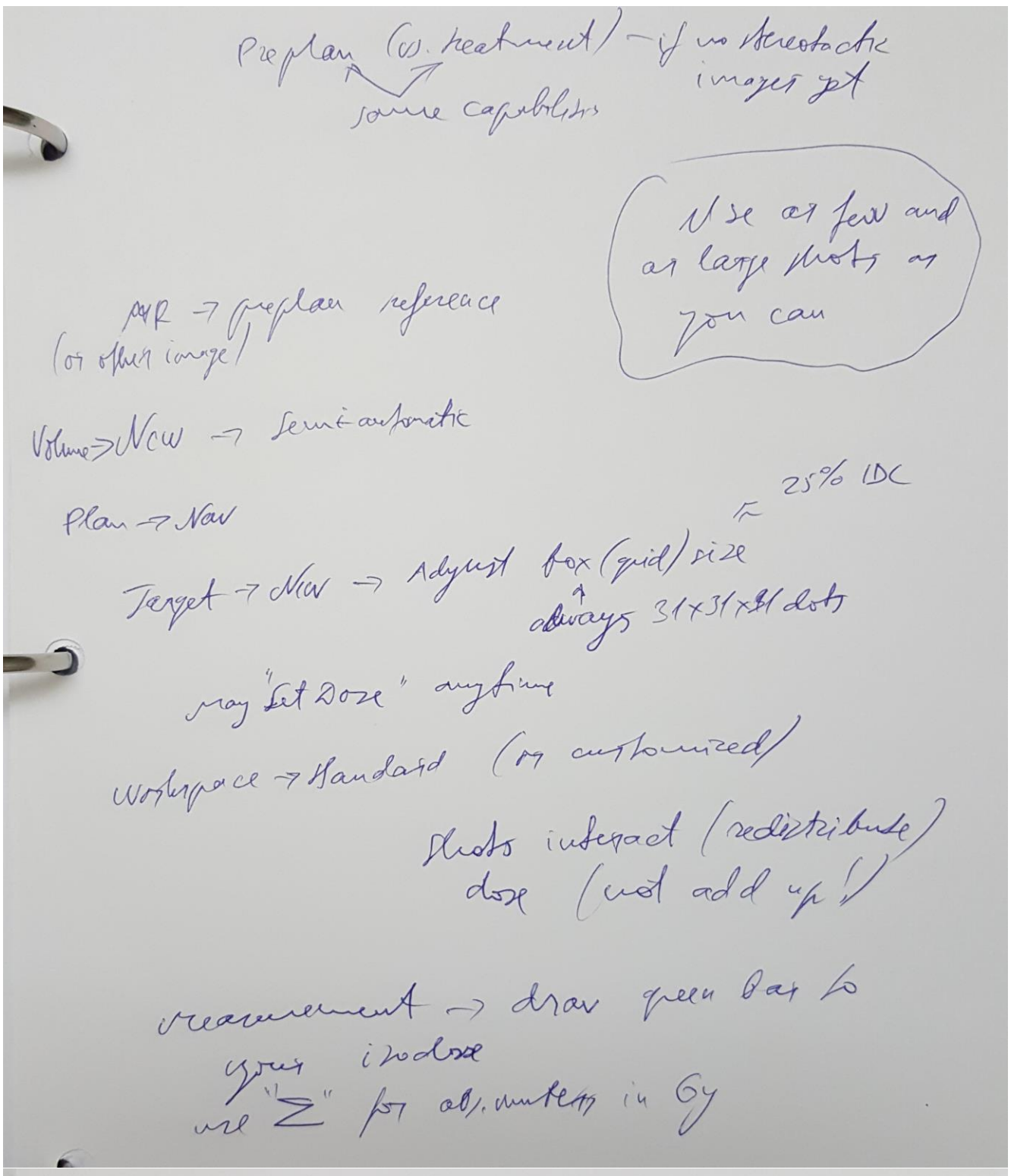
Follow Up

XXVI. Select patient file: **Patient** → **Patient Management:** Click on patient name in database → **New** → **New Examination for selected patient:** Verify demographic data, selecting **Follow-up** as type and identify operator → **OK**

XXVII. Import previous examination: Select exam to be followed up from the list

XXVIII. Import images as described in step II

XXIV. Co-register images as described in step XVII bullet point 4

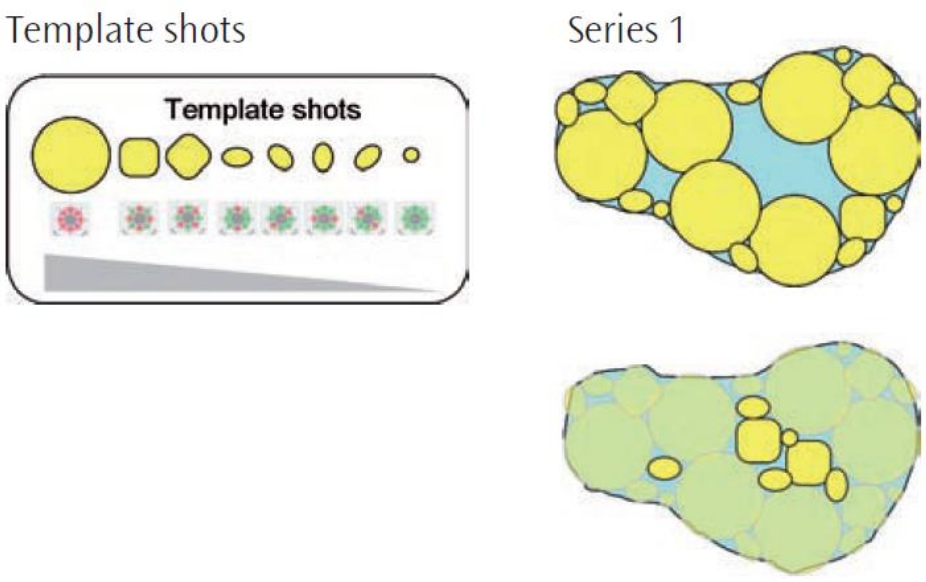


INVERSE PLANNING

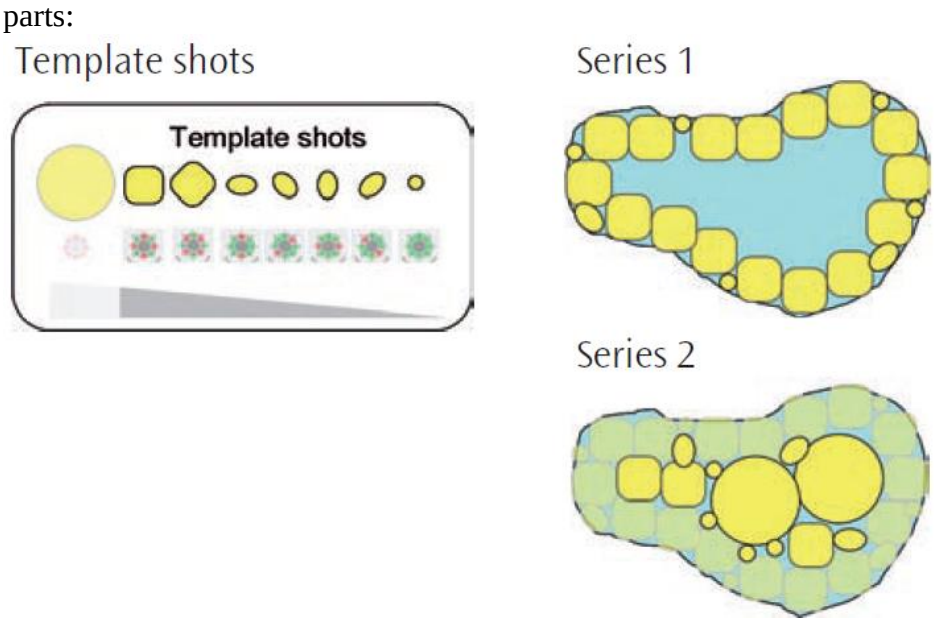
- intrinsically more automatic than forward planning.
- may manually add or remove shots in the same manner as in the forward process.

Fill step - main purpose is to automatically create a starting point for the optimization process

- after the target has been outlined a fill algorithm will place shots within the target volume based on geometrical criteria - this is a packing method, but in contrast to most volume filling algorithms the shots are not described as spheres. Instead, the algorithm determines the shape at the planning isodose level of a number of shots with a selection of collimator set-ups. These "template shots" are then placed in the target to fill the volume in an ingenious manner. The filling process will add a number of shots to the plan giving a reasonable start to the optimization.
- use ***as large shots as possible*** and place shots in positions where the selected isodose touches the target volume periphery, without overlapping other shots too much.
- when no more such shot positions exist even for the smallest shot, the volume covered so far is treated as non-target, and the procedure is repeated with the reduced target volume, starting over with the largest shots - thus, the target is filled from the surface and inwards, trying to place as large shots as possible:



- the user can ***restrict the usage of the largest shots in the first series***, where shots are placed at the target periphery - conformity is expected to depend most on the shots close to the target surface, and to avoid an explosion of the number of shots as few shots as possible are used in the central parts:

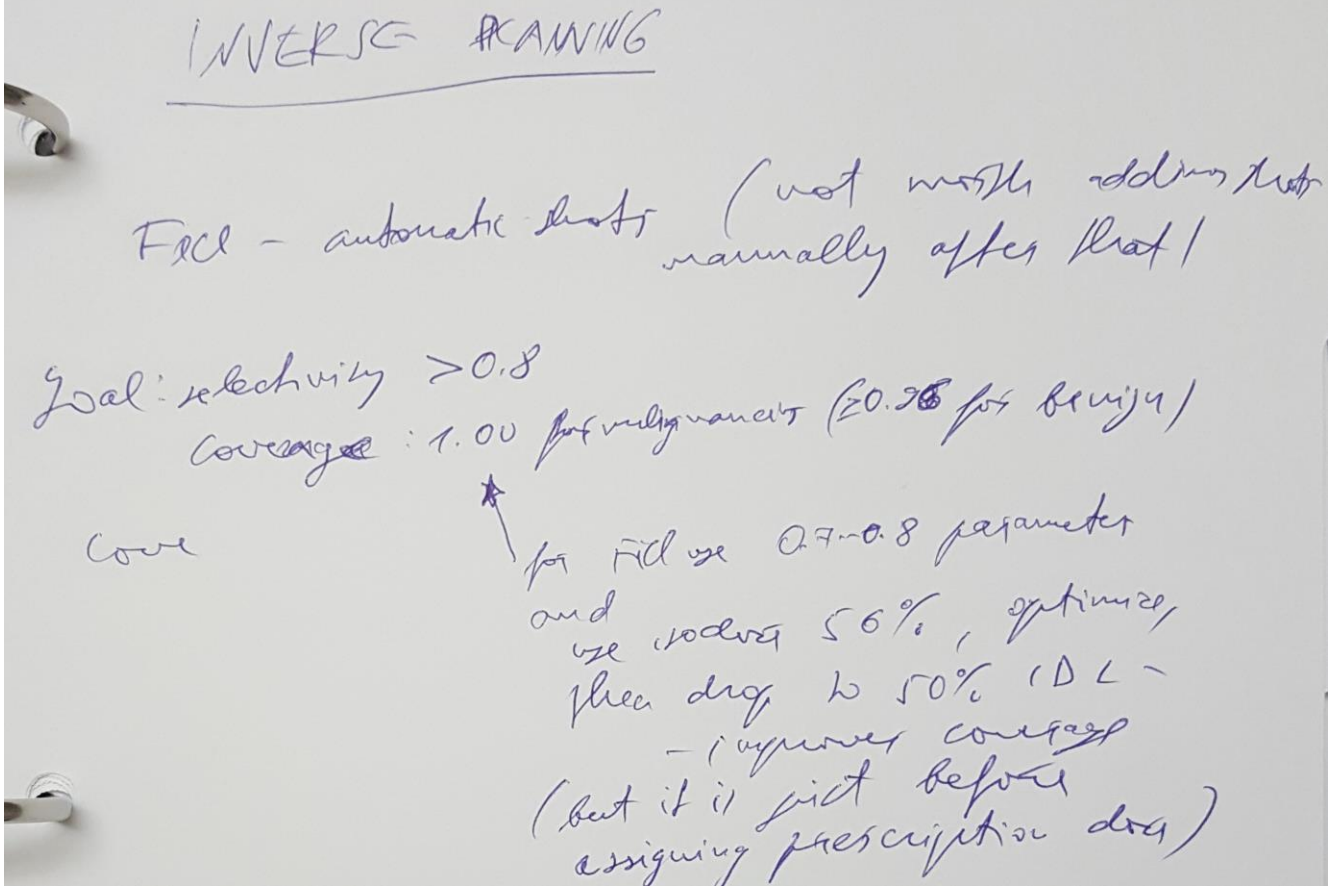


Algorithm:

1) For SHAPE in shot template shapes in decreasing volume
   Iterate over all voxels inside the target volume
   If SHAPE 'touches' the target volume surface AND SHAPE overlaps with existing shots with at most Y % Accept current position
2) Remove the volume covered by existing shots from the target volume and repeat from 1).

Optimization step - does not change the number of shots in the treatment plan (so it is important to start with a reasonable number of shots, which will depend on the selected isodose level, the target volume size and shape, and the requirements on the dose distribution such as fall-off, homogeneity and treatment time).

Postoptimization step - address organs at risk - dynamic shaping and manual blocking of shots close to the structure.



CONVOLUTION

(s. heterogeneity correction) – corrects beam doses by tissue electron density; i.e. much more reflects reality (vs. **TMR10** – default simple water volume normalization) – on average it is 7% difference.

Convolution is an optional software module - enables accurate dose calculation for the treatment of heterogeneous tissue – such as tissue-air and tissue-bone interfaces – to facilitate rapid generation of dose plans for these tissues.

- convolution provides dose calculation accuracy that approaches the quality of the Monte Carlo algorithm.
- users can choose TMR (tissue-maximum ratio) or Convolution depending on target localization.

PATIENT FLOW

Traditional	Perfexion	PFX – Co-reg	PFX - Multiday
			MRI
		MRI	Preplan
Frame	Frame	Frame	Frame
CT	CT	CT	CT
MRI	MRI	Coreg/Finalize	Coreg/Finalize
Plan	Plan	Treat	Treat
Treat / Multiple Interventions	Treat		

PREOP

- NPO after midnight preop
- urine HCG on all menstruating females ≥ 12 y/o
- Cleveland Clinic gives 10 mg of DEXAMETHASONE before treatment.
- MIDAZOLAM for anxious patients.

POSTOP

Discharge Instructions >>

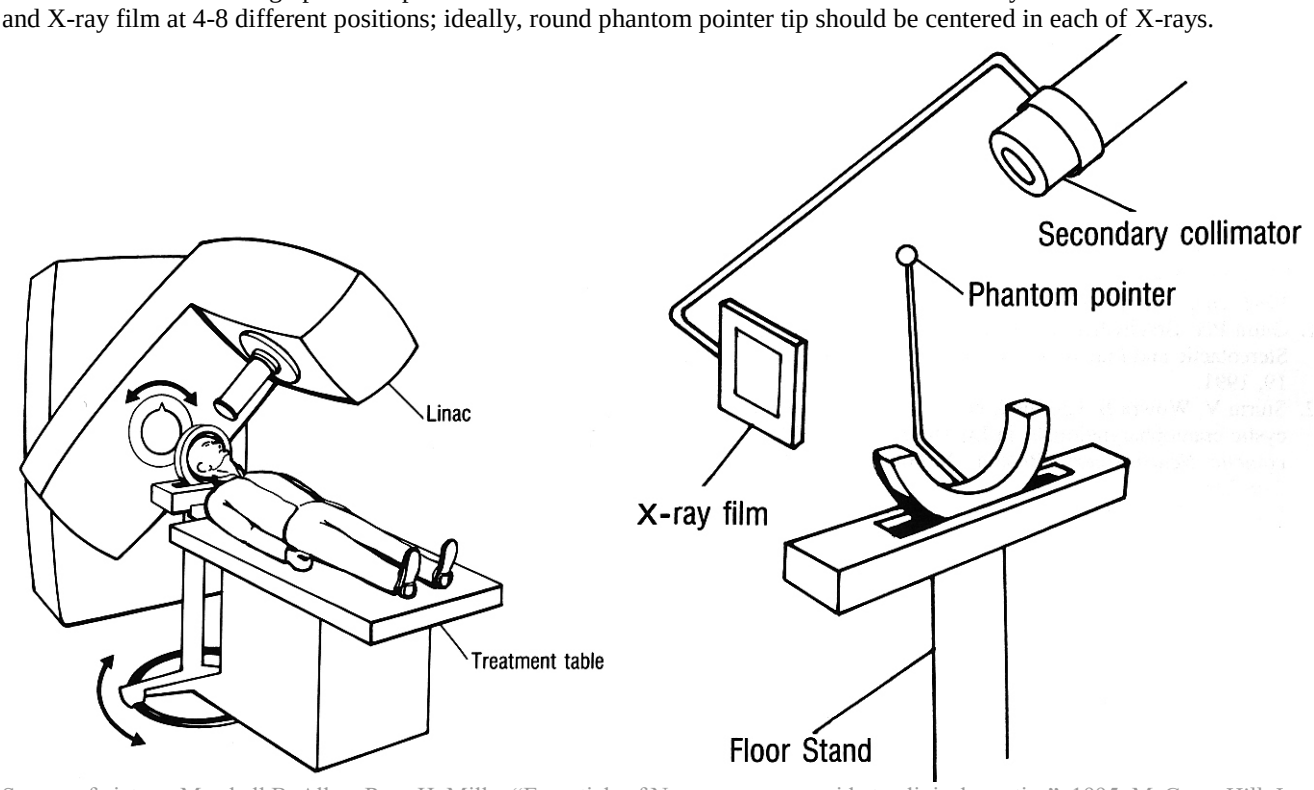
- patients are observed for a few hours in the same day surgery unit and are discharged within 24 hours.
- adult drive/accompany patient home.

PLATFORMS – B. X-RAYS (LINAC)

- modified linear accelerators [LINACs] (rotational high-energy X-ray photon beam) – mechanical accuracy comparable to gamma knife.

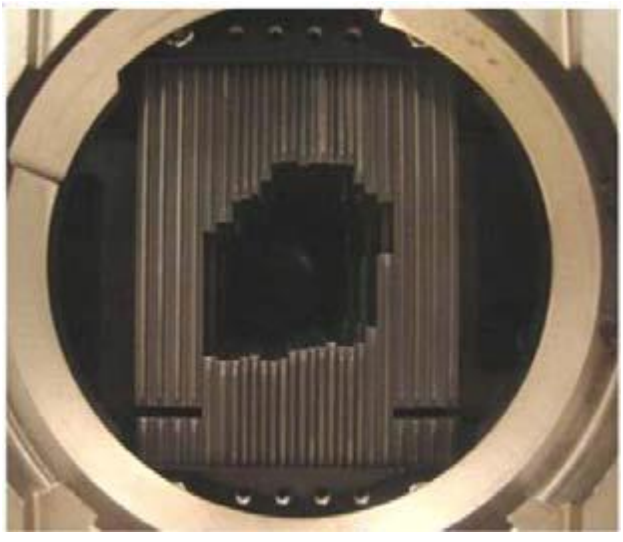
- LINAC emits spectrum of photons (so unit is MV, not MeV) in circular or dynamically shaped beams in multiple non-coplanar arcs.

A. LINAC-based radiosurgery system; LINAC moves through variable degree treatment arc, usually five more times. With each treatment arc, patient and treatment table are rotated into different position.
B. Many LINAC-based radiosurgery centers perform recollimation before each procedure; this consists of passing X-ray beam from LINAC through phantom pointer fixed at isocenter of stereotactic instrument. X-rays are obtained with LINAC and X-ray film at 4-8 different positions; ideally, round phantom pointer tip should be centered in each of X-rays.



Source of picture: Marshall B. Allen, Ross H. Miller "Essentials of Neurosurgery: a guide to clinical practice", 1995; McGraw-Hill, Inc.; ISBN-13: 978-0070011168 >>

Multi-leaf Collimator:



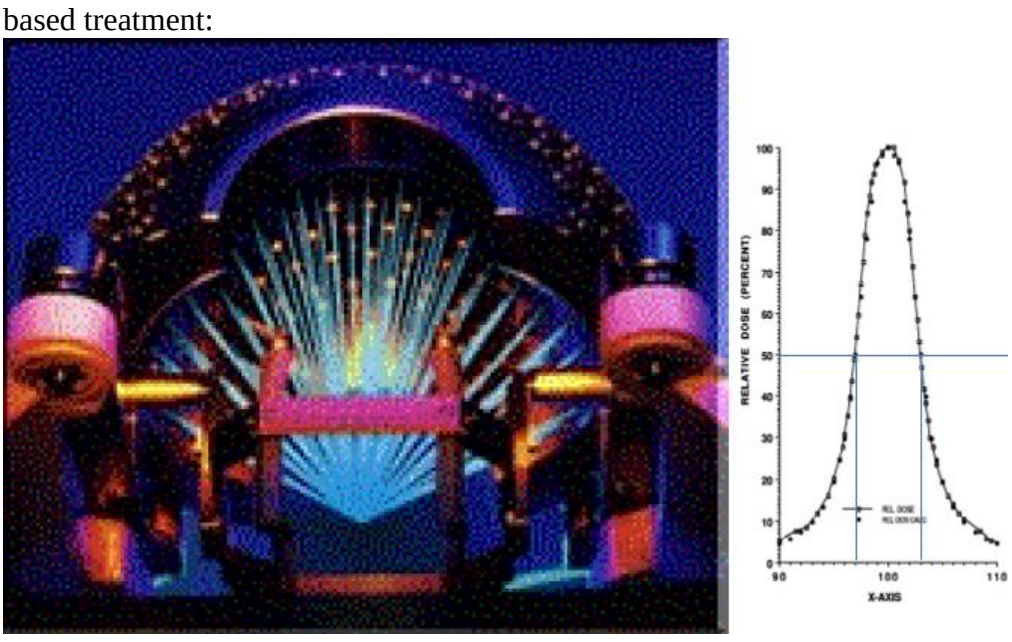
GK VS. LINAC

- two techniques could be used interchangeably for brain lesions.
- differences:

Gamma Knife	LINAC
Largest and longest clinical experience	
Higher cost	
Radiation source is always on – needs replacement of Co-60 source every 5 years	Radiation is off when treatment is finished or paused
Can only be used to treat intracranial brain lesions and nothing else	Much more flexible and can treat "head to toe"
Securing head to treatment table, using fixed head frame – it is minimally invasive, because screws must be inserted into the patient's scalp. Because it is not practical to leave head frame in place, treatment with Gamma Knife is usually completed in one session	LINAC uses firm plastic mask – completely noninvasive, conforms to head, and is much more comfortable for the patient; mask can be easily removed and replaced for multisession treatment

Steepest gradient index is around the 50% isodose line*	Steepest gradient index is around the 80-90% isodose line*
Dose rate 3 Gy/min	Higher dose rate (up to 24 Gy/min) – faster treatment
Less moving parts - possible increased accuracy and precision.	
Local brain tumor control same or better (than with LINAC)	Local brain tumor control same or worse (than with GK)
Lower peripheral normal brain tissue dose	

*Gamma Knife dose plan has more heterogeneity within the target volume than a LINAC-based treatment:



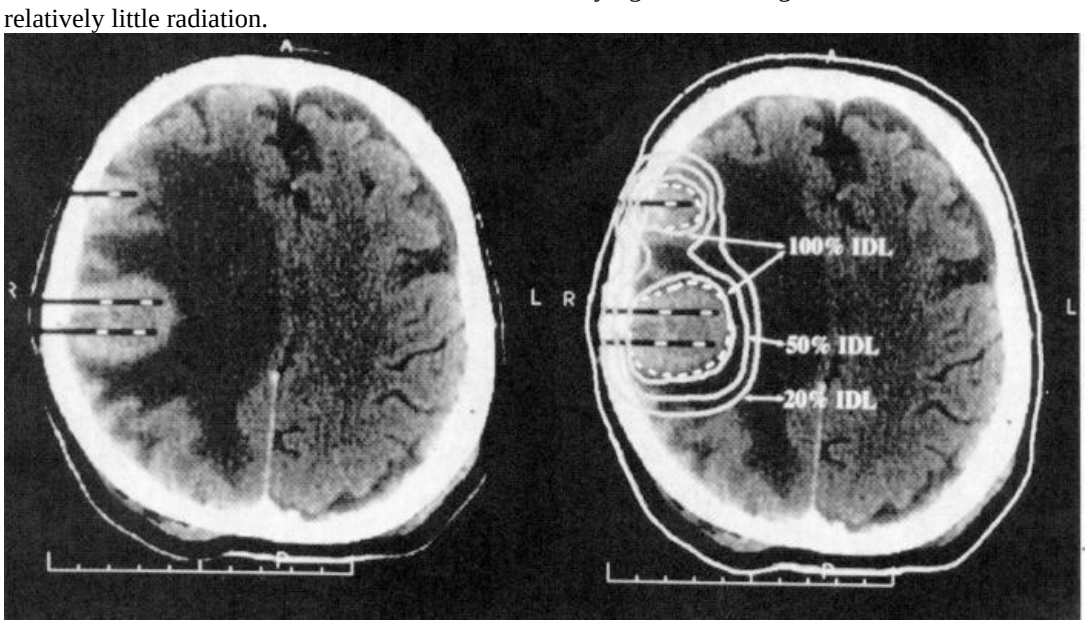
N.B. absolute precision can be slightly better for the Gamma Knife. "If a patient has small lesion that is near optic nerve or brainstem, and we want to be as precise as possible, Gamma Knife may be a little better".

BRACHYTHERAPY (INTERSTITIAL / IMPLANTED RADIATION THERAPY)

No role in neurosurgery!!!!

- $^{125}I_3$ or $^{192}Ir_4$ "seeds" placed by stereotactic techniques.
  Invasive! (vs. radiosurgery)
- rapid dose falloff around "seeds" - localized high-dosage (40-120 Gy) radiation with sharp edges and sparing of adjacent brain.
- effectiveness as of radiosurgery.
- ideal candidate - unifocal, well-defined, supratentorial tumor < 5 cm* in diameter that does not involve corpus callosum, brain stem, or ependymal surfaces.
  *treatment of larger tumors can lead to life-threatening edema
- patient wears lead-lined helmet when others enter his private room.
- **steroids** are given during the period of treatment (to prevent surrounding reactive edema).
- typically, sources (along with stereotactically placed afterloading catheters) are removed after 5-6 days of treatment.
- high incidence of *radiation necrosis*!

Stereotactic implant of bilobed brain tumor - hollow catheters placed inside tumor-bearing region; radioactive seeds are then loaded into catheters; dose distribution is extremely tight around target volume and remainder of normal brain receives relatively little radiation.



RADIOCOLLOIDAL SOLUTIONS

- placed ***into cystic cavities*** (to control fluid reaccumulation, to decrease cystic tumors and consolidate their capsule → safer surgery):
  a) ^{90}Y - maximum range of β particles is 8 mm; > 50% dose absorbed by first 1.1-1.5 mm of tissue.
  b) ^{32}P - half-value layer penetration 0.8 mm - lower risk of injury to surrounding vascular / neural structures.
  c) ^{186}Re
  d) ^{198}Au
- no significant radiation dose to associated solid tumor components.
- suspension is aspirated after several days.

BIBLIOGRAPHY for "Radiotherapy" → follow this LINK >>