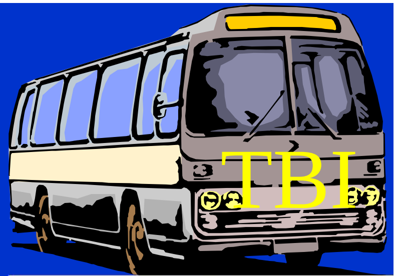
Total Body Irradiation

Subhashini John

Total Body Irradiation (TBI) History



1905	Dessauer - “X-ray bath”
1923	Chaoul & Lange - Lymphomas
1920s	Animal experiments to determine biological effects
1931	“Heublein therapy”, New York
1930s-40s	Used for nearly every malignant disease
	- Limited success
1942	Medinger & Craver reviewed 270 cases treated at Memorial between 1931-1940

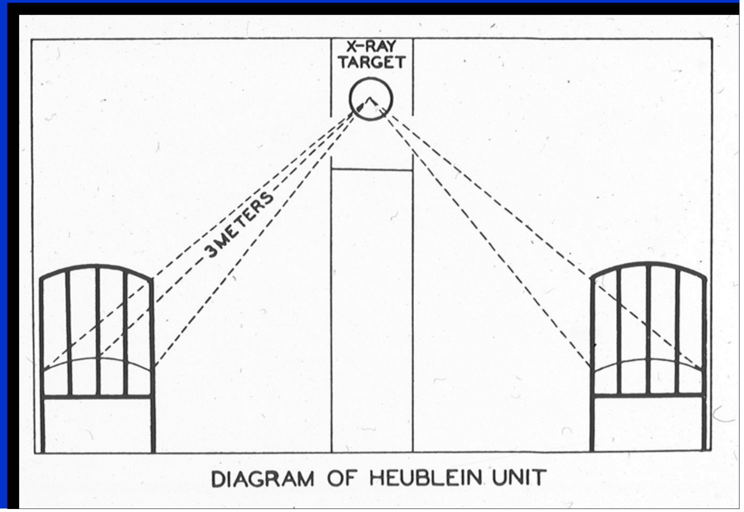
Total Body Irradiation (TBI) History

Early 1950s :Introduction of chemotherapy
- TBI declined

1954 Barnes & Loutit - Observed immune response after TBI in animals

1955-56 TBI & BMT in animals

1957- TBI & BMT in humans
- Leukemias
- Aplastic anemia
- Ewing's sarcoma
- Others



Total Body Irradiation (TBI) History

- 1970 – Pioneering work of Donald Thomas in Seattle
  - Proved usefulness of TBI
  - Increasing use and demand for TBI
- Dedicated equipment costly
- Modified standard Megavoltage RT equipment developed – less expensive

Total Body Irradiation (TBI) History

- Rationale for use of TBI not changed
- Tremendous change in
  - Delivery of TBI
  - Radiation sources used - Co60/ Linac
  - Dose measurement techniques - more reliable and accurate rather than erythema dose for determination of dose delivered

Indications for TBI

- Acute Leukemia – ALL, AML
- Chronic Leukemia – CML
- Myelodysplastic Syndromes
- Non-Hodgkin’s Lymphoma
- Multiple Myeloma
- Aplastic Anemia
- Autoimmune Diseases

ACR Practice Guidelines for the performance of TBI (Revised 2006)

Describes a quality assurance program for TBI

Supplementary to the ACR Practice Guideline for Radiation Oncology & the ACR Technical Standard for the Performance of Radiation Oncology Physics for External Beam Therapy

Introduction

Prior to transplantation of hematopoietic stem cells or peripheral blood progenitor stem cells, when Combined with intensive Chemotherapy TBI enables

– Myeloablative high dose therapy
– Immuno-ablative conditioning treatment

Tasks of TBI

- Immunosuppression - lymphocyte elimination to allow grafting of donor bone marrow
- Eradication of malignant cells - leukemia, lymphoma, rarely solid tumors
- Eradication of cells with genetic disorders - Fanconi's anemia, thalassemia major, Wiskott - Aldritch syndrome

Unique features of TBI

Valuable component of transplant preparative regimens vs chemotherapy

1. No sparing of "sanctuary" sites (testes, brain)
2. Dose homogeneity regardless of blood supply
3. No known cross-resistance with other agents
4. No problems with excretion or detoxification
5. Ability to tailor the dose distribution by shielding specific organs or by "boosting" sites

Interventions and Practices Considered

1. Process of Total body irradiation (TBI)
   - Clinical evaluation
   - Obtaining informed consent
   - Treatment planning
   - Simulation of treatment
   - Dose calculations
   - Treatment delivery and treatment aids

Interventions and Practices Considered

2. Qualifications & responsibilities of personnel
3. Patient and personnel safety measures
4. Types of equipment needed
5. Documentation
6. Continuing medical education programs for medical staff
7. Quality control and improvement & patient education

Clinical Evaluation

- Detailed history - issues that may impact upon treatment tolerance
  - Previous radiotherapy to sensitive organs
  - Factors affecting pulmonary, renal or hepatic function
  - Exposure to infectious agents
- Physical examination
- Review of all pertinent diagnostic and laboratory tests

Clinical Evaluation

- Communication with the referring physician and other physicians involved in the patient's care in accordance with the ACR Practice Guideline for Communication: Radiation Oncology

- Careful review of the applicable protocol for the particular disease being treated is essential since standardized institutional or cooperative group protocols are the norm for transplantation

Informed Consent

- Prior to simulation and treatment, informed consent must be obtained and documented and must be in compliance with applicable laws, regulations, or policies
- Detailed discussion of
  - Benefits
  - Potential tissue-specific acute and late toxicities
  - Details of, rationale for, and alternatives to TBI

Treatment Planning

Specific treatment parameters

- field size
- dose per fraction, dose rate, total dose, fractions per day, interval between fractions
- if relevant, beam energy, geometry to achieve dose homogeneity
- bolus or beam spoilers to increase skin dose
- shielding and dose compensation requirements (e.g., lungs, kidneys)
- boost specifications (e.g., testes)

Treatment Planning

Specific treatment parameters contd

- Patient thickness measurements at

  - The prescription point (often at the level of the umbilicus)

  - Other points of interest for dose calculations and homogeneity determinations - head, neck, mid-mediastinum, mid-lung, pelvis, knee, ankle, etc.

- Patient height - to determine the appropriate source-to-patient distance to appropriately fit the patient within the beam with sufficient margin around the patient (>5 cm, usually)

Simulation

- For lung or other organ blocking, simulation or other treatment planning is generally done in the treatment position
- If the planning session is performed in another position, positional differences in organ location should be taken into account, and the medical physicist should be consulted
- Reference points for block placement at the time of treatment should be marked on the patient's body for reproducibility

Calculation

- Medical physicist - to achieve the prescribed dose, dose homogeneity in locations specified by protocol & doses at any other points of concern
- A second medical physicist - independently checks the calculation before the first fraction
- In vivo dosimetry may aid in assessment of dose homogeneity
- Every effort should be made to maintain dose inhomogeneity to within +/-10%

Treatment Aids

Special TBI stands or tables are often used to aid in

- Immobilization
- Placement of organ shields
- Patient support and comfort

Treatment Delivery

- Fractionated or hyperfractionated regimens (twice a day or three times a day) in order to
  - Minimize both acute and chronic toxicities
  - Minimize overall treatment time
- Prior to treatment, any shielding of normal organs should be checked with portal images
- In the setting of single fraction low-dose TBI, total doses are typically only 200 cGy, organ shielding is not utilized

Treatment Delivery

- Dosimetry should be checked against department protocols to verify dose delivery at the extended distances that are usually used for treatment
- A medical physicist should be available during all treatments in case of questions regarding
  - dosimetric details
  - equipment function
  - patient setup, etc.
- Treatments are carried out by the radiation therapist per the ACR Practice Guideline for Radiation Oncology

Qualifications & Responsibilities of Personnel

Application of this guideline should be in accordance with the ACR Practice Guideline for Radiation Oncology

- Radiation Oncologist
- Qualified Medical Physicist
- Dosimetrist
- Nurse

Equipment

- High-energy photon beams
  - Linear accelerators in the range of 4–18 MV or
  - Co-60 unit
- Additional equipment may include a fluoroscopy or computed tomography (CT) simulator
- Immobilization devices
- Equipment to fabricate shielding blocks

Equipment

- Computers for dose calculations
- Beam spoiler
- Custom bolus, Custom compensators
- Dosimetry and calibration devices
- A backup beam delivery system must be available in case of unanticipated machine failure

Bone Marrow Transplant Procedure

1. High Dose Chemotherapy
2. Total Body Irradiation
3. Bone Marrow Transplant
4. Reverse Isolation For Bone Marrow Recovery
5. Long Term Observation and Management of Complications

Total Body Irradiation
Intent & Dose

Low dose TBI

- No transplant, generate immune response
- Lymphocytic leukemia, lymphoma, neuroblastoma
- Total dose of 100-150 cGy in 10-15 fractions

Total Body Irradiation
Intent & Dose

High dose TBI

- Intent
    - Preparatory for bone marrow transplant
        - Leukemia, myeloma, lymphoma, aplastic anemia
    - Kill tumour cells, Reduce immune response
- Dose
    - Single Fraction
        - 500 to 900 cGy
    - Fractionated
        - 1200 cGy in 2 # over 2 days
        - 1200 cGy in 6 # over 3 days (2#/day)

Advantages of Fractionated TBI

- Most Common schedule
  - 1200cGy in 6 Fractions over 3 days
    - dose/ Fractions =200cGy
    - Separated by minimum six hours
- Less side effects during treatment
- Lesser probability of pulmonary complications
- Generally maintains a high imunosuppressive effect
- Improves the therapeutic ratio

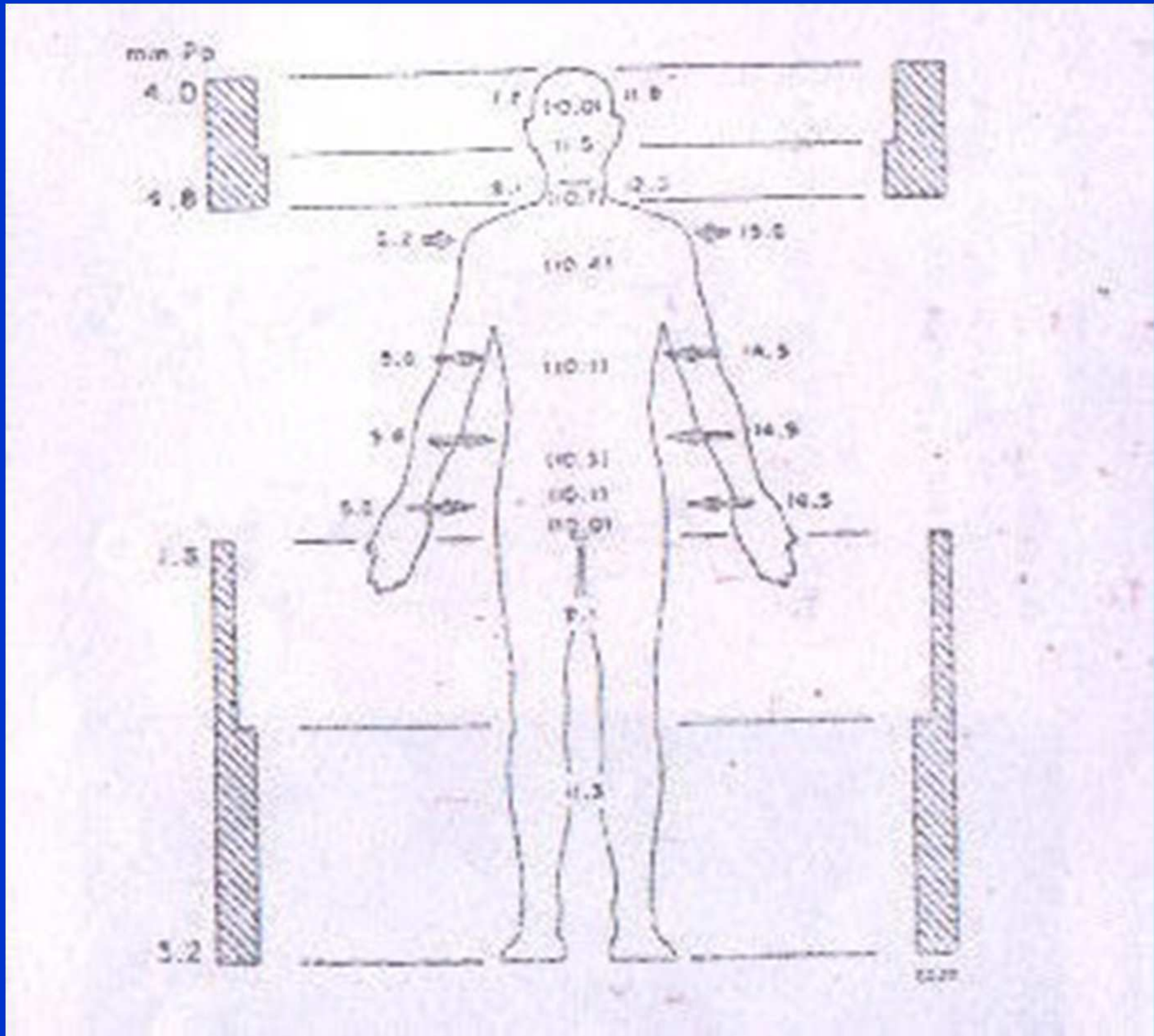
TBI Requirements - Clinical

- Dose Prescription point
- Intersection point of Line 1 and 2
  - Line 1 – intersection between the midsagittal and midaxial planes
  - Line 2 intersection between the mid corronal and mid axial planes

TBI Requirements - Clinical

- Required dose uniformity ± 5%
- Realistic ± 10%
- Low dose rate
- Less dose to Lung
  - < 700 cGy for single fraction of 900cGy
  - < 950cGy for 2 fractions of 600cGy (1200cGy)
  - <14Gy for fractionated TBI

Compensators for improved Homogeneous Dose



TBI Requirements - Physical

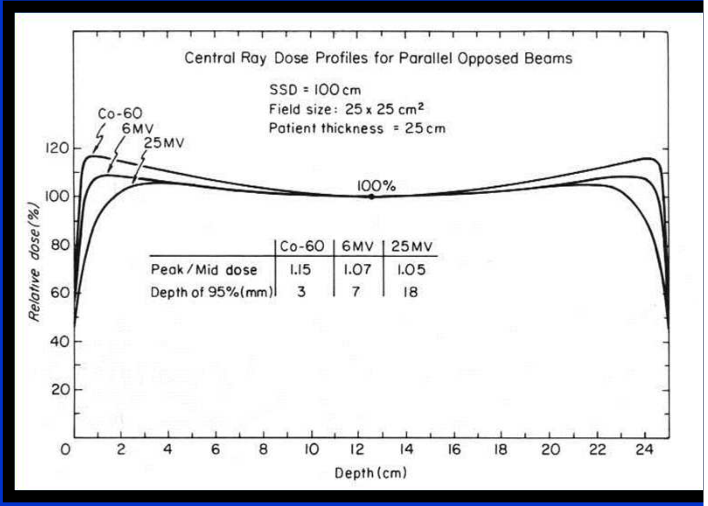
- Treatment Unit
  - Dedicated unit
  - Modified Conventional Machines
- Beam Energy
  - Mega-voltage (Cobalt unit or Linac)
- Field size - 50 x 200 cm^2
- SSD - 200 cm to 400 cm

TBI Requirements - Physical

- Technique
  - Parallel opposed (AP-PA or Lateral)
- Shielding
  - Partial lung shielding (1 HVL)
  - Kidney & liver may require shielding
- Dose Rate

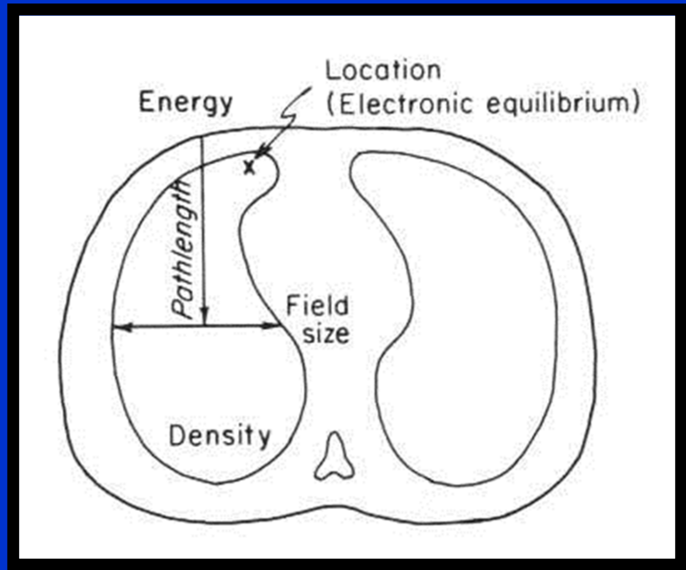
  Average 8 to 10 cGy / minute

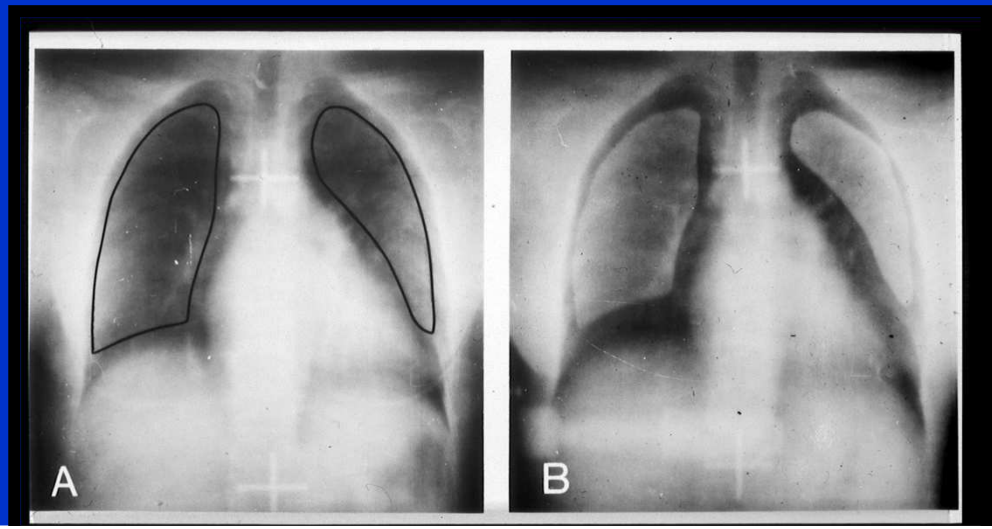
  Maximum up to 15 cGy)



Radiation Pneumonitis

- Major concern for whole lung irradiation
  - Especially TBI and HBI
- Factors affecting lung dose





TBI Treatment Variables

- Machine (Energy-Co60,4MV,6MV,10MV)
- Total Dose
- Fractionation
- Dose Rate
- Prescription point
- Compensators or bolus

TBI Treatment Variables

- Treatment fields: AP-PA, laterals, AP-PA sweep, combination, others
- SSD
  - – Vertical 150-200 cm
  - – Horizontal 240-550 cm

TBI Techniques

Dedicated Machines

- Single, dual & mulltiple sources
- Track mounted mobile sources
- Specially designed flattening filter
- Max. field size of $75 \times 210 cm^2$

TBI Techniques

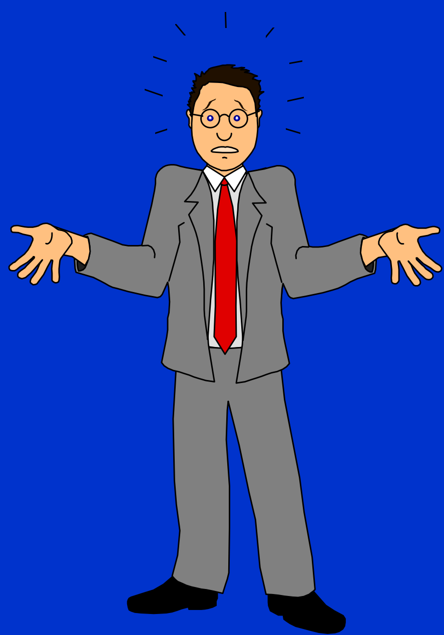
Modified Conventional Machines -

Large Stationary Beam, Stationary Patient

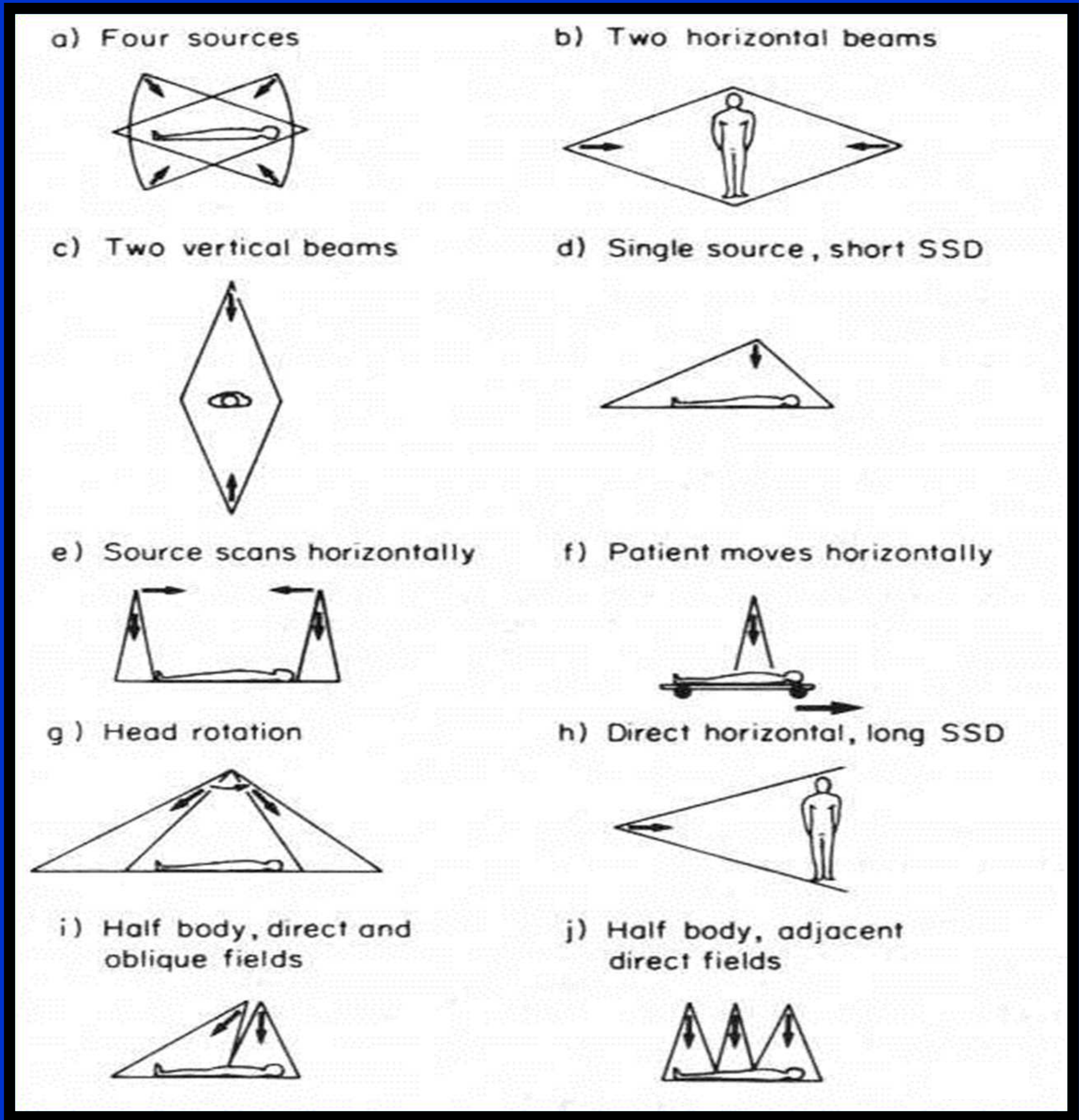
- – Extended SSD Technique
- – Collimator removal method

Moving Beams produced by

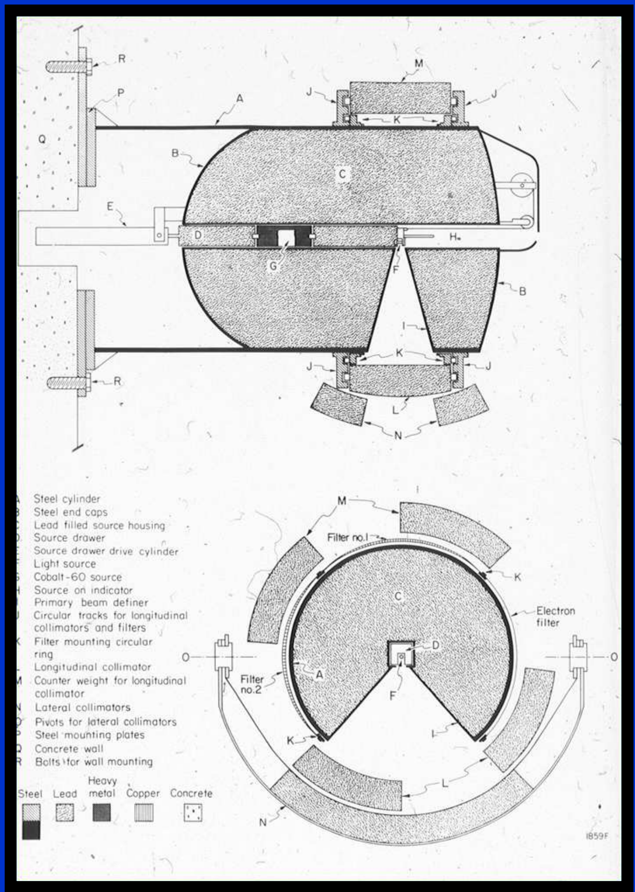
- – Translational beam method
- – Sweeping beam TBI
- –



TBI-Irradiation Methods



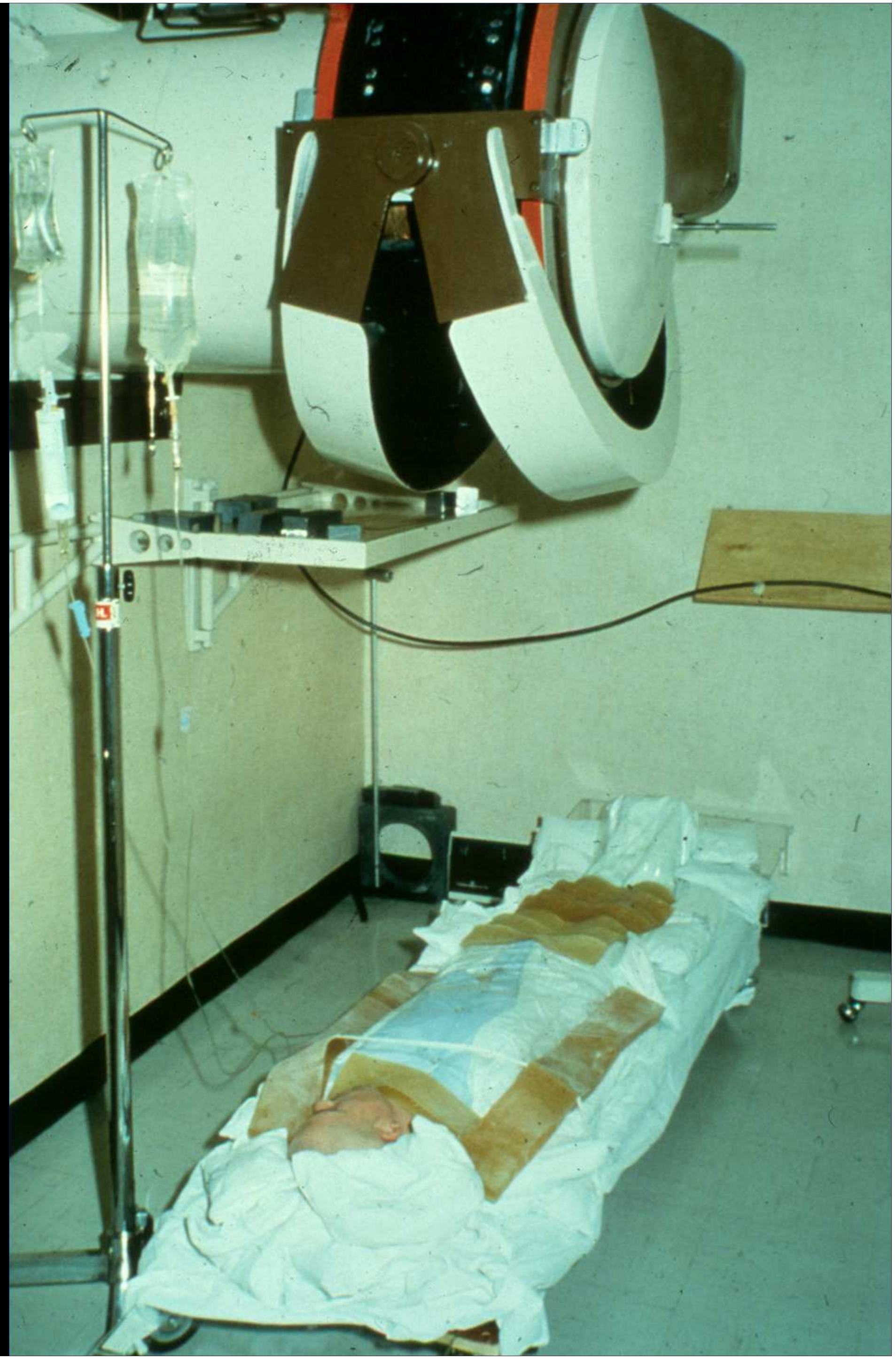
Princess Margaret Hospital (PMH), Toronto - Hemitron



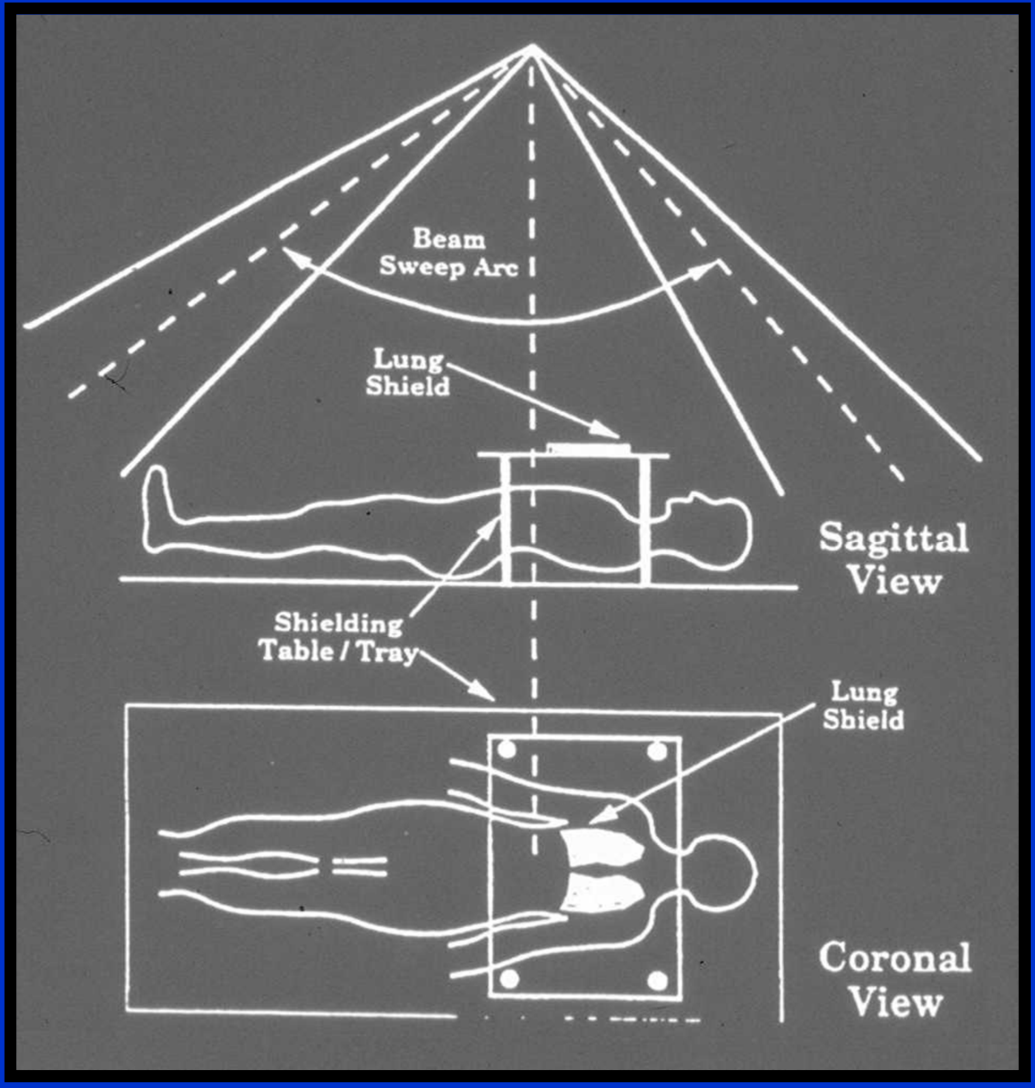
Princess Margaret Hospital, Toronto

Hemitron

- Cobalt-60
- 80×250 cm^2 @ 150 cm

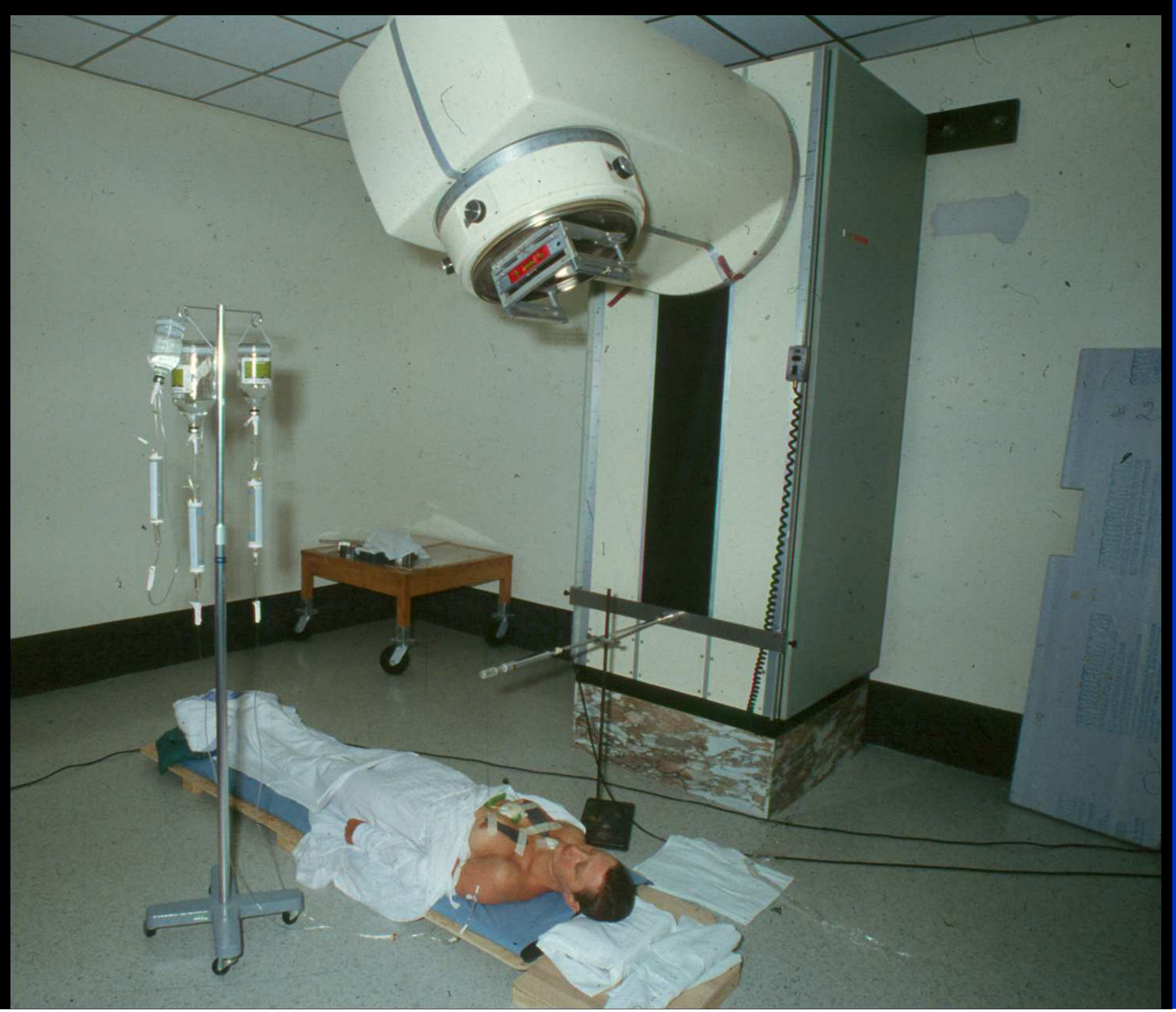


McGill University
Sweeping Beam Technique



TBI: McGill Technique

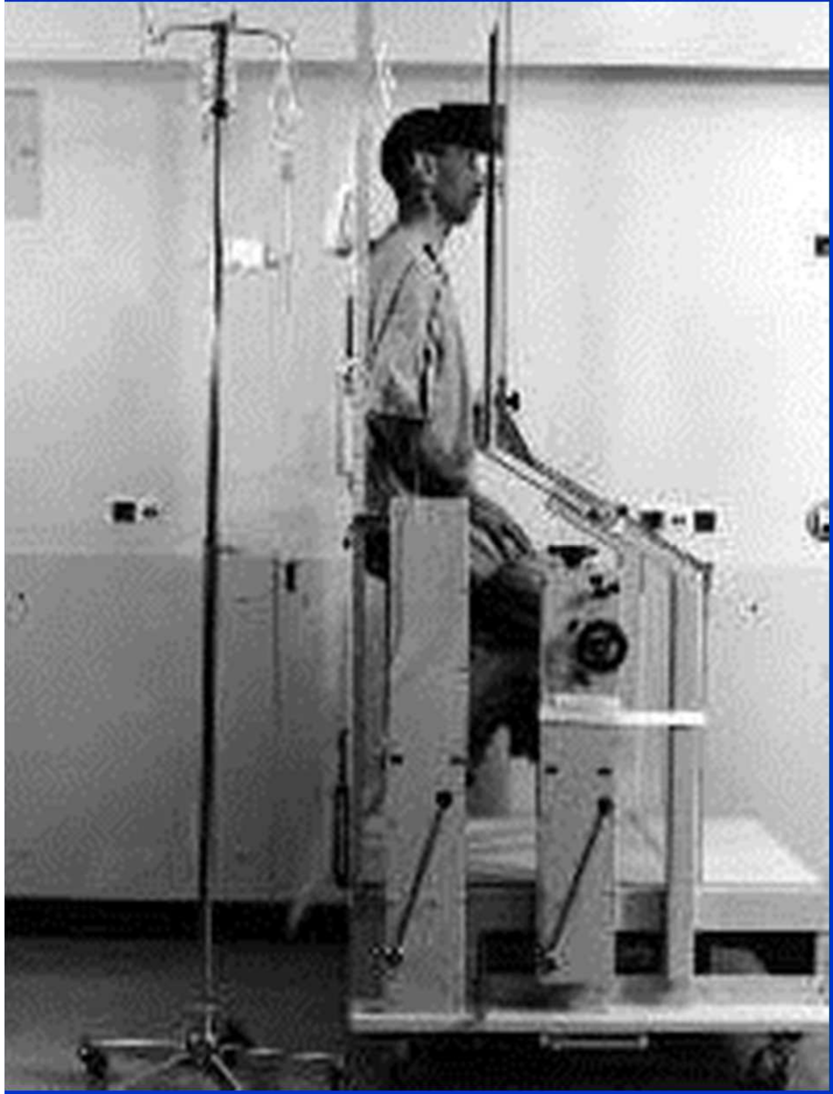
McGill University
Sweeping Beam Technique



Translational Couch

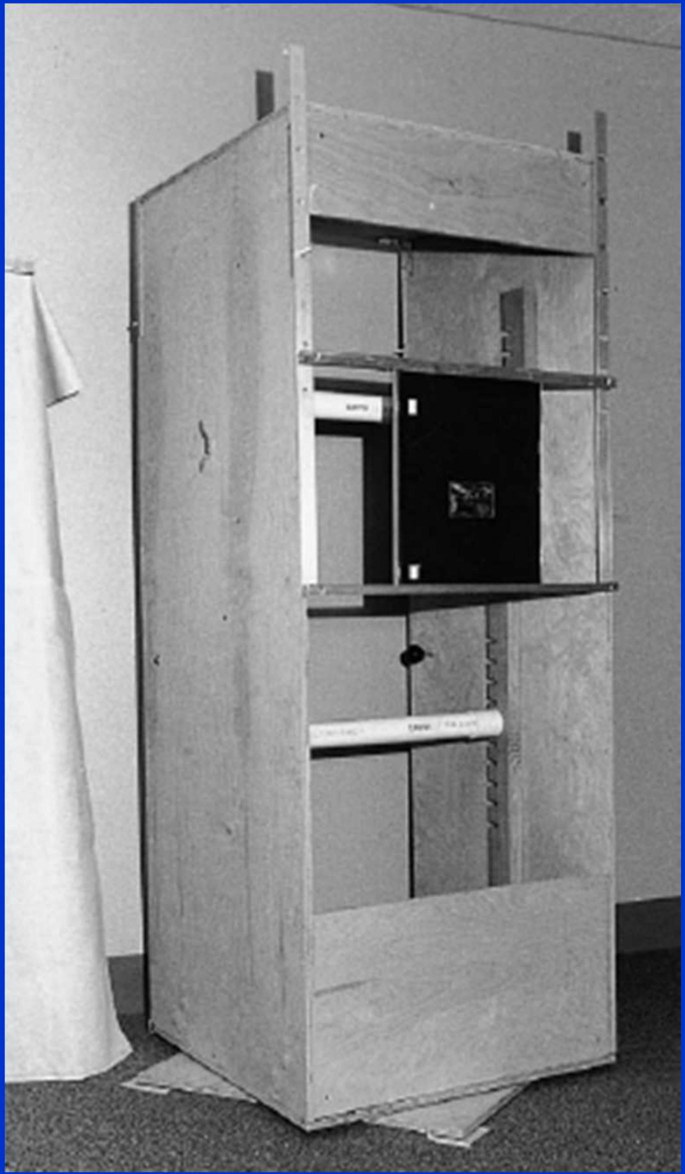
Computer controlled

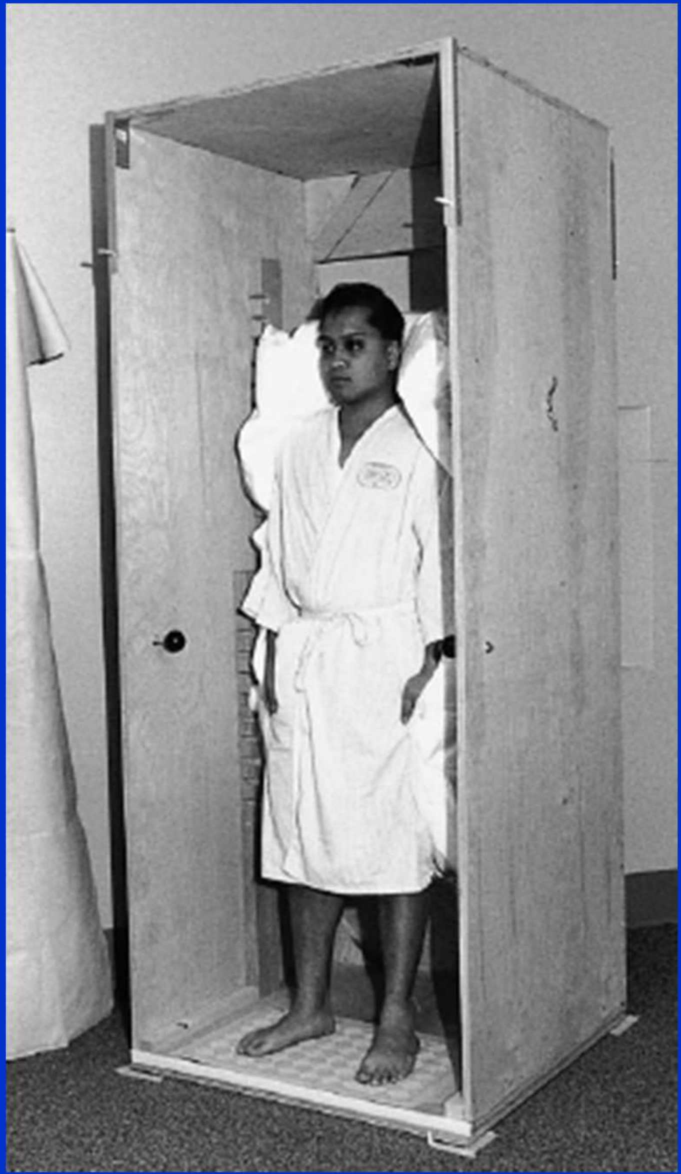
The Utrecht TBI Chair



- Devoloped at the University Hospital of Utrecht
- To have equal sagittal thickness both in trunk and legs
- Perspex attenuators to guarantee maximum skin dose

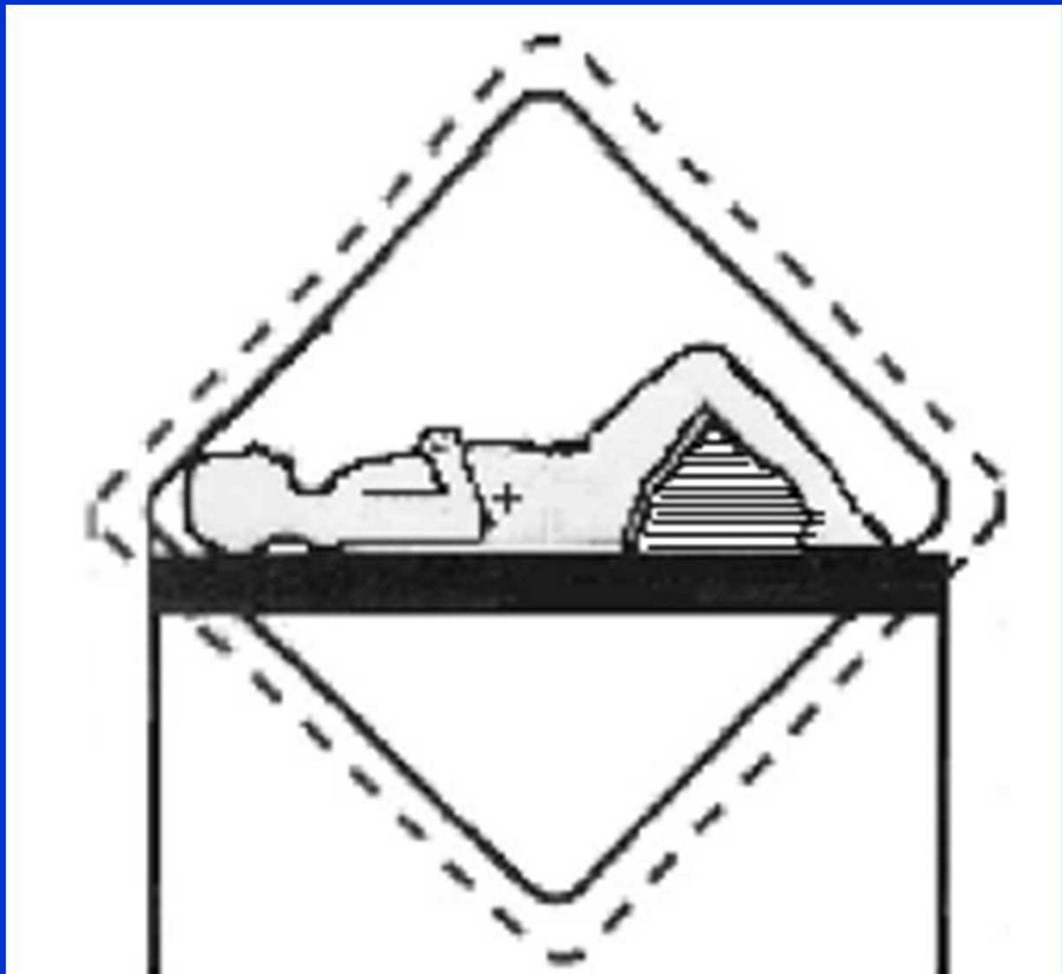
Isocentrically mounted stand





Lateral on Couch – extended SSD

TBI at Vellore – Lateral Couch extended SSD



TBI – Commissioning measurements at CMC,Vellore

- Choice of Unit & energy
  - Linac & 6 MV beam
- Output Calibration at Extended SSD
- Beam profiles measurement for the extended SSD
- Measurement of depth dose (PDD/TMR)

TBI – Commissioning measurements at CMC,Vellore

- Skin dose
  - choice of beam spoiler position & thickness
- Calibration of Diodes for in vivo dosimetry at Treatment conditions
- Preparation of Protocol for patient positioning
- Measurement of attenuation coeff for aluminium and perspex to be used as tissue compensator

Beam spoiler
to enhance surface dose

Output Measurement at extended SSD (at D_{max})

- Dosimeter
  - SSD meter Capintec .6cc farmer chamber
- Phantom
  - Perspex
- Beam spoiler
  - 1cm perspex
- Protocol

  IAEA TRS 398
- SSD = 385 cm

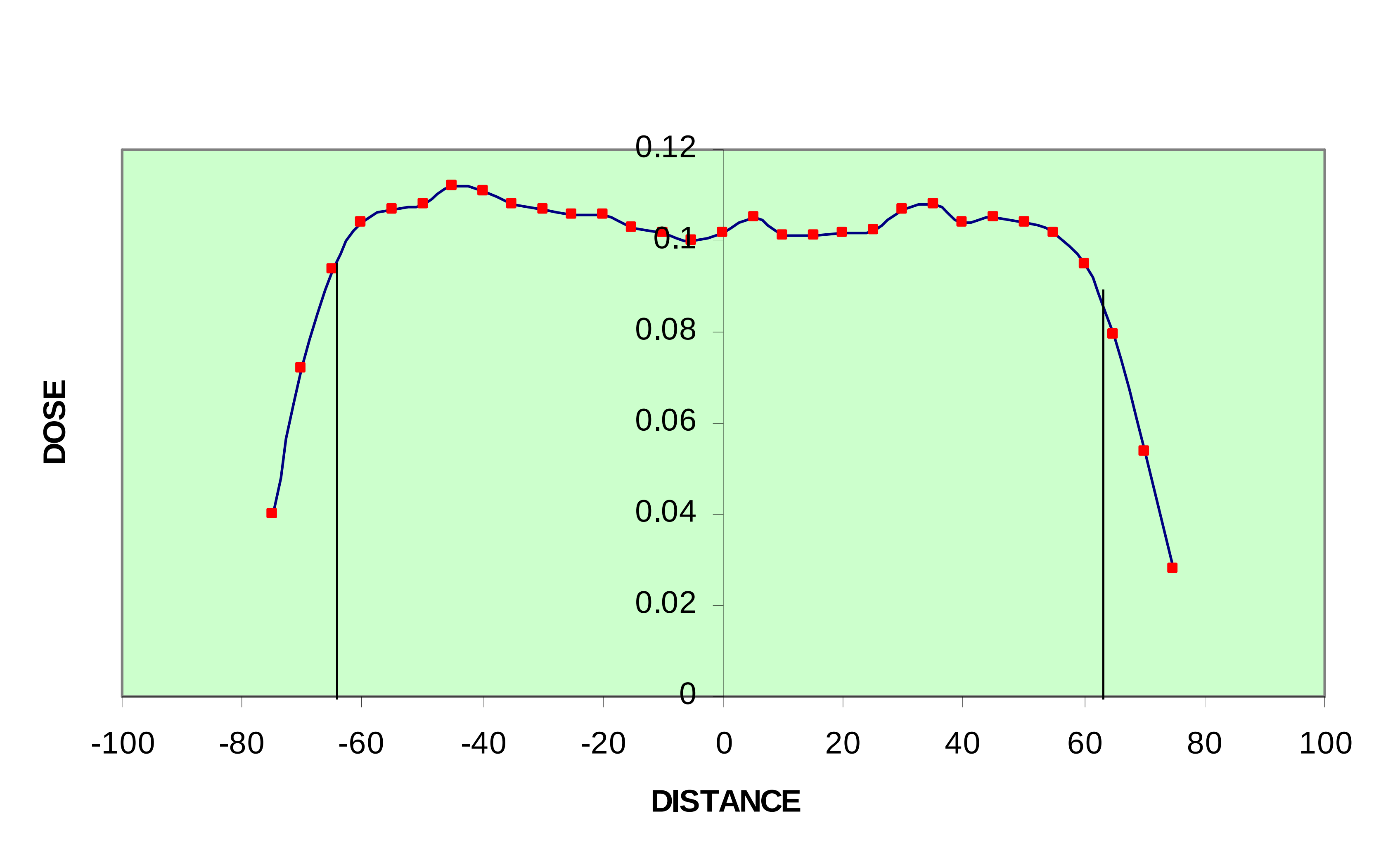
Beam Profile Measurement

- Detector
  - PTW Diodes 8 nos
- Placed 10 cm apart
- Profile for 150 cm measured by moving the diodes by 5 cm.
- Acrylic sheets used as back scatter material
- Profile measured at SSD 385cm

Verification of the Beam Profile

The patient setup is simulated with perspex sheets

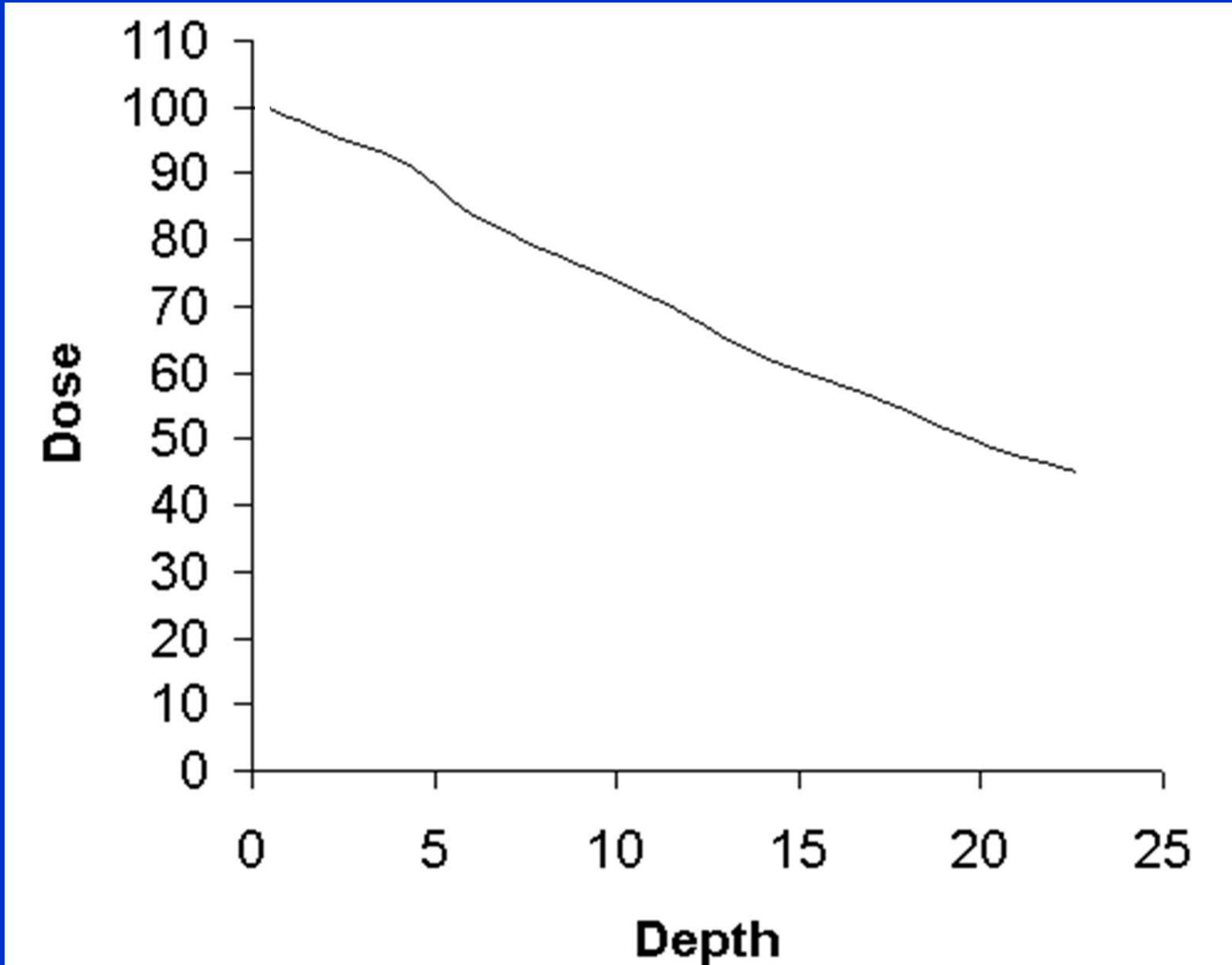
Profile at extended SSD with Beam spoiler

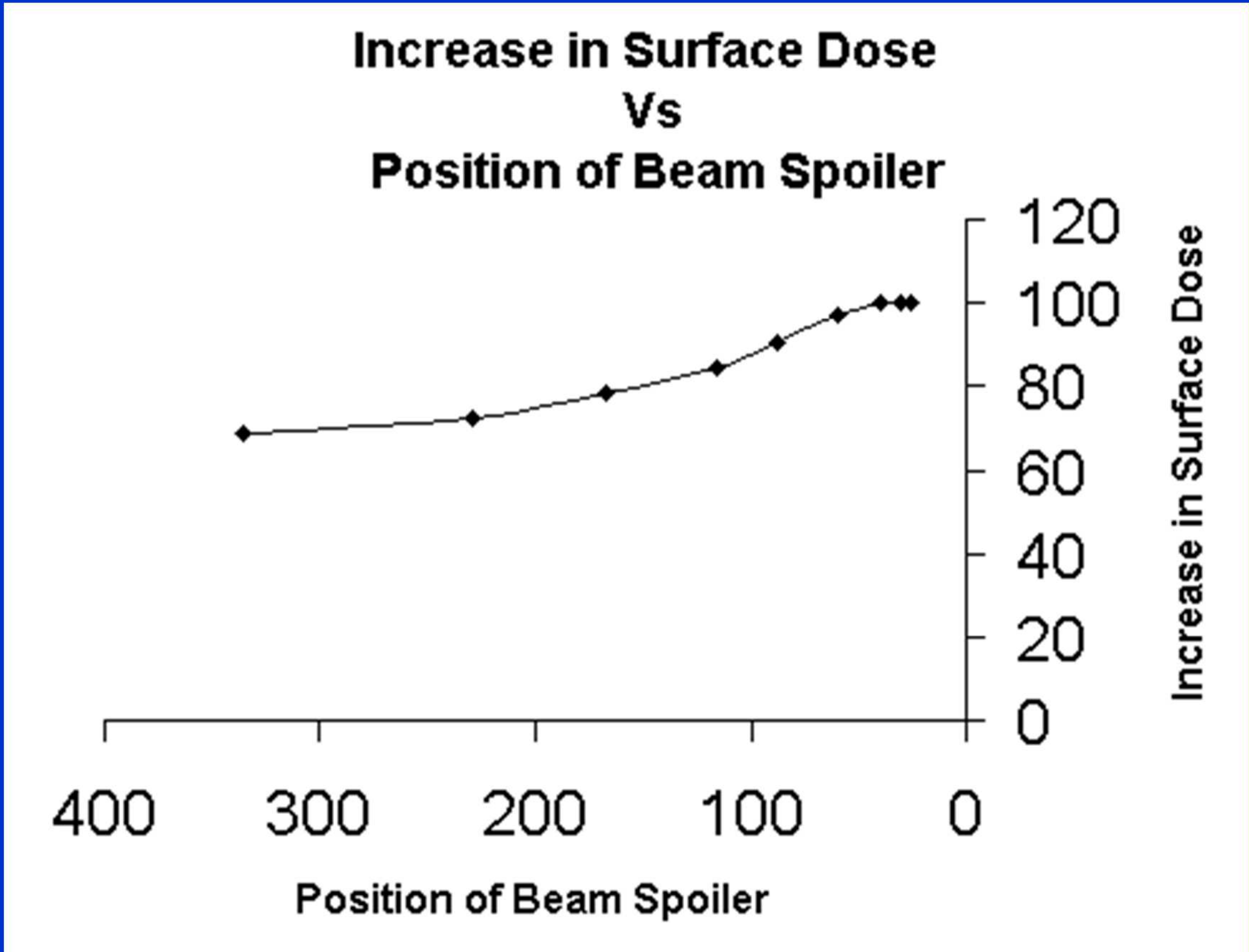


Percentage Depth dose at extended SSD

- Dosimeter
  - SSD meter Capintec .6cc farmer chamber
- Phantom
  - Perspex
- Beam spoiler
  - 1cm perspex
- Chamber placed at different depths
- SSD = 385 cm

Percentage Depth Dose at Extended SSD




Increase in Surface Dose
Vs
Position of Beam Spoiler
120
100
80
60
40
20
0
Increase in Surface Dose
400
300
200
100
0
Position of Beam Spoiler

Calibration of Diodes for In vivo-Dosimetry

- PTW diodes were placed at the middle of the phantom
- Exposed to known dose at D_{max}
- Calibration factor determined for each diode

TBI Treatment Protocol CMC Vellore

- Day – 5
  - Set-up measurements
  - Measurements of separation of different regions
- Day – 4
  - Calculation of attenuator thickness & MU
- Day – 3
  - TBI first fraction with in-vivo dosimetry (AM)
- Verification of Attenuator thickness
  - TBI second fraction with corrected attenuator thickness (if required)

TBI Treatment Protocol CMC Vellore.

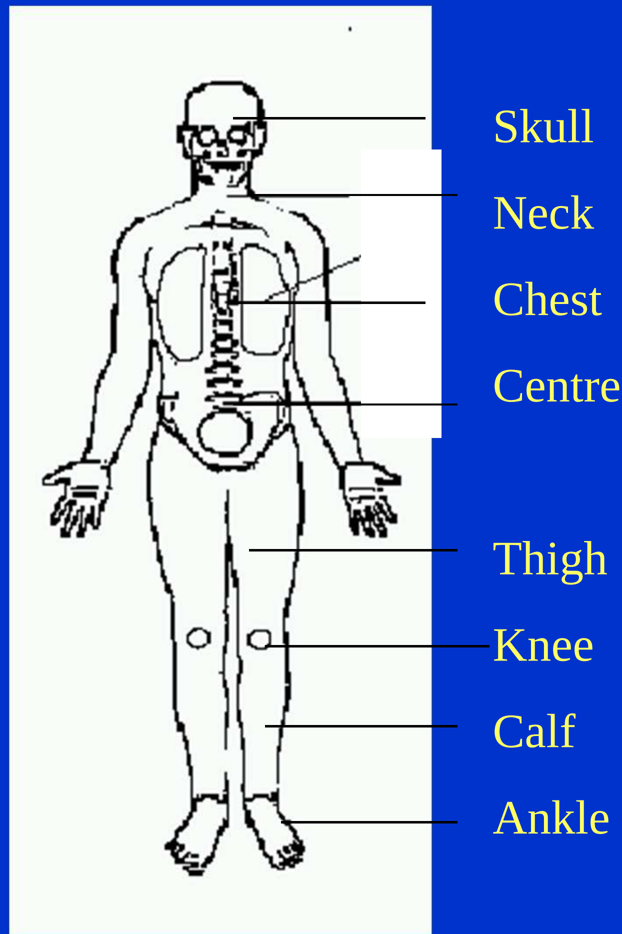
Day – 5:Patient Setup and Positioning Measurements

	Patient Name:		Patient No:	
1	Position the height of linac couch		121	cm
2	Collimator angle		45	^{0}
3	Gantry angle		90	^{0}
5	Measure patient length		135	cm
6	Fix source to surface distance **(SSD)**		285	cm
7	Check the patient with light beam			
8	Place the Diodes			
9	Measure the distance			
	I	EAM level	298	cm
	II	Centre level	285	cm
	III	Knee level	294.4	cm
	IV	Ankle level	298.5	cm
10	Distance between beam spoiler and isocenter		254	cm

Measurement of Separations

Day – 5

Regions	Separation (cm)
Skull	15.50
Neck	11.00
Shoulder	45.00
Chest	31.00
Center	35.00
Thigh	32.00
Knee	21.00
Calf	20.50
Ankle	13.50



Compensator Thickness

Day – 4

- The formula used is

$$I = I_o e^{-\mu t}$$

where, I - Transmitted intensity of radiation

I_o - Incident intensity of radiation

μ - Linear attenuation coefficient

t - Compensator thickness

Calculation of Compensator Thickness

Day – 4

Sl. No	Position	PDD	Mid Plane Dose (cGy)	Thickness of Aluminium	Thickness of Perspex (cm)
1	Skull	85.8	129.02	26.8	4.7
2	Neck	90.5	136.09	32.4	5.7
3	Shoulder	50.5	75.94	-29.0	-5.0
4	Chest	66.5	100.00	0.0	0.0
5	Umblicus (Center	66.5	100.00	0.0	0.0
6	Thigh	69	103.76	3.9	0.7
7	Knee	73.5	110.53	10.5	1.8
8	Calf	75.5	113.53	13.4	2.3
9	Ankle	88	132.33	29.5	5.1

Treatment setup - check sheet

Day – 3

	Patient Name:		Patient No:		Date	
					F/N	A/N
1	Position the height of linac couch		121	cm		
2	Collimator angle		45	^{0}		
3	Gantry angle		90	^{0}		
4	Measure patient length		135	cm		
5	Fix isocentre to surface distance **(SSD)**		285	cm		
6	Check the patient with light beam					
7	Place the Diodes					
8	Measure the distance					
	I	EAM level	298	cm		
	II	Centre level	285	cm		
	III	Knee level	294.4	cm		
	IV	Ankle level	298.5	cm		
9	Distance between beam spoiler and isocenter		254	cm		
10	Place the compensators					
	I	Head	4.70	cm		
	II	Neck	5.70	cm		
	III	Knee	10.53	mm		
	IV	Calf	13.36	mm		
	V	Ankle	29.49	mm		

Patient Positioning

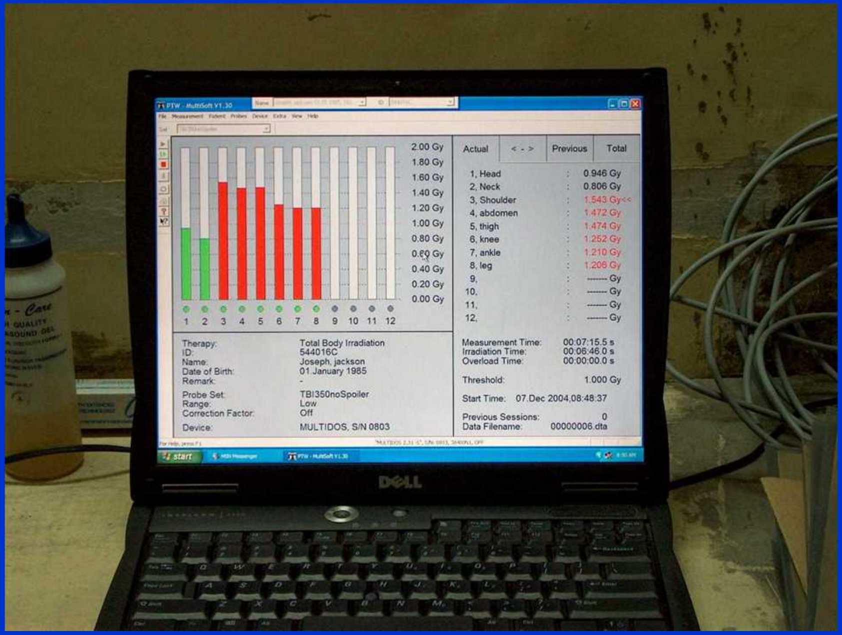
Day – 3

- **40 x 40 cm Field Size, Gantry 90º**
- **SSD 385 cm, Measurements**

In-vivo Dosimetry with Diodes

Day – 3

Diodes placed on patient



On-line dosimetry

Dose Guided Radiotherapy (DGRT)!!!!!!

In-Vivo Measurements

REGION	MID PLANE DOSE				
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Skull	92.5	102.7	90.8	99.3	97.0
Neck	102.2	97.7	93.7	87.6 +	101.1
Chest	104.9	98.6	98.0	100.6	89.6
Umbilicus	100.0	100.0	100.0	100.0	100.0
Thigh	98.4	104.4	106.6	98.5	102.2
Knee	90.7	94.9	91.9	94.5	95.7
Calf	93.1	91.2	95.4	92.3	91.9
Ankle	109.6	100.8	95.4	101.1	98.0

Acute Complications of TBI

- Mucositis
- Hair loss
- Bone marrow suppression
- Veno-occlusive disease of liver
- Interstitial pneumonitis
- GI toxicity

Chronic Complications of TBI

- Pulmonary
  - Restrictive disease (8%)
  - Alteration in DLCO (12%)
- Ocular (29.5%) – cataract, dryness, keratitis
- Thyroid – Hypothyroidism, thyroiditis, Basedow's disease
- Infertility
- Secondary malignancies
- Radiation nephropathy

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Thank You