# New innovations in Radiation Therapy

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IAEA
International Atomic Energy Agency

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# COMING TECHNICAL ADVANCES IN RADIATION ONCOLOGY

**HERMAN SUIT, M.D., D.PHIL**

Table 1. Technical advances in radiation oncology in the recent 50 years

| | |
|---|---|
| 1. Portal Films | 2. Gantries |
| 3. Simulators | 4. $^{60}$Co Units and Linear Accelerators |
| 5. Electron Beams | 6. CT, MRI, PET and US |
| 7. Computerized Treatment Planning | 8. Intra-operative Electron Beam Therapy |
| 9. Stereotactic Radiosurgery and Radiation Therapy | 10. IMRT [IMXT] |
| 11. Image Guided Brachytherapy | 12. Proton Beams |

# Preface

- Is it Advanced  Techniques or Recent Technologies ?
- New advanced technologies needed for dosimetry and imaging.
- Few studies have been published to date comparing patient / clinical outcomes using different technologies

# Common Sense Assumptions

- Better dose distribution leads to better clinical outcomes.
- Escalate dose to clinical target volume.
- Minimize treated volume ( reduced normal tissue toxicity) .

CHALLENGES

- Unnecessarily complex?
- Quality assurance critical?
- Geographical misses?
- Value for money?
- Staffing issues?

# Goals of Radiotherapy

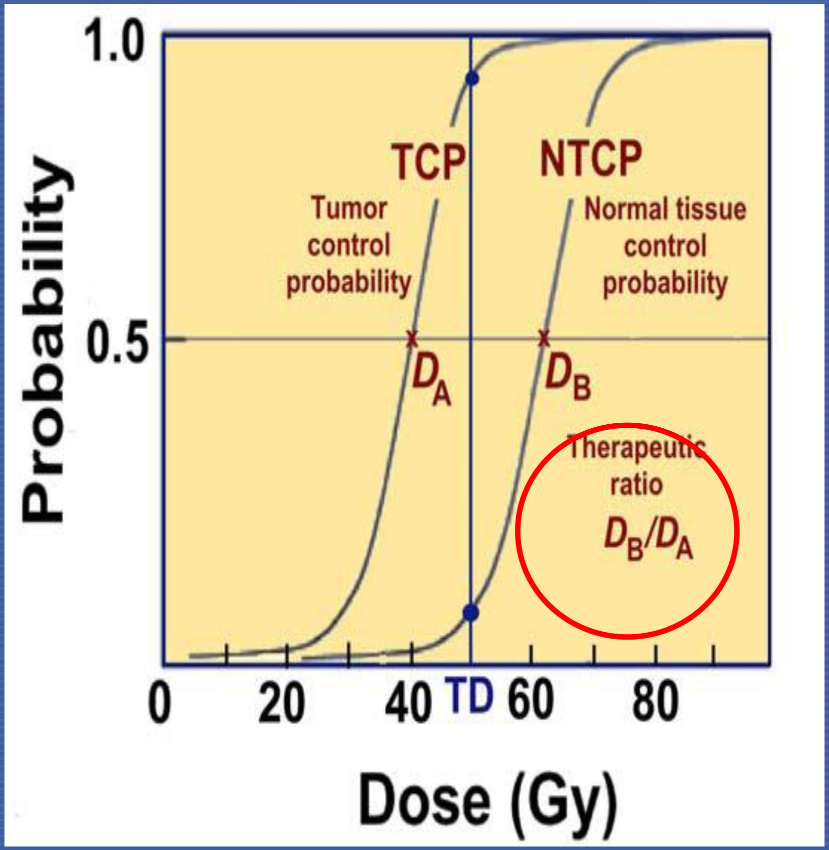
- To Improve Tumor Control

  through an increase in tumor dose,
  i.e., through an increase in TCP

- To Reduce Morbidity

  through decreased dose to normal tissue,
  i.e., through a decrease in NTCP

(1)More complex treatment techniques
(2)New technology



# Dose should be accurate & Precise ….

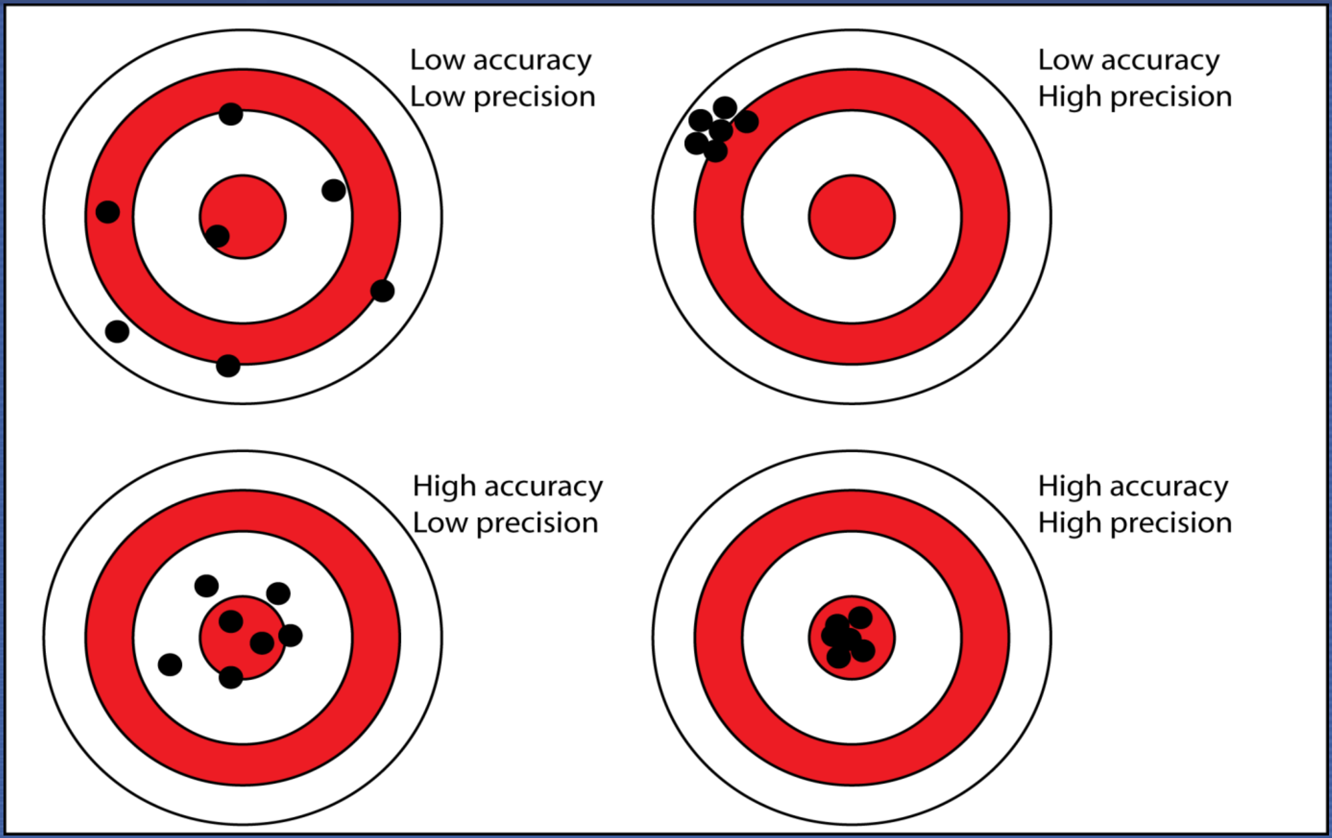
- To target:

  5% too low - may result in clinically detectable reduction in tumor control (*e.g.* Head and neck cancer: 15%)

- To normal tissues:

  5% too high - may lead to significant increase in normal tissue complication probability = morbidity = unacceptable side effects

# Precision *versus* Accuracy




Dosimetry

I.G.R.T

# Technological Challenges

- Make sure that the right dose is delivered at the right place = improved dosimetry + improved imaging

- The challenge of early diagnosis
- “See” smaller tumours = improved imaging
- New advanced technologies needed for dosimetry and imaging

# Dosimetric Challenge

- The requirements for new dosimeters:
  - Measure dose at tumor site and not at skin.
  - Measure total dose (including dose during imaging procedures).
  - Measure in real-time and not long time after each treatment fraction.
  - System easy to use.

- <u>The answer</u>: in-vivo dosimetry

# Imaging Challenge

- The requirements for new imaging systems:
  - More accurate, more quantitative and highly repeatable imaging
  - Imaging during treatment: organ movement (breathing), patient set-up, tumor shrinkage
  - Image smaller lesions (early diagnosis)
  - Treatment specific requirements (for ex. Bragg position in proton/light ion therapy)

- <u>The answer</u>: higher spatial resolution, higher linearity, lower noise, less drift, faster imaging.

# Volumetric Modulated Arc Therapy
# Rapid Arc / VMAT

MLC 120/160

F.F.F dose rate up 20 Gy/min

KeV CB-CT

TPS- Inverse
TPS-Algorithm

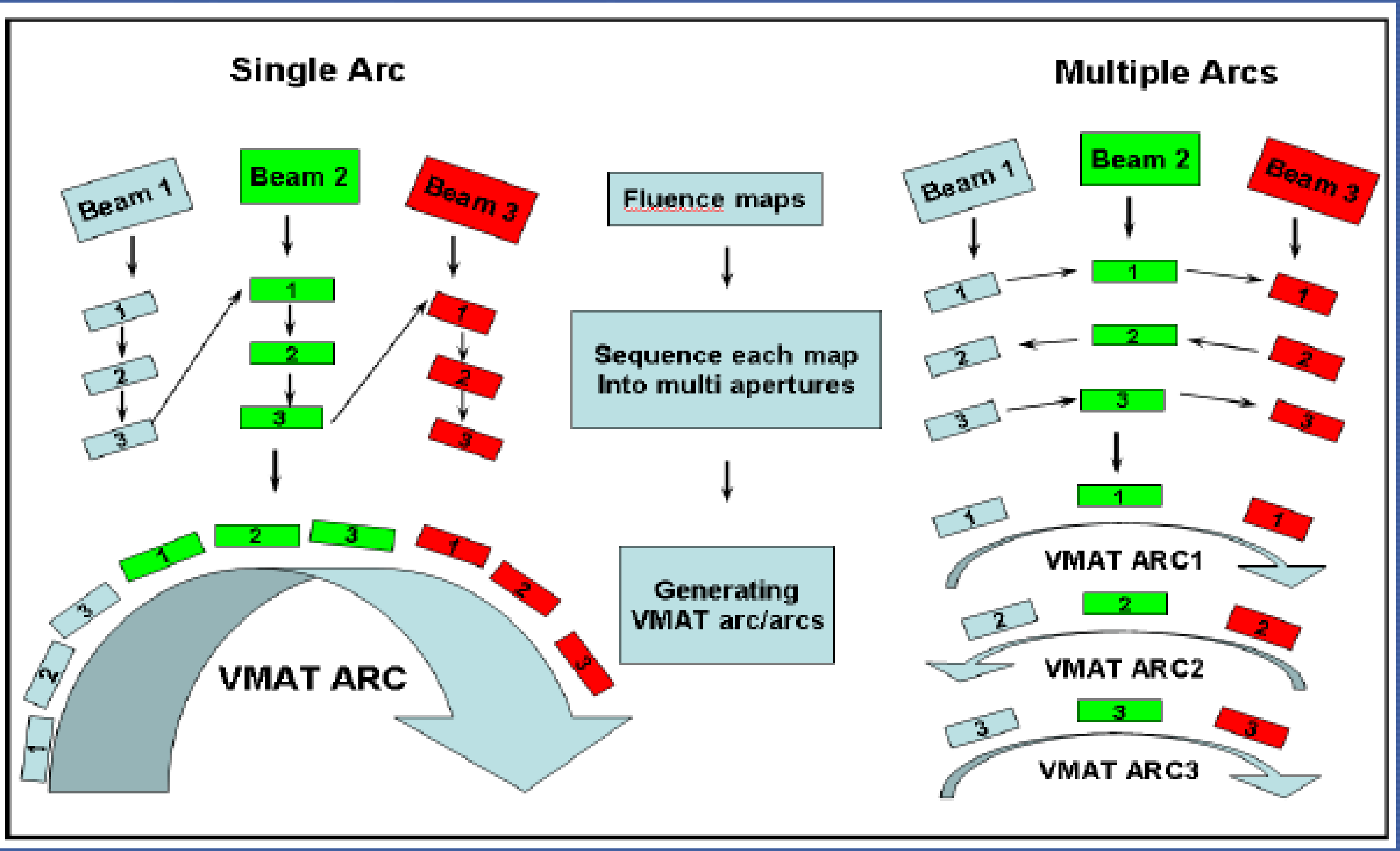
V & R Integration

# Volumetric Modulated Arc Therapy Rapid Arc / VMAT

First proposed by Cedric Yu, Ph.D., in the mid-90's, but only adopted recently by Elekta

- VMAT Slower than RapidArc, but will allow for more modulation, and should allow for improved dose distributions vs. Rapid Arc
- Disadvantage: Much slower than either Rapid Arc or Tomotherapy.

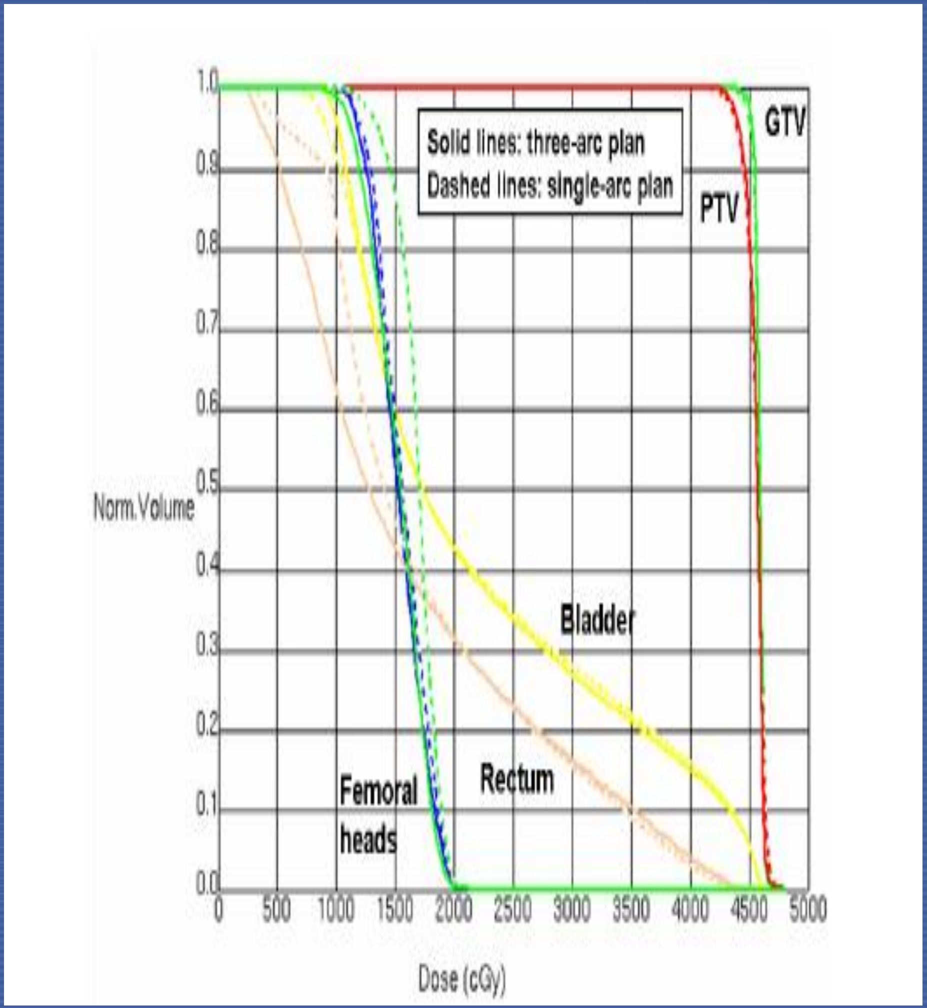
# Single Arc vs. Multiple arcs



# Single Arc vs. Multiple Arcs

- The V95 (target volume covered by 95% of prescribed dose) are 99.1% and 99.6% for the 1-arc and 3-arc plans, respectively

- Delivery times are 2.5 and 5.1 minutes for single-arc and three arc plans, respectively.



# Neutrons

- The energy required to accelerate these particles is quite high
- The machines are quite expensive thus these beams are not commonly available.

- Advantages
  - Neutron beams are less affected by tumor hypoxia and repair of sublethal damage is lessened.
- Disadvantage
  - Despite encouraging local control outcomes, neutron studies have shown high rates of adverse effects and their use has been largely discontinue.

# Neutrons

A C T A   O N C O L O G I C A

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## NEUTRON THERAPY—THE HISTORICAL BACKGROUND

Hans Svensson and Torsten Landberg

Neutron therapy was first introduced by Stone et al. in 1938, i.e. more than 10 years earlier than electron beam therapy and only 6 years after the discovery of neutrons. In spite of the impressive accomplishment in generating an adequate therapy beam, time was also found for careful radiobiological studies of neutron beams. However, it was not considered that for a certain early reaction the late effects were much greater with neutrons than with x-rays. The severe late sequelae in proportion to the few good results motivated the closure of this therapy. Neutron therapy was again introduced in Hammersmith hospital at the end of the 1960's. The major reason seems to have been to overcome the oxygen effect. Encouraging results were reported. It was argued that the very favourable statistics on local tumour control were obtained at the expense of more frequent and more severe complications. A clinical trial in Edinburgh seemed to indicate this, but it was not proved in the end as the two trials differed regarding fractionation. Today about 16 000 patients have been treated with neutrons. The neutron beams now used differ significantly, both regarding dose distributions and microdosimetrical properties, from those utilized earlier. The advantage of neutrons is still, however, controversial. There are indications that neutron treatment may be favourable for some tumours. A careful cost–benefit study ought to be performed before the creation of a neutron therapy centre in Sweden as the group of patients suitable for neutrons is limited, and there may be new possibilities for improvement of photon and electron treatment with much smaller resources.

The major reason seems to have been to overcome the oxygen effect.

For most tumors there seem to be a stronger radiobiological rationale for using photons and electrons than neutrons as the irradiated normal tissue is less affected.

# Neutron Therapy

- First trials of neutron therapy in 1938 used lower energy neutrons than what is used today.

- The energy required to accelerate these particles is quite high.
- The machines are quite expensive thus these beams are not commonly available.

## Where are Neutrons Needed ?

- Large radioresistant tumors are not well controlled by photon (or proton) therapy
- Hypoxic (low oxygen) cells are radioresistant

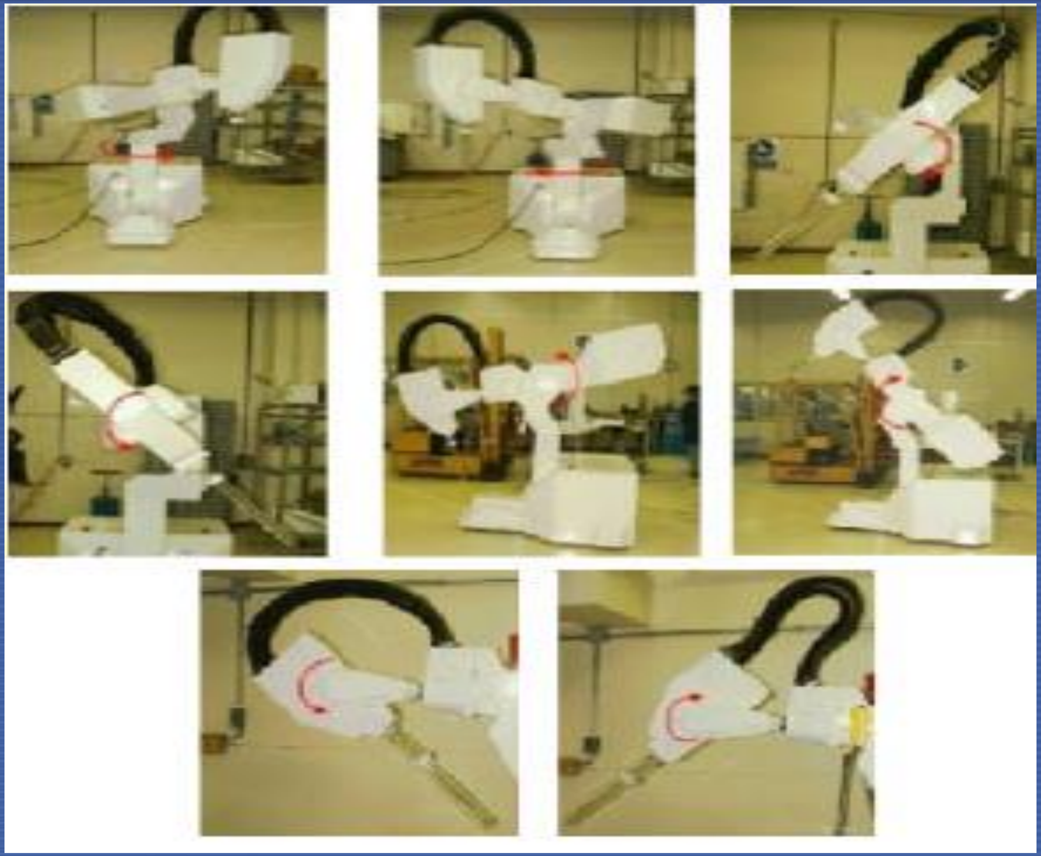
# INTRA OPERATIVE RADIOTHERAPY

- Electron beam /or KeV X-ray with variable applicator size
- Target tumor bed ; Direct visualization
- Avoid organs at risk ; Convenient
- Short duration < 2 min

# INTRA OPERATIVE RADIOTHERAPY

## New-Novac 7

- Mobile and dedicated linac
- Electron beam: 4 energies ( 4, 6, 8, 10 MeV)
- very high dose per pulse
- conventional surgery room
- 6 degree of freedom



Collimators: 30, 40, 50, 60, 70, 80, 100 mm diameter
Angles: 0°, 15°, 22,5°, 30°, 45°

# IGRT Systems

- Port film
- Emergence of MV portal imagers
- In-room ultrasound localization
- Marker-based localization
- Fluoroscopic tracking
- Flat panel imaging (EPID)
- KV digital imaging
- CT –on rail ;
- KV-CBCT
- MV-CBCT

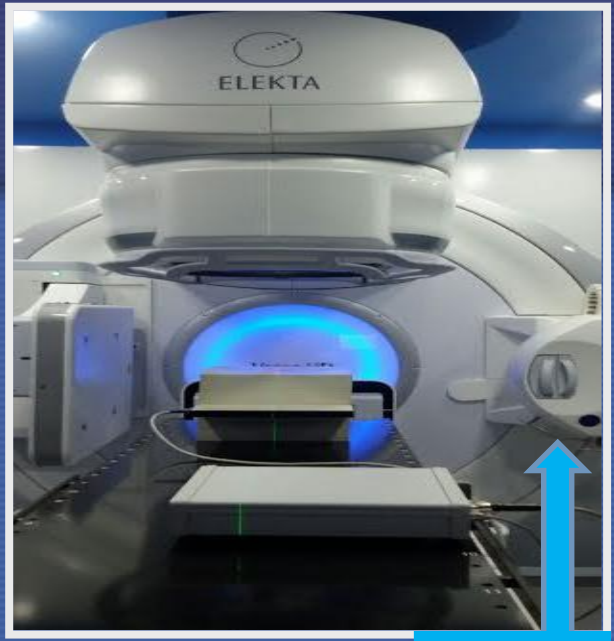
❖ IGRT systems are based on direct integration of:

- Kilovoltage or Megavoltage imaging system and an isocentric linac (Cone Beam CT - **CB CT**).
- CT scanner and an isocentric linac.
- Megavoltage Computerized tomography (MVCT) and a Tomotherapy machine (miniature linac mounted on a CT-type gantry).
- 2-D or 3-D Ultrasound system and an isocentric linac.
- On-line imaging with paired orthogonal planar imagers and a miniature linac mounted on a robotic arm.

# Cone Beam Computed Tomography

- CBCT system integrated with an isocentric linac and based on Kilovoltage X-ray beams consist of:
  - Conventional X-ray tube mounted on a retractable arm at 90º to the high energy treatment beam.
  - Flat panel X-ray detector mounted on a retractable arm opposite to the x-ray tube.
- In addition to cone beam images, the X-ray system can also produce radiographic and fluoroscopic images.
- Volumetric data are then compared with the planning CT data and the associated optimized dose distribution, and the patient position is fine tuned to account for:
  - Tumor volume motion.
  - Set-up error

# Cone Beam Computed Tomography

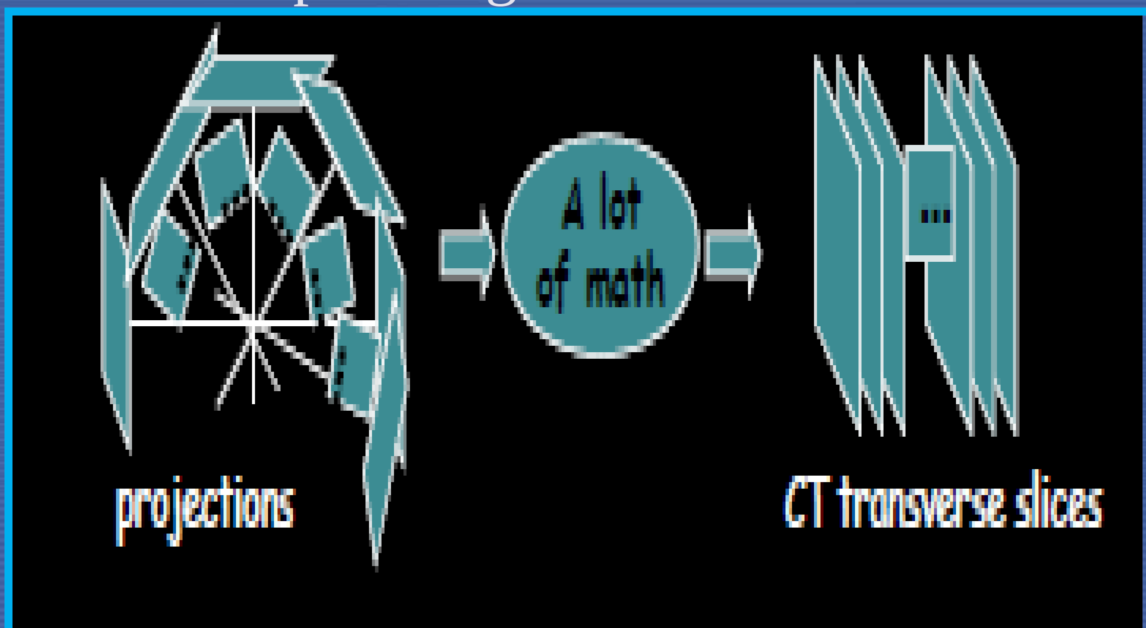



- In CBCT, a filtered back-projection algorithm, similar to CT scanning algorithms, is used to reconstruct the volumetric images of:
  - Target volume.
  - Sensitive structures.
  - Landmarks in the patient or markers on patient's skin.

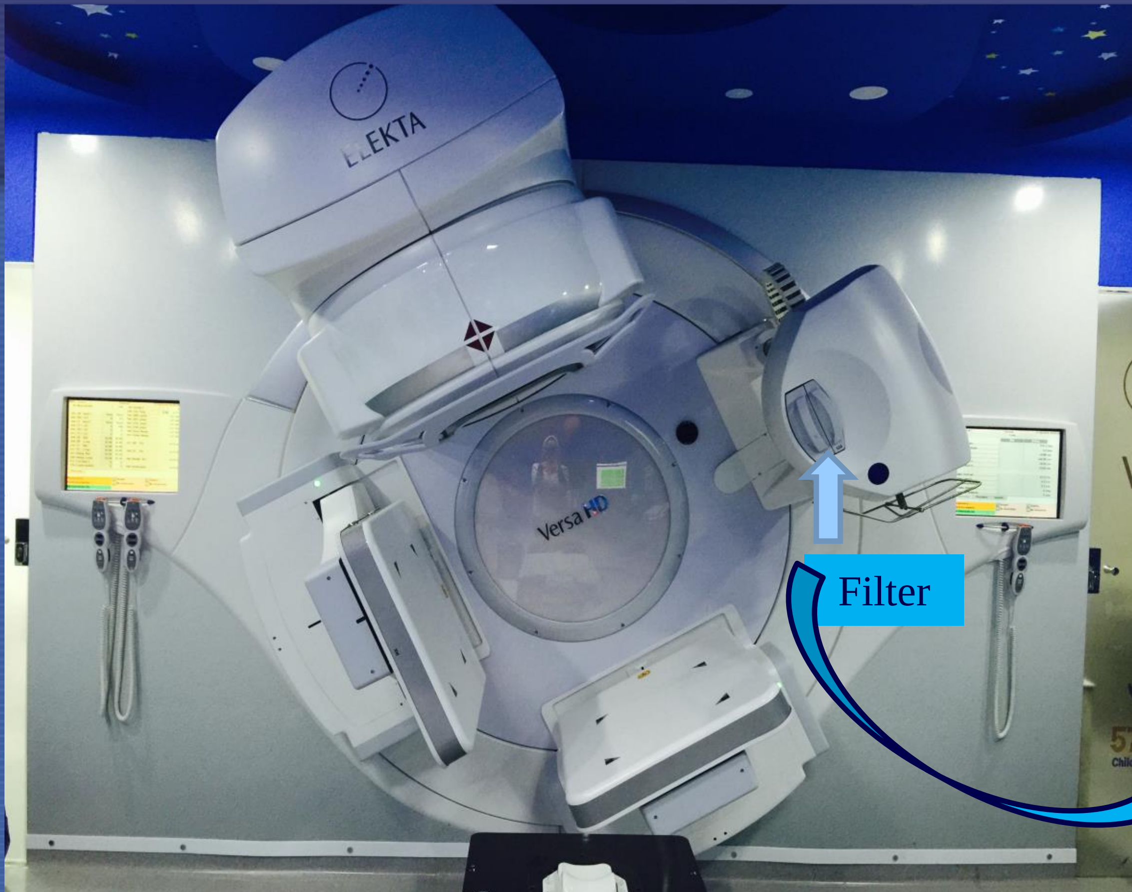
- CBCT images can also be produced with megavoltage X-ray beams (MVCT) produced with isocentric linacs.
- **Advantage of megavoltage CBCT** is that no additional equipment is required for producing the cone beam since:
  - Beams come from the linac beam line.
  - MVCT systems use the detector panel that is already installed on the linac for use in electronic portal imaging.
- **Disadvantage of MVCT** systems is that, in comparison with KVCT systems, the MVCT systems produce an inferior tissue contrast.

# KV- Computed Tomography

- Gold-Standard for RT planning
- Use of volumetric kV-CT data for planning and localization allows for "accurate" automated image registration process
  - – Accurate patient re-positioning
  - – Preplanning

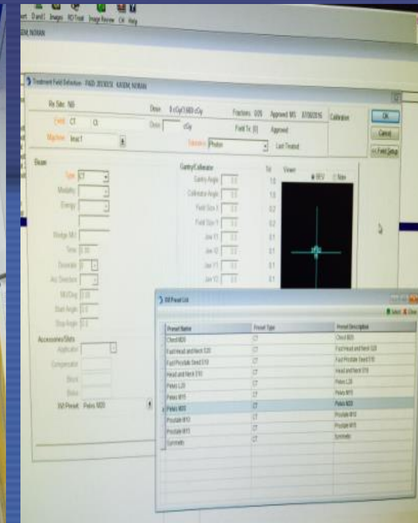



**Varian-image-guidance system.**

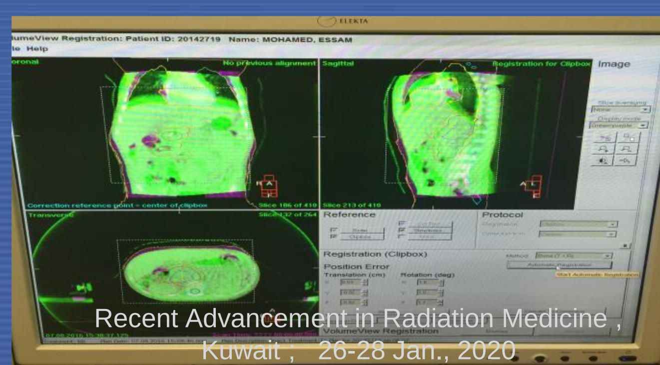


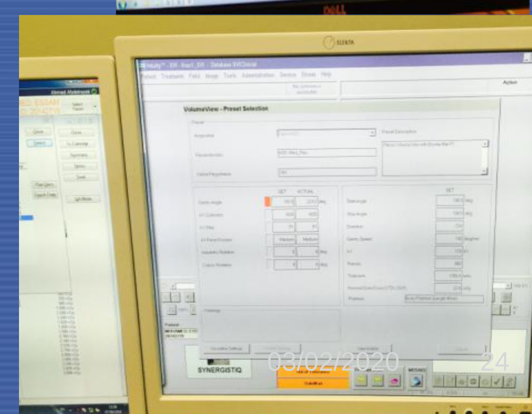

Filter

Filters



# Versa image-guidance system.

# CT on rail-track Computed tomography Primatom

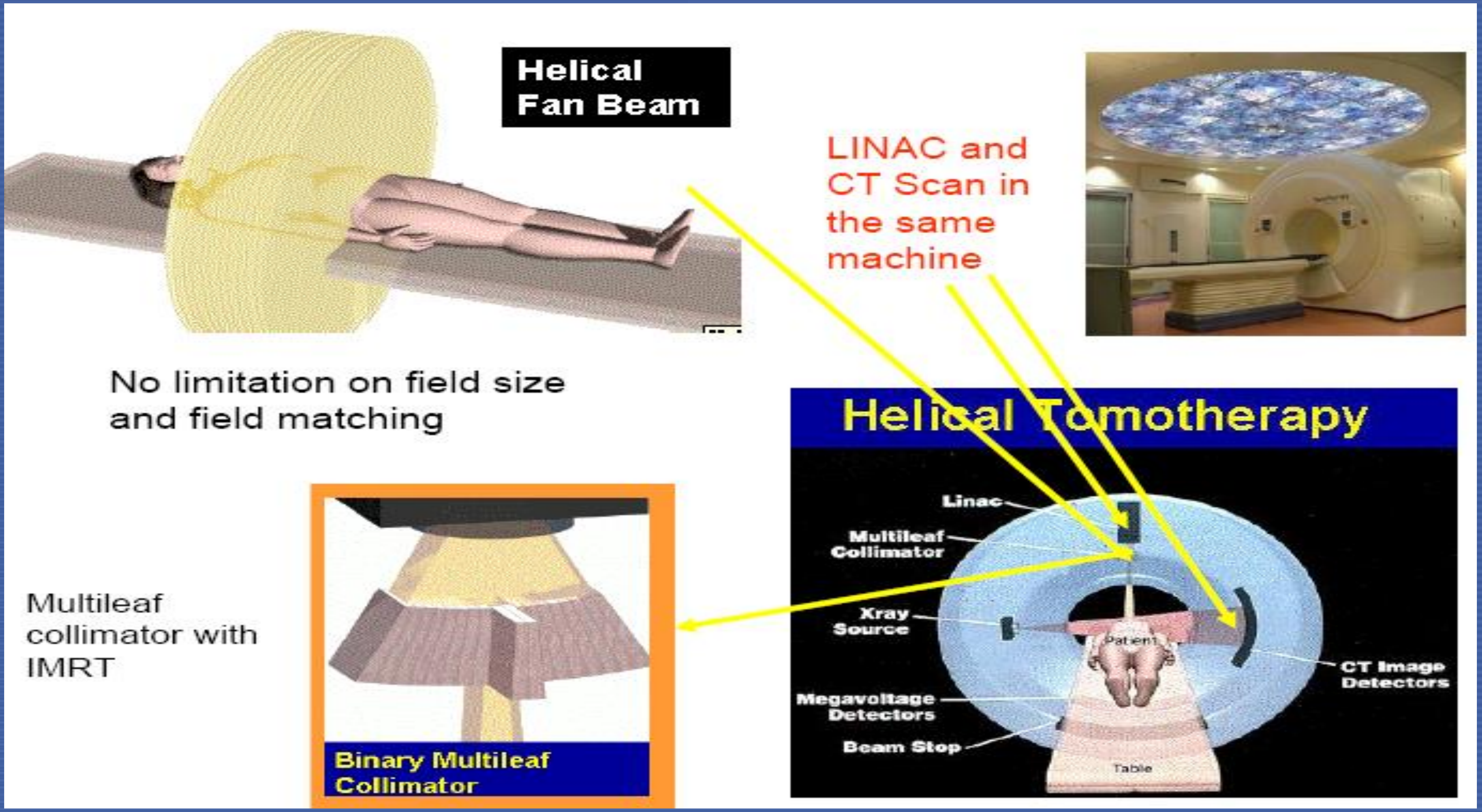
- A system comprised of a linac and a CT unit at opposite ends of a standard radiotherapy treatment table has been developed and is marketed by Siemens.
- Main features of the system are:
  - System allows precise CT imaging of patient anatomy prior to each fraction of radiotherapy.
  - Patient can be shifted to compensate for target motion and setup inaccuracies.
  - System allows clinicians to account for changes in target volume size and shape over a multifraction course of radiotherapy treatment.

a rail-track–mounted system: Siemens PRIMATOM™ system. (Courtesy of Lisa Grimm, Ph.D., Morristown Memorial Hospital, NJ)

# Tomotherapy

- Tomotherapy concept for delivering image guided radiotherapy was developed by T.R. Mackie and colleagues at the University of Wisconsin in Madison.
- In the tomotherapy system the IMRT is delivered with a 6MV X-band miniature linac mounted on a CT type gantry ring, allowing the linac to rotate around the patient.
- Beam collimation is accomplished with a computer controlled MLC that is also mounted on the gantry and has two sets of interlaced leaves that rapidly move in and out of the beam to constantly modulate the intensity of the radiation beam as the linac rotates around the patient.

# TOMOTHERAPY

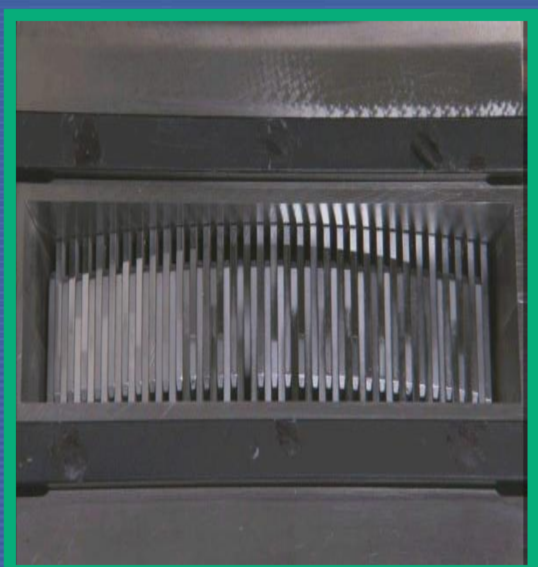



- No traditional external gantry
- Max 5 cm field width
- Patient moves into bore.

# Helical Tomotherapy

- MLC leaves that move at 250 cm/s to open or shut in milliseconds
- Thousands of beamlets throughout multiple 360 degree rotations
- Coverage of a target extent up to 160 cm in length with no matching

Fast Binary MLC

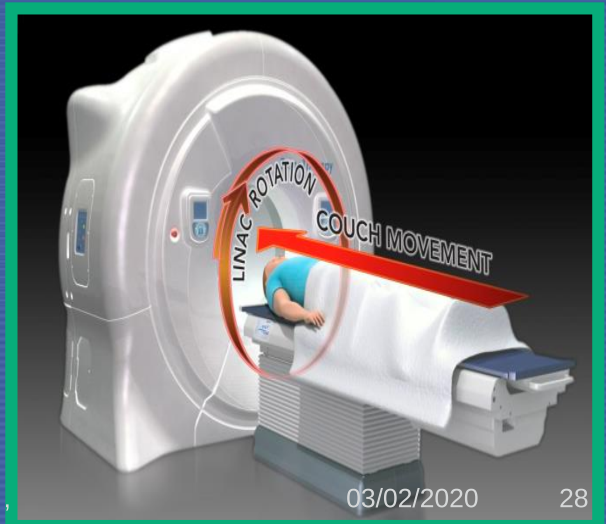


+

Continuous Gantry Rotation

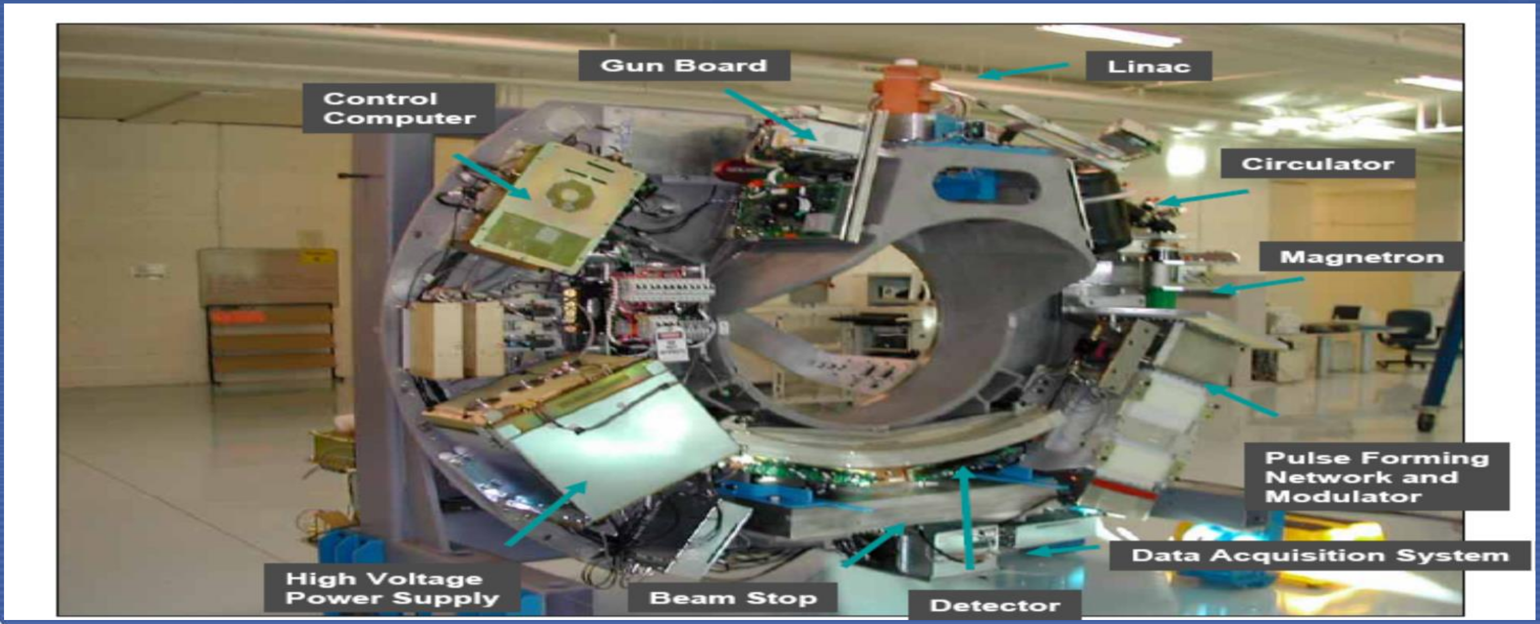
+

Simultaneous Couch Movement



# Tomotherapy

- During treatment, the table advances the patient through the gantry bore so that the radiation beam dose is delivered in a helical geometry around the target volume.
- System is designed to obtain an MVCT scan of the patient anatomy at any time before, during or after dose delivery.
- MVCT image data are acquired with a 738 element xenon ionization chamber array that rotates on the gantry opposite the linac.



# The BAT system

- B-Mode Acquisition and Targeting (BAT) system is based on 2-D ultrasound images acquired prior to dose delivery. The images are used to realign the patient into the appropriate position on the treatment table.
- System consists of a cart-based ultrasound unit positioned next to a linac treatment table and is used by the radiotherapist to image the target volume prior to each fraction of radiotherapy treatment.

- Relationship of the target volume to a reference point, usually the linac isocentre, is determined interactively by the user and compared with the target volume originally contoured in the CT data set.
- Recommendations for required patient translation to move the target volume into the same position relative to the isocentre as in the treatment plan are made by the system and the patient is moved, based on this information, to gain better treatment accuracy.

# BAT Ultrasound

- External probes used to acquire images
- Planning CT structures overlaid on the US images to calculate couch shifts
- Used mainly for prostate and breast patients

Trans abdominal US

Table Shift x, y, z

# The Exac Trac Ultrasonic and X-ray modules

- Tumor positioning conventionally relies on external skin markers that are subject to inter-fraction shifts compromising the accuracy of dose delivery.
- Exactrac by BrainLAB is designed to address precise patient positioning by providing imaging of the target area around the tumor.
- Ultrasound or X-ray images are taken just before treatment and the ExacTrac system automatically compensates for any patient misalignment.

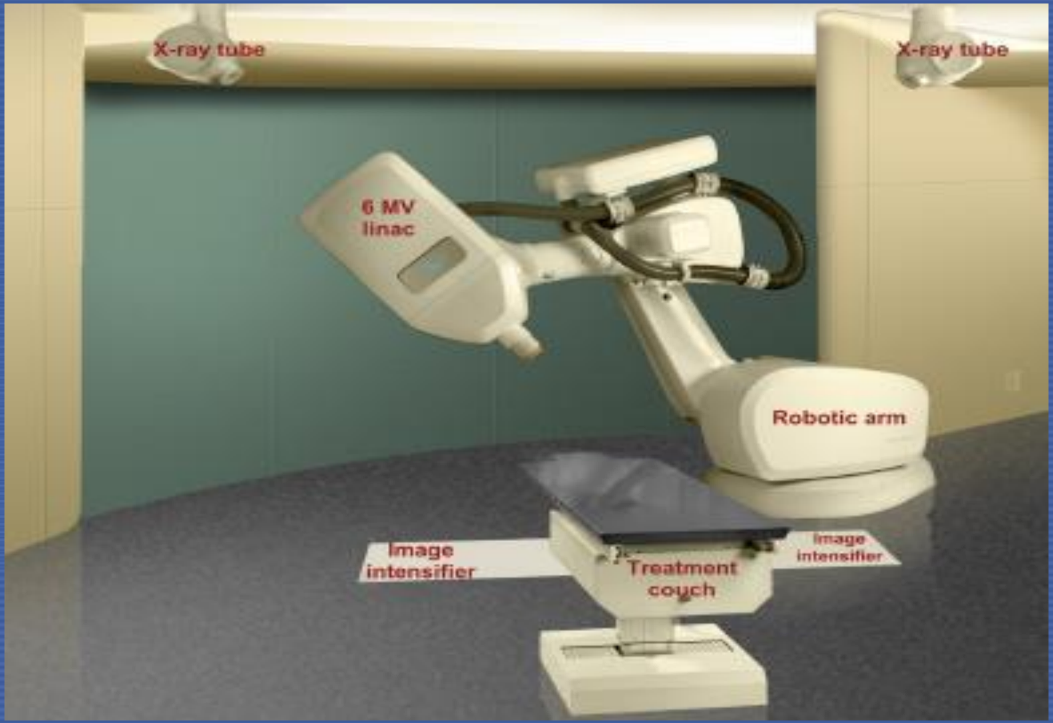
- Ultrasound-based ExacTrac system can be used with any ultrasound unit and is comprised of a reflective marker array attached to an ultrasound probe. The marker array is calibrated by the ExacTrac infrared tracking system relative to reflective markers attached to patient's body.
- System works similarly to the BAT system and allows fine adjustment of the patient's position to compensate for target motion and set-up inaccuracies.

# ExacTrac X-ray imaging

- Radiofrequency Tracking
  - Calypso system
  - Small beacons transmitters implanted in patient
  - Beacons are marked on the planning CT & their positions relative to the isocenter are calculated
  - An electromagnetic array excites the Beacon transponders and receivers which detect each transponder's frequency
  - Frequencies determine the location coordinates of Beacons relative to the iso during txt
- ExacTrac X-ray imaging module provides high-resolution imaging of internal structures and organs.
- During the positioning process the system calculates the discrepancy between the actual and the planned target position and compensates for any discrepancies with automatic treatment table motions.

# The CyberKnife

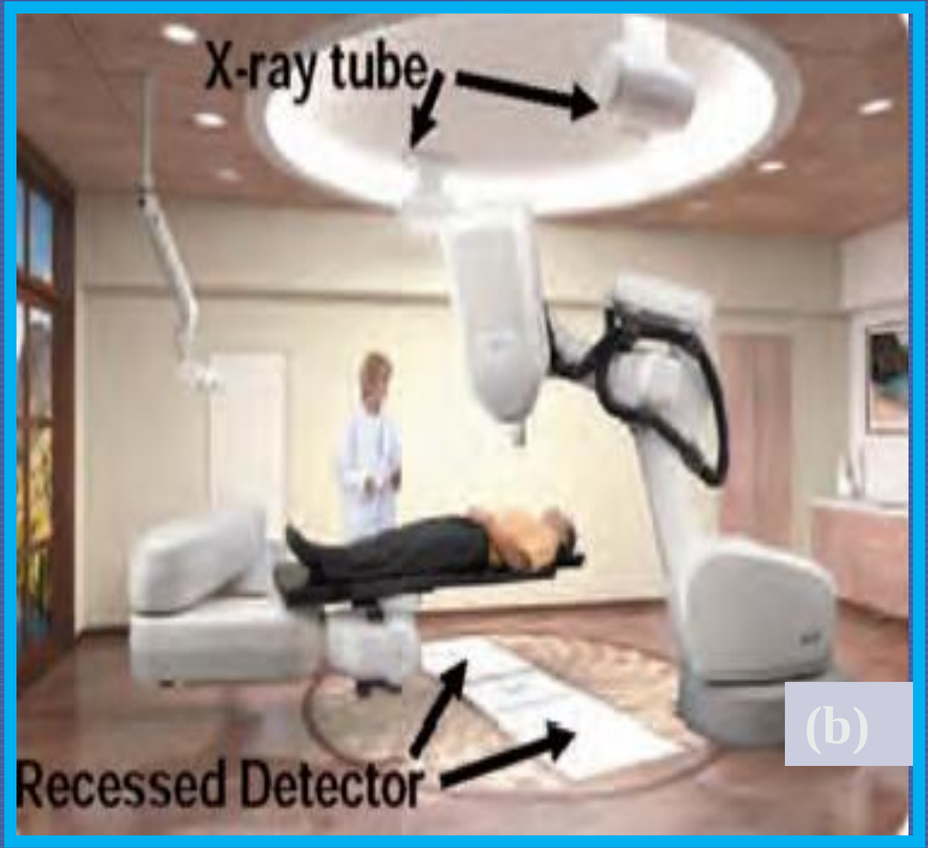
- CyberKnife was developed in the mid 1990s as an innovative tool for intracranial stereotactic radiosurgery.
- Dose is delivered with a miniature X-band (104 MHz) linac mounted on an industrial robotic arm in a combination that:
  - Offers excellent spatial accuracy in dose delivery




Main components:

6 MV linac
Robotic arm
Treatment couch
Imaging system

# CyberKnife


**CyberKnife image-guidance system with two detectors mounted** (a) above the floor and (b) under the floor. (Courtesy of Accuray, Inc.)

# CyberKnife

- CyberKnife radiosurgery system provides an innovative approach to image guided dose delivery that is based on:
  - On-line orthogonal pair of digital x-ray imagers.
  - Patient axial CT data set possibly fused with MR and PET images.
  - Miniature 6 MV X-band linac.
  - Industrial robotic arm.

- This new approach to highly accurate intracranial as well as extracranial delivery of high radiation doses with small radiation fields opens the field of radiosurgery to exciting new IGRT techniques.

- Target localization is achieved through a family of axial CT images that serves as a base for the determination of a set of digitally-reconstructed radiograph (DRR) images.
- A set of paired orthogonal X-ray imagers determines the location of the lesion in the room coordinate system and communicates these coordinates to the robotic arm, which adjusts the pointing of the linac beam to maintain alignment with the target.

# CyberKnife

- Compact 6 MV linac mounted on a robotic arm
- Robotic arm, max collimator 6 cm
- Isocentric and non-isocentric
- 150-200 per fraction, small beamlets
- Treatment time for a fractionated case is about 60 min/day.

The CyberKnife is a frameless robotic radiosurgery system invented by John R. Adler of Stanford University.

Radiotherapy technology developments – such as, for example, the latest CyberKnife Robotic Radiosurgery System from Accuray (above) – will continue to make a significant impact upon patients' quality of life.

IAEA

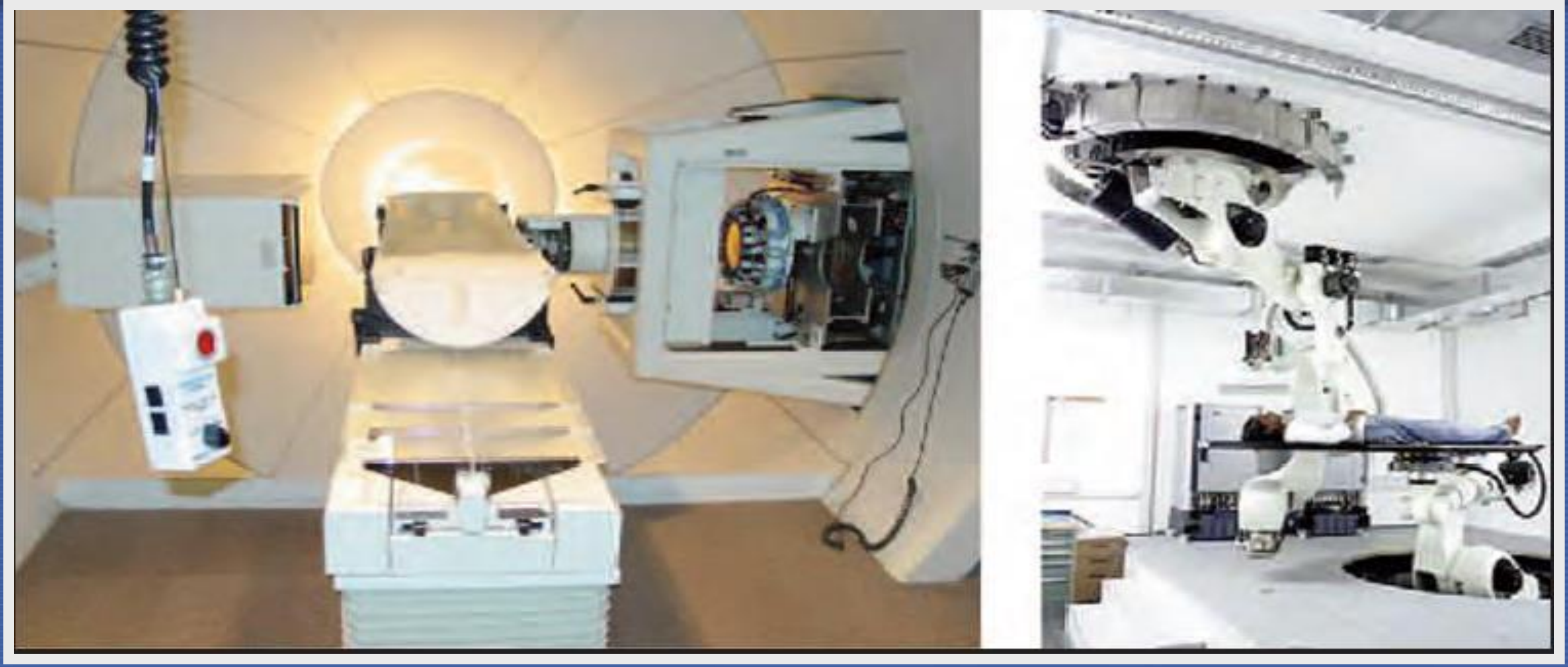
# Strengths

1. Intracranial and extracranial tumors can be treated
2. Large number of beam angles are available
3. Frameless immobilization (more comfortable and allows fractionated treatment)
4. Monitors and tracks patient position during treatment

# Weaknesses

1. No posterior beams (below couch) are possible
2. Treatment times are long
   - 3-4 hours to deliver single-shot SRS
   - 60-90 minutes per session to deliver fractionated treatment
3. Significant quality assurance (QA) is required prior to treatment to ensure that the robotic arm performs as expected
4. No interface to record and verify systems

# IGRT Proton Therapy

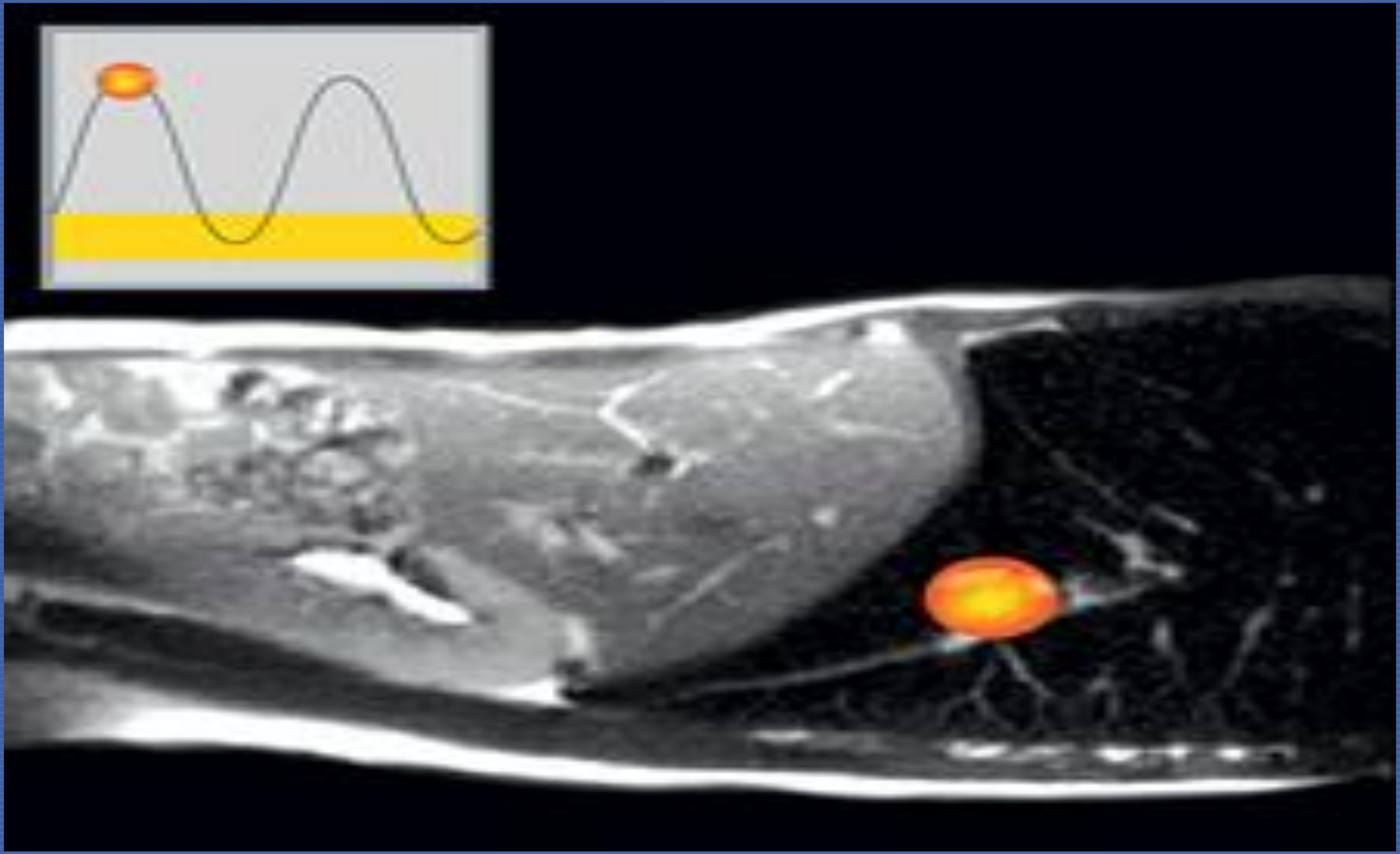


kV X-ray imaging system used at Loma Linda University Proton Treatment Center; (b) a CBCT imaging system with robotic arm used at Heidelberg University heavy ion particle treatment facility. (Courtesy of Michael Moyers, Ph.D.)

# ADAPTIVE RADIOTHERAPY

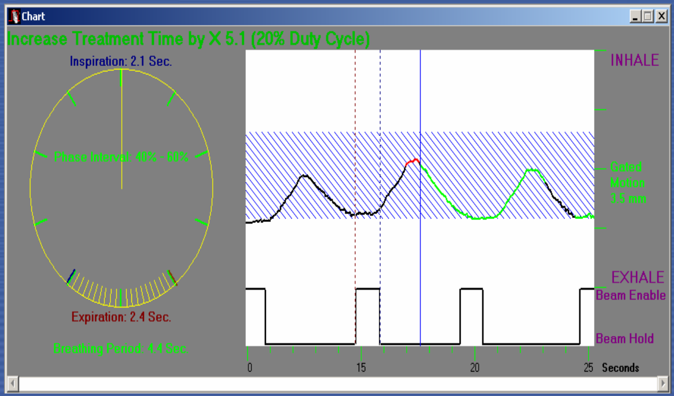
- A full implementation of image guided radiotherapy will lead to the concept of adaptive radiotherapy (ART).
- In ART the dose delivery for subsequent treatment fractions of a course of radiotherapy can be modified to compensate for inaccuracies in dose delivery that cannot be corrected simply by adjusting the patient's positioning like in the IGRT.
- Causes of these inaccuracies may include:
  - Tumour shrinkage during the course of treatment.
  - Patient loss of weight during the course of treatment.
  - Increased hypoxia resulting during the course of treatment.

# Adaptive Radiotherapy



# Gating and ABC

- Camera systems required
- External fiducials often used to predict internal motion
- Patient must wear goggles/spirometer – must be “trainable”
- Only select patients can tolerate treatment
- Significant cost from vendor
- According to Varian users gating can increase treatment times by a factor of 5





Multiple Computer Systems and hardware components must work in synchrony

# The MR-guidance hypothesis

- CBCT has limiting soft-tissue contrast
- Issue of CT Doses
- MR is applicable to EBRT and brachytherapy

## Systems:

- MRL (Utrecht – Elekta – Philips)
- View Ray
- Australian MRI-Linac
- Rotating biplanar Linac-MR
- Princess Margaret MRgRT

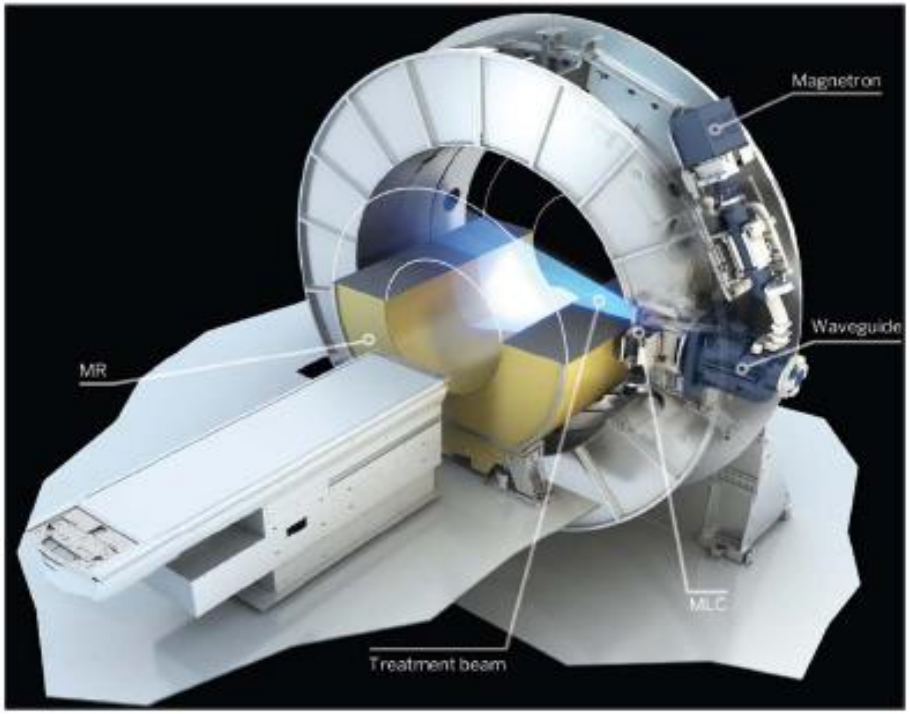
# MRI - Linac

## Systems Comparison

| | Jaffray | Mutic | Fallone | Keall | Lagendyk |
|---|---|---|---|---|---|
| | *Varian MRgRT* | *ViewRay* | *Bi-planar linac-MR* | *Australia MR-Linac* | *Elekta MRL* |
| **Field strength [T]** | 1.5 | 0.35 | 0.56 | 1 | 1.5 |
| **Radiation** | 6 MV | Co-60 | 6 MV | 6 MV | 6 MV |
| **In-line imaging** | no | yes | yes | yes | yes |
| **Bore size [cm]** | 70 | 70 | 85 | 82 | 70 |
| **Room configuration** | Adjacent rooms | bunker | bunker | bunker | bunker |

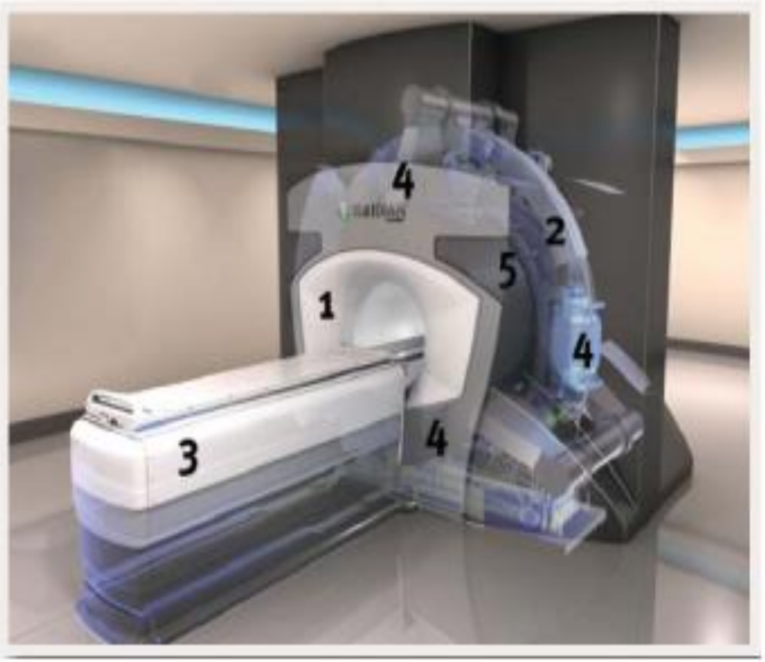
# Elekta MRL

- Utrecht-Elekta-Philips consortium

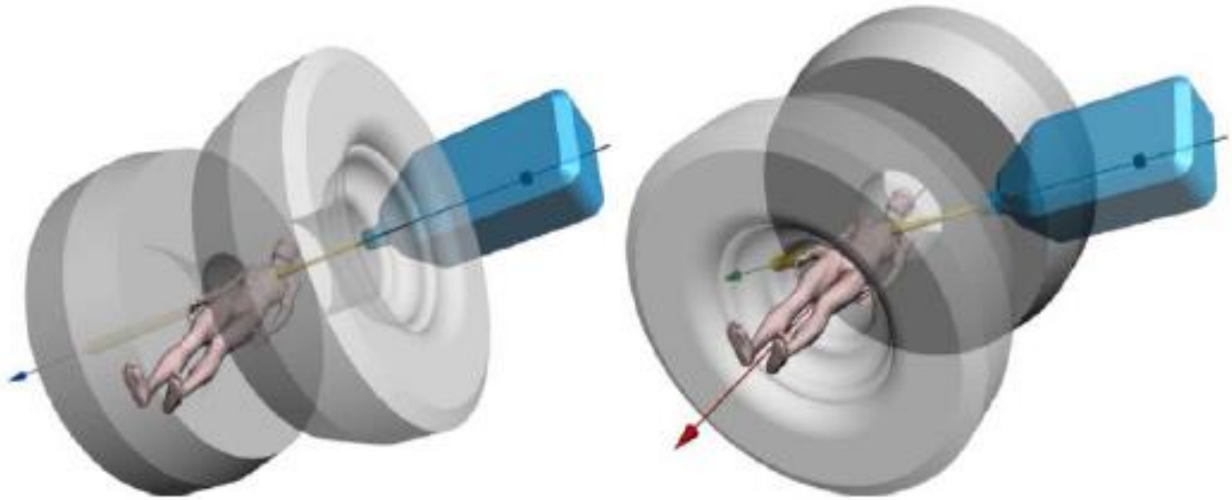


# ViewRay

1. Split superconducting magnet
2. Gantry
3. Patient handling system
4. 60-Co source heads
5. Split gradient coil

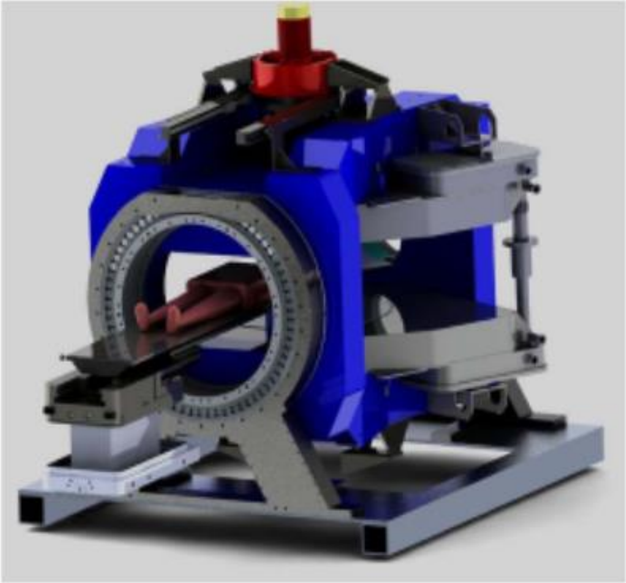


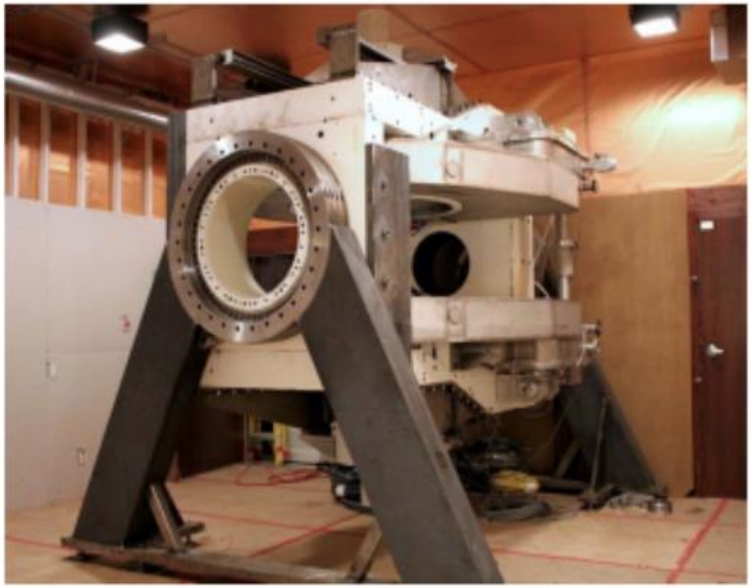
# Australian MRI-Linac Program



- Test facility for a 1-T open-bore MRI 6-MV linac
- In-line and perpendicular geometries

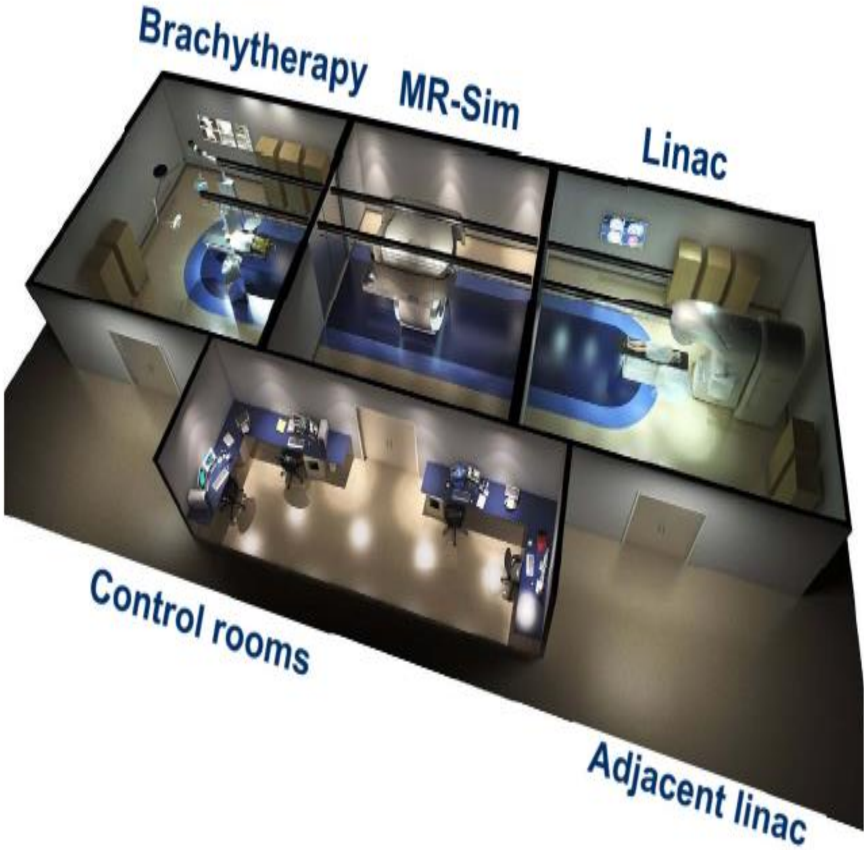
# Rotating Biplanar Linac – MRI System



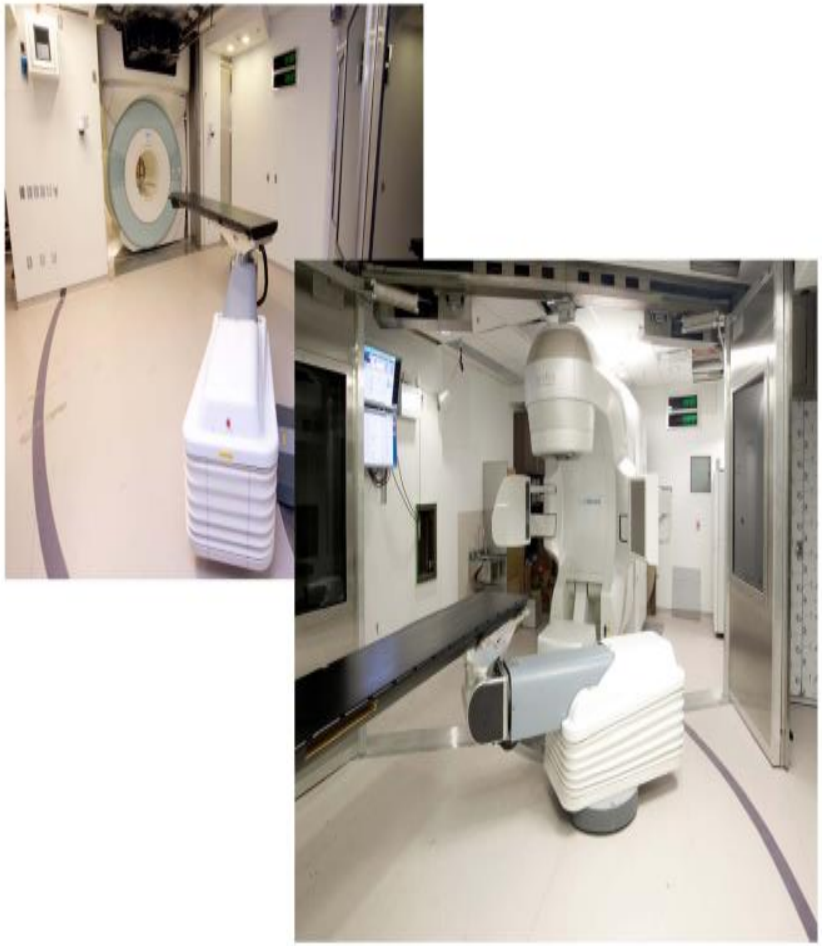


- 6 MV Linac and 0.2 T open-bore MRI
- high-quality MR images during irradiation
- simultaneous linac and MR rotation in parallel configuration
- cryogen-free superconducting magnet not requiring a helium vent

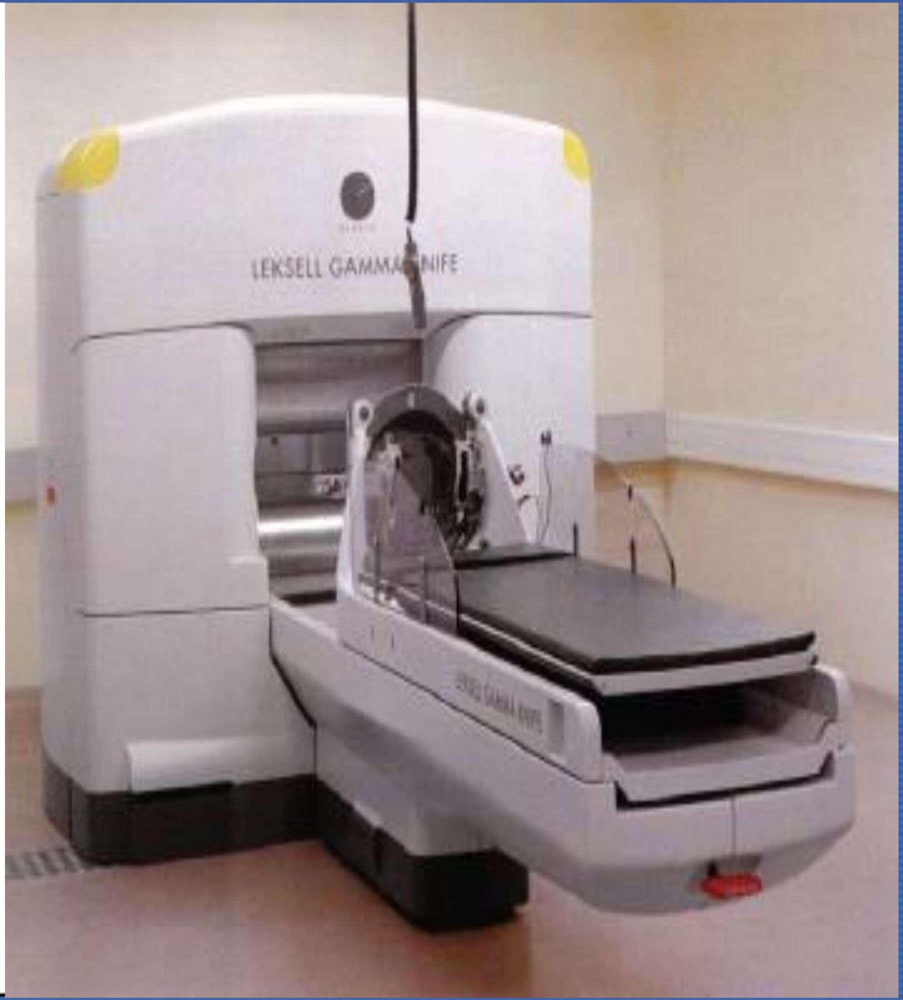
PM MRgRT




PM MRgRT

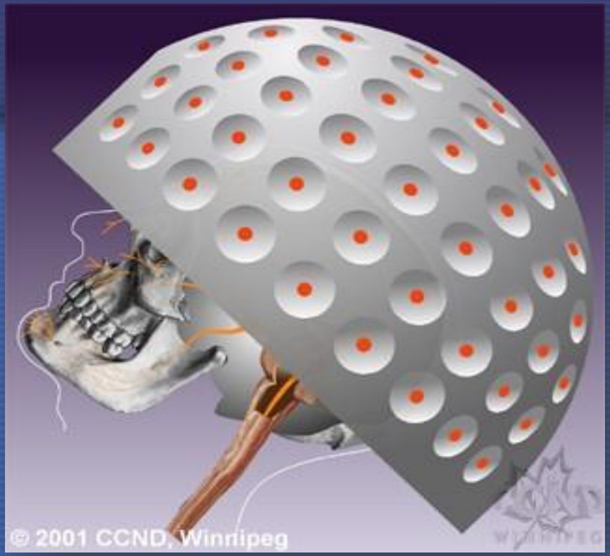


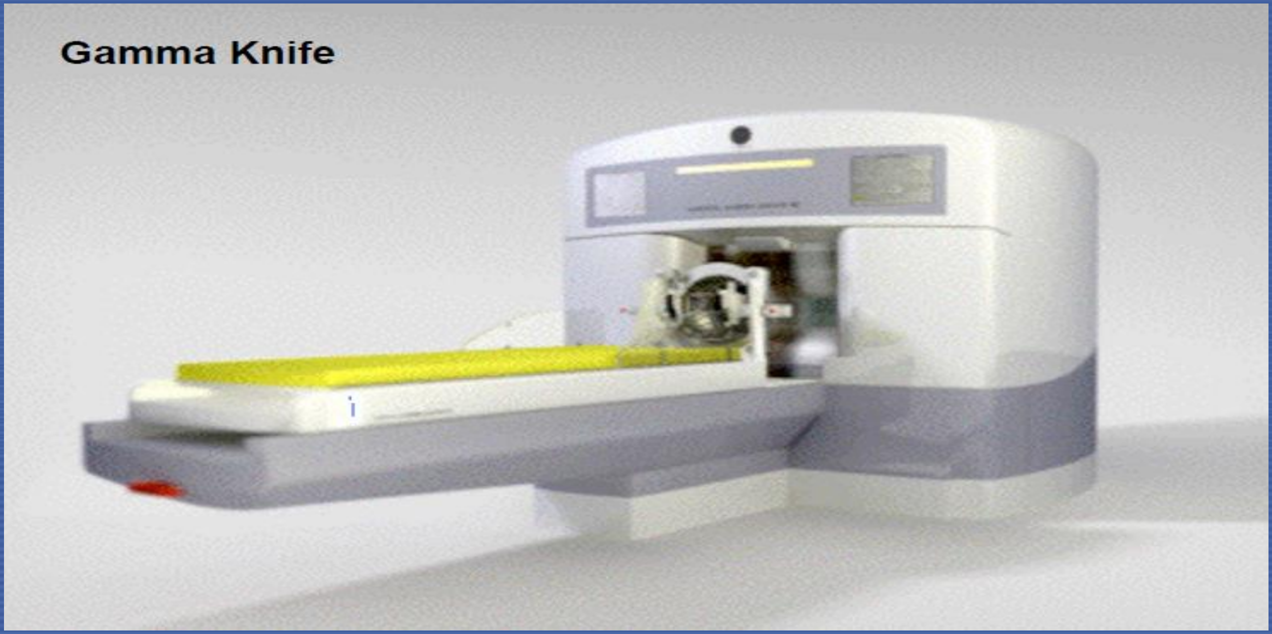
# Gamma Knife


LEKSELL GAMMA KNIFE
LEKSELL GAMMA KNIFE

LEKSELL GAMMA KNIFE

# Gamma Knife

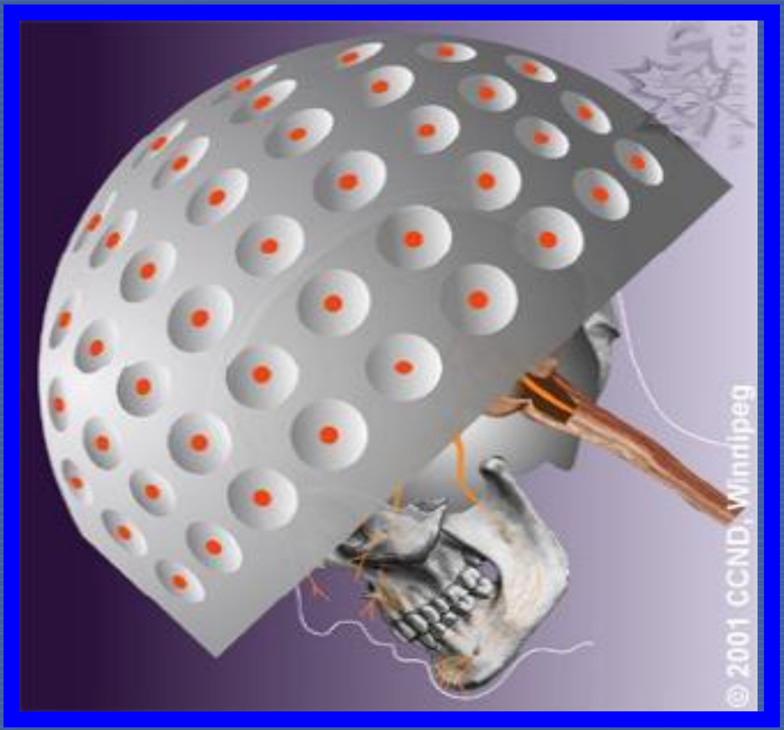
- Gamma Knife® by Elekta
  - Uses 192 to 201 beams of highly-focused gamma rays
  - Different helmets produce different beam sizes
  - All beams aim at target region



# Gamma Knife

## Treatment process




only sources which shall contribute to the irradiation are ‘unplugged’

1. Head frame is attached to the skull with screws.
2. MRI(or CT) scan is acquired for planning
3. Head frame is attached to a helmet.
4. Shielding door slides open and table moves into the Gamma Knife unit.
5. Irradiation times run 40-60 minutes or longer depending on dose, number of isocenters and source strength.

# Strengths

- Has been the gold standard
- Large clinical experience
- High accuracy: 0.2 mm
- Very stable mechanical attachment of patient
- Intracranial SRS is done well
  - ✓ No moving sources and patient is rigidly immobilized
- Treatment planning is relatively straightforward
- Dedicated Neurosurgery tool
  - ✓ Well accepted by the Neurosurgery community

# Weaknesses

- Limited to intracranial targets.
- Bolted head frame is necessary.
- Fractionated treatments are not possible.
- Large targets with complicated shapes require treatment plans with multiple isocenters increasing complexity and treatment time.
- Co-60 sources decay, increasing treatment times, and need to be replaced.
- Radioactive source replacement is a major undertaking and expense.
- No interface to record and verify software systems.

# Heavy Ion Therapy

## Carbon ions

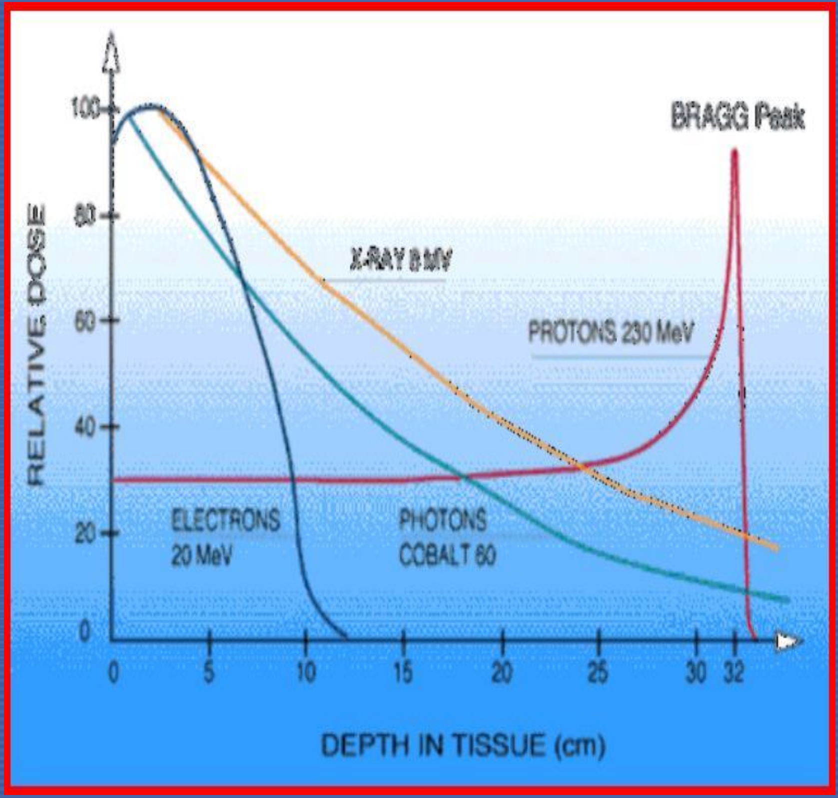
- Carbon ion therapy attempts to capture the 'best of both worlds,'
  - Presence of the proton's Bragg peak
  - Advantage of their high RBE to increase the tumor control probability

- The RBE of carbon ions has a estimated value of 3

# Protons

- Dr. Robert R. Wilson was the first propose the medical use of protons for cancer therapy in 1946
- 29 proton radiotherapy facilities worldwide (April 2010)
- More than 67.000 patients had been treated { nearly half for eye- Ocular melanoma }

1. Potentially better dose distribution
2. More expensive.($200 million)
3. Often combined with basic research (*e.g.* nuclear physics) or other applications (*e.g.* radiation testing for space applications) to be more cost efficient.
4. Large facility required.




Comparison to other radiation types

# Physical Properties

- A disadvantage of heavy ions is the extension of a small portion of dose behind the Bragg peak (the so-called **fragmentation tail**)

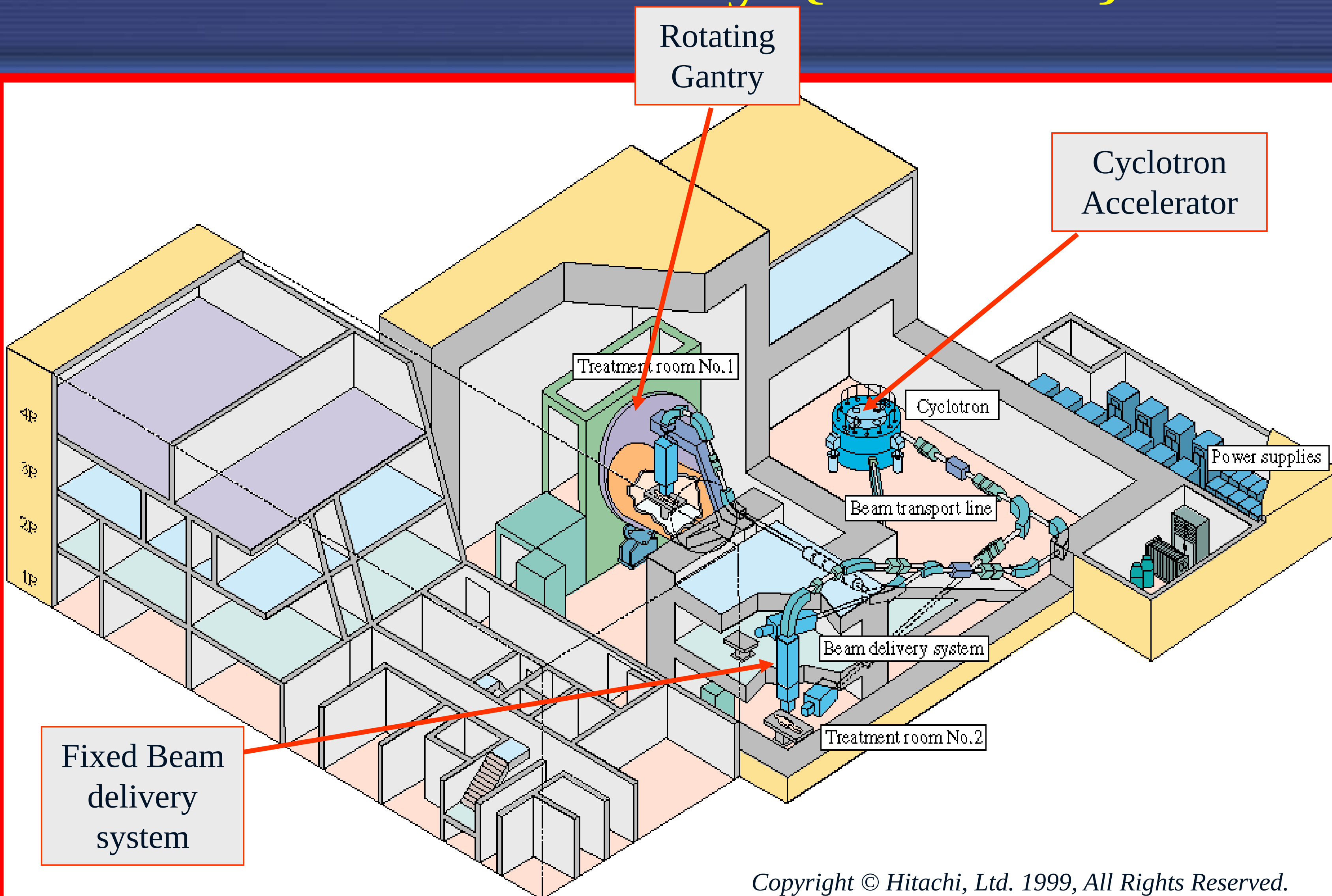
- In most clinical situations, however, the dose in the fragmentation tail is not higher than 10% of the dose to the target and thus causes no severe restrictions to the treatment plan.

# Spread out Bragg peak

- Bragg peaks are usually not wide enough to cover most treatment volumes.
- By superimposing a set of beams with decreasing energies and weights, a “spread out break peak” (SOBP) is generated:

1. Passive-beam shaping (using compensator)
2. Active-beam shaping (using Pencil beams)

# Tsukuba Facility {JAPAN}



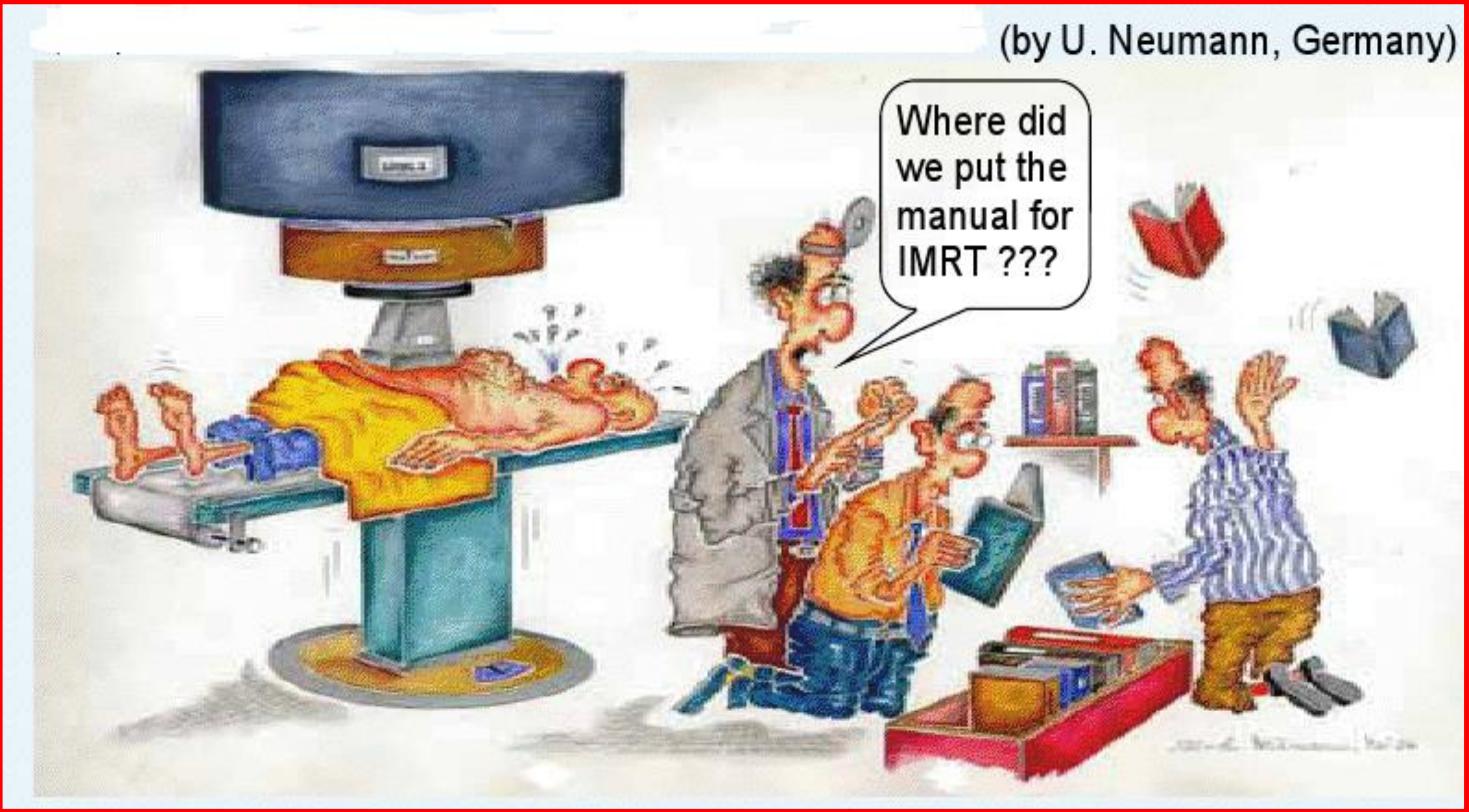
# Rotating Gantry at Loma Linda Proton Radiotherapy Centre {U.S.A}

# Beam production

1. Beam Production With Cyclotrons and Synchrotrons.
2. For protons, energies between 80 and 250 MeV are required.
3. To accelerate particles to such high energies, synchrotrons are better suited than cyclotrons.
4. Synchrotrons produce pulsed beams, and the energy can be varied from 1 cycle to the next in steps of a few MeV.
5. In most proton facilities, cyclotrons are used to produce proton beams with sufficient energy and beam intensity.

# Beam-Delivery Systems

- Although the weight of a proton gantry is around 100 tons and has a diameter of 10 meters.
- The size and weight of such a gantry together with the high spatial accuracy required for the beam position at the isocenter is probably the reason why no such gantry has been built up to now.
- Beams with 45° inclination are available together with horizontal beams.
- Another possibility is to move the patient rather than the beam. At some proton, treatment chairs and molds that can be rotated around the patient’s longitudinal axis by about 15° are available.




Thanks for your attentions