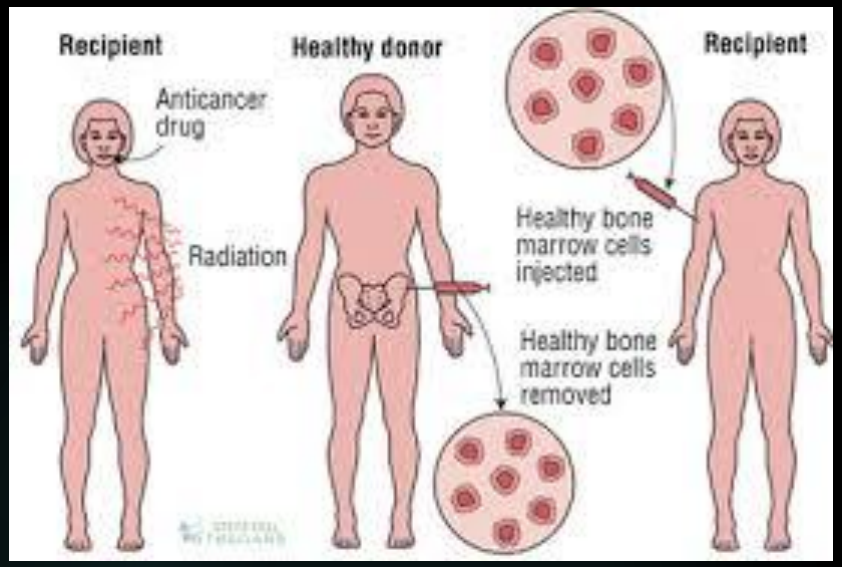
PLANNING OF TOTAL BODY IRRADIATION

DR. SAURABHA KUMAR

Outline

- What is TBI
- Indications
- Radiobiology
- Physics
- Techniques
- Pre-planning
- Planning
- Dosimetry
- AAPM guidelines
- Toxicities



- **Definition**
- **It is a type of Magnafield radiation where the entire body is irradiated to ablate the bone marrow and cause immunosuppression prior to bone marrow transplantation.**

Indications

Myeloablative Task
Uses high doses of radiation for irreversible elimination of the clonogenic cells causing complete and lasting bone marrow suppression, which requires stem cell support for recovery

Non-Myeloablative Task
Employs lower doses of radiation to induce immunosuppression and minimal cytopenia. Its better tolerated, especially in older and frail patients.

Myeloablative-Hematolymphoid

- ✓ ALL
- ✓ AML
- ✓ CML
- ✓ Hodgkin Lymphoma at relapse or PD
- ✓ NHL at relapse or PD
- ✓ Multiple myeloma
- ✓ Mantle cell lymphoma

- **Myeloablative Solid Tumours**

✓ Ewings sarcoma/PNET

✓ Neuroblastoma

✓ Medulloblastoma

- **Non-Myeloablative**

✓ Aplastic Anemia

✓ Myelofibrosis

✓ Fanconi' anemia

✓ Thalessemia

Advantages

- No sparing of ‘sanctuary sites’ such as testes and CNS.
- Dose delivered is fairly homogenous & independent of blood supply.
- No cross resistance with other agents .
- No detoxifications / excretion of a chemical agent necessary, therefore no alteration of dose if these mechanisms are impaired.
- Dose distribution within body may be tailored by either blocking normal tissue that are more sensitive or boosting areas at greater risk of recurrence .

Radiobiology

Intrinsic Radiosensitivity

- **The D_0 of normal lymphocytes has been reported to be 0.5 to 1.4 Gy.**
- **This D_0 suggests that normal lymphocytes cells are very sensitive to ionizing radiation.**

Repair

- **A very small shoulder on the radiation cell survival curve has been noted suggesting little repair between fractions of radiation.**

Reoxygenation

- **Radiobiologically relevant levels of hypoxia are unlikely in the hematopoietic compartment.**

Repopulation

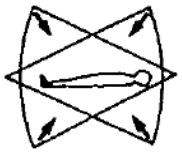
- **It is not likely to influence hematopoietic cell survival, given the short duration of most TBI regimens (1-5 days).**

Technique of TBI

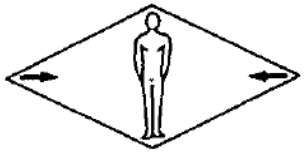
Practically, the choice will depend on –

- **The equipment available.**
- **Its workload with conventional treatments .**
- **Construction of a dedicated facility is not always practical, therefore use of existing unit is more reasonable alternative.**

a) Four sources



b) Two horizontal beams

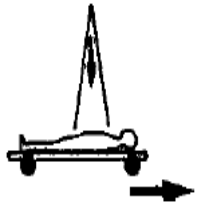


c) Two vertical beams

d) Single source, short SSD

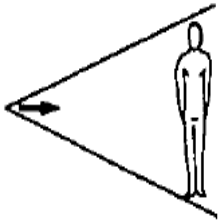
e) Source scans horizontally

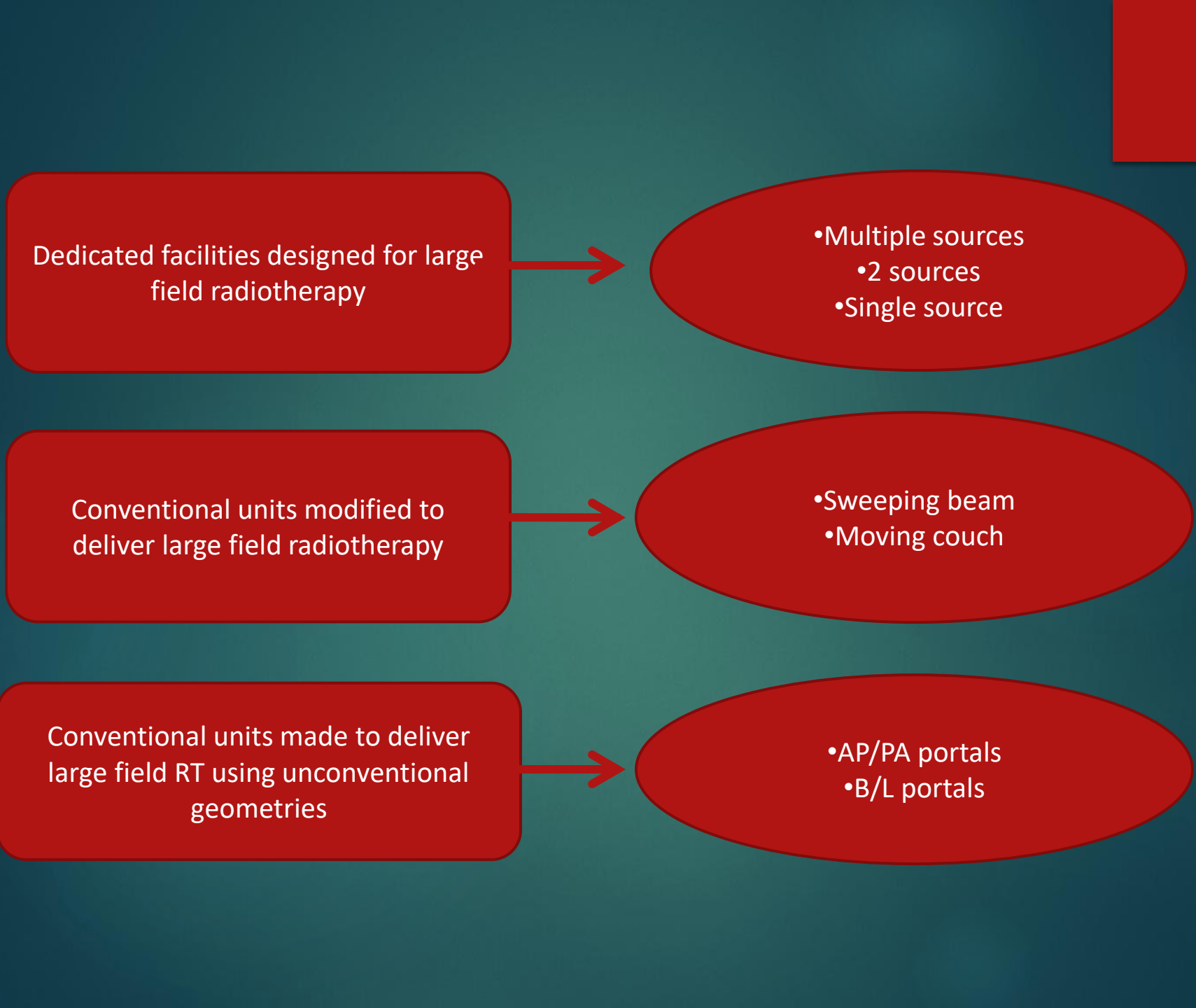
f) Patient moves horizontally



g) Head rotation

h) Direct horizontal, long SSD




Dedicated facilities designed for large field radiotherapy
•Multiple sources
•2 sources
•Single source
Conventional units modified to deliver large field radiotherapy
•Sweeping beam
•Moving couch
Conventional units made to deliver large field RT using unconventional geometries
•AP/PA portals
•B/L portals

Stationary beam TBI technique

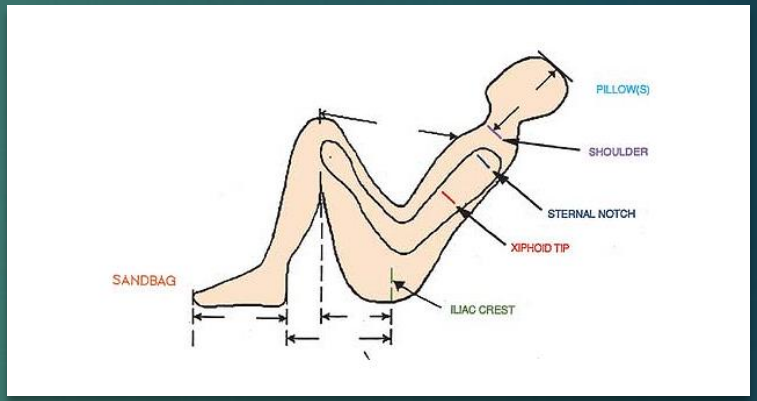
1. **Bilateral Technique**

- **Advantages:**

  - Easier to set up

  - More comfortable to patient in sitting / supine position

  - Posterior lung compensation easily achieved in adults using upper arm



- **Disadvantages :**

  - Dose variation is greater

  - Compensators are usually necessary

2. AP/PA Technique

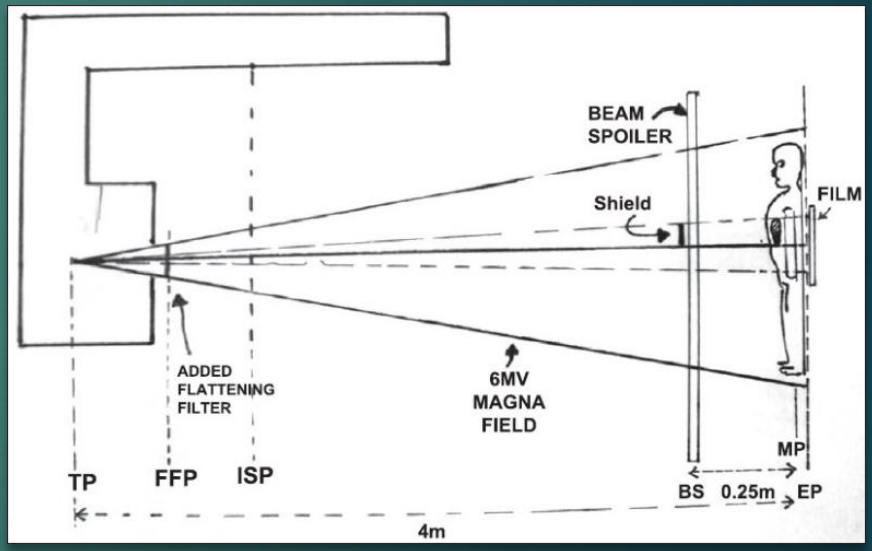
- **Advantages**

  - Minimizes patient thickness along the central axis of beam

- **Disadvantages:**

  - Needs lung block or other means to reduce lung doses

  - Requires patient to stand/ sit perfectly still.



	Bilateral technique	AP/PA technique
Patient position	More comfortable Easier to set-up	Less comfortable
Thickness along long axis beam	More	Less
Dose variation	Greater	Less
Lung shielding	Arm can provide lung shielding (posteriorly)	Lung block is needed

Preplanning

- H/O previous radiotherapy to sensitive organs, h/onpulmonary, renal or hepatic dysfunction, and exposure to infectious agents may impact treatment tolerance.
- Physical examination.
- Review of all relevant diagnostic and laboratory tests.
- Communication with the referring physician and other physicians involved in the patient's care .
- Whether a female patient is pregnant before initiating any component of a transplant program, including TBI

-If the patient is pregnant, alternative therapies in an effort to preserve the pregnancy versus termination of pregnancy and continuation with transplantation must be decided upon.

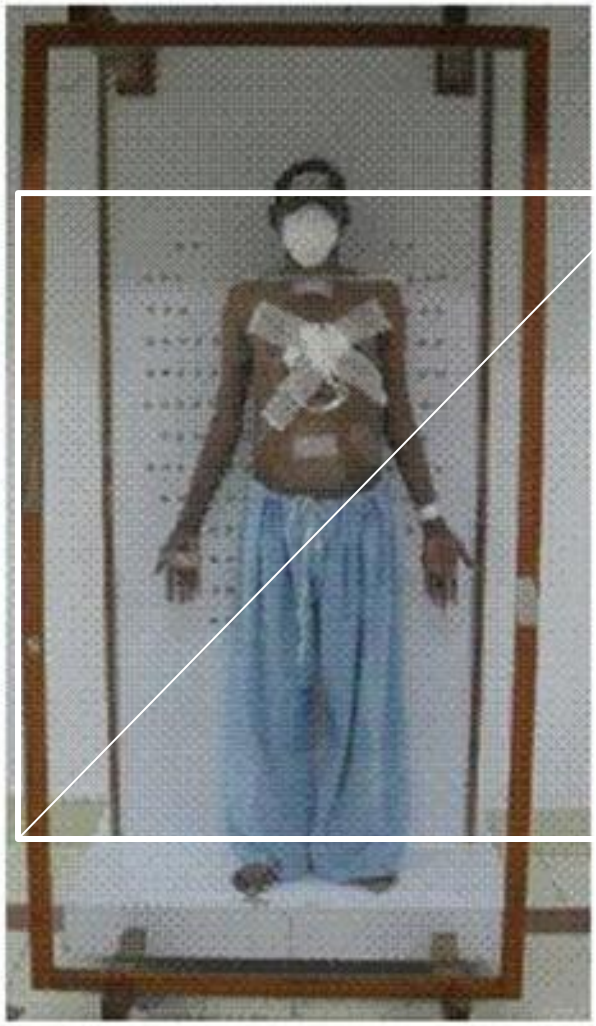
- Informed Consent : Prior to simulation and treatment.
- This should include a detailed discussion of the benefits and potential tissue-specific acute and late toxicities of TBI, as well as the details of rationale for and alternatives to TBI.

Treatment Planning

Specific treatment parameters to be determined -

- **Field size - Height of patient, SSD**
- **T/D/F parameters - dose per fraction, dose rate, total dose, fractions per day.**
- **Beam energy – Thickness of the patient**
- **Geometry to achieve dose homogeneity.**
- **Bolus or beam spoilers to increase skin dose,**
- **Shielding and dose compensation requirements (e.g., lungs, kidneys), and boost specifications (e.g., testes).**

Field size, SSD, Pt height



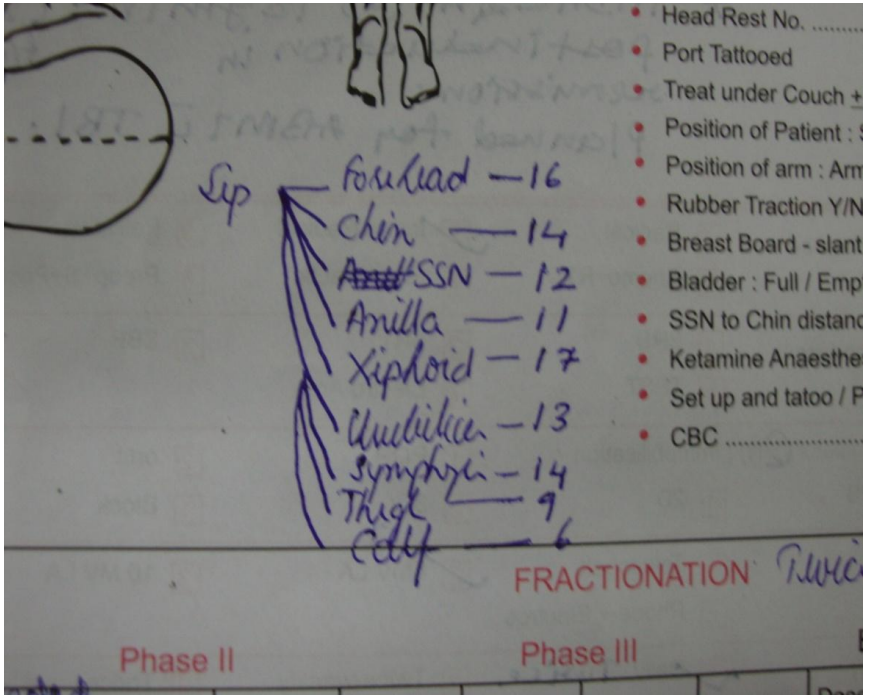
- **Patient height - to determine the appropriate source-to-patient distance to appropriately fit the patient within the beam with sufficient margin around the patient (>5 cm, usually)**
- **Target volume- whole body, including the skin, as the target cells are widely disseminated, all manifest or occult clones of malignant cells, including those circulating and the whole cellular immune system**
- **Collimate by 45 degree**

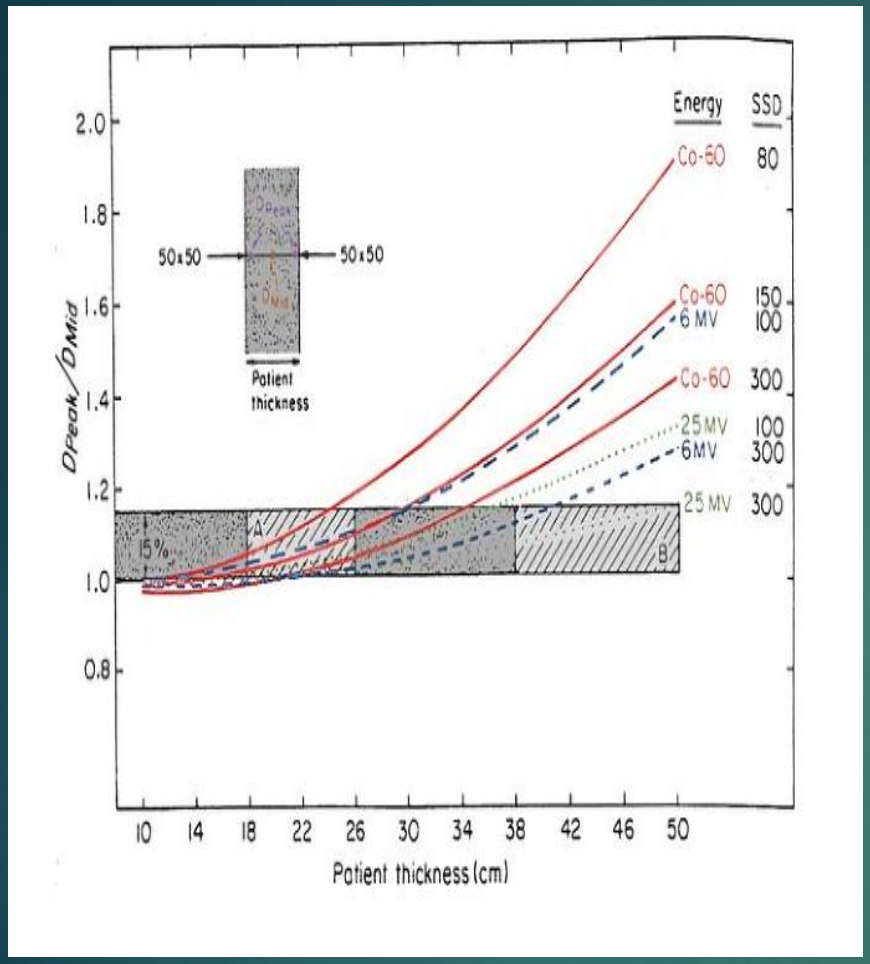
T/D/F Parameter

- **Retrospective data –Lowering dose rate [<0.025Gy-0.09Gy] reduces the incidence of pneumopathy.**
- **Dose >13.2Gy :higher incidence of VOD.**
- **Fractionated regimen decreases incidence of VOD.**
- **Randomized study [Seattle] –Fractionated TBI 2Gy x 6# is superior in terms of event free survival as compared to single dose TBI [10Gy] .**
- **Fractionated TBI to a total dose of 13-15Gy roughly equivalent to 10Gy single dose TBI .**

Pt thickness, beam energy, SSD

- Patient thickness measured at the prescription point (often at the level of the umbilicus), and at other points such as :
  - Forehead
  - Chin
  - SSN
  - Axilla
  - Xiphoid
  - Symphysis pubis
  - Thigh
  - Calf



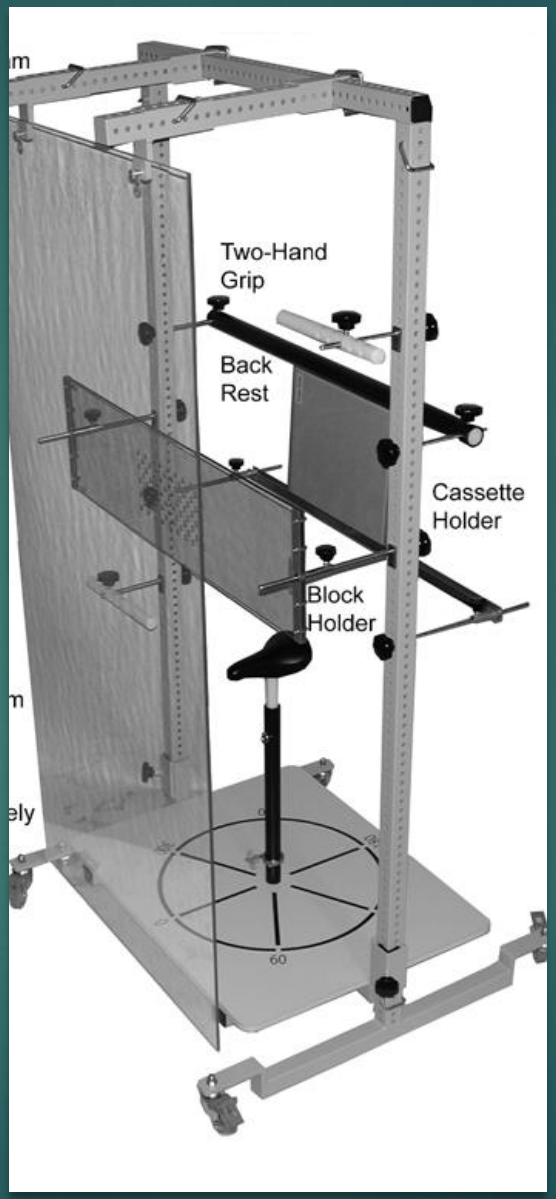


- **Ratio of peak dose to the midline dose on the central ray as a function of patient thickness for parallel opposed radiation fields**

- ✓ Higher the energy, lower the dose variation.
- ✓Larger the treatment distance, lower the dose variation.
- ✓Larger the patient diameter, larger the dose variation.
- ✓AP/PA treatments will yield a variation not larger than 15% for most megavoltage energies and distances.
- ✓Greater dose variation for lateral opposed beams compared to AP/PA treatments especially for adult patients.

Treatment Aids

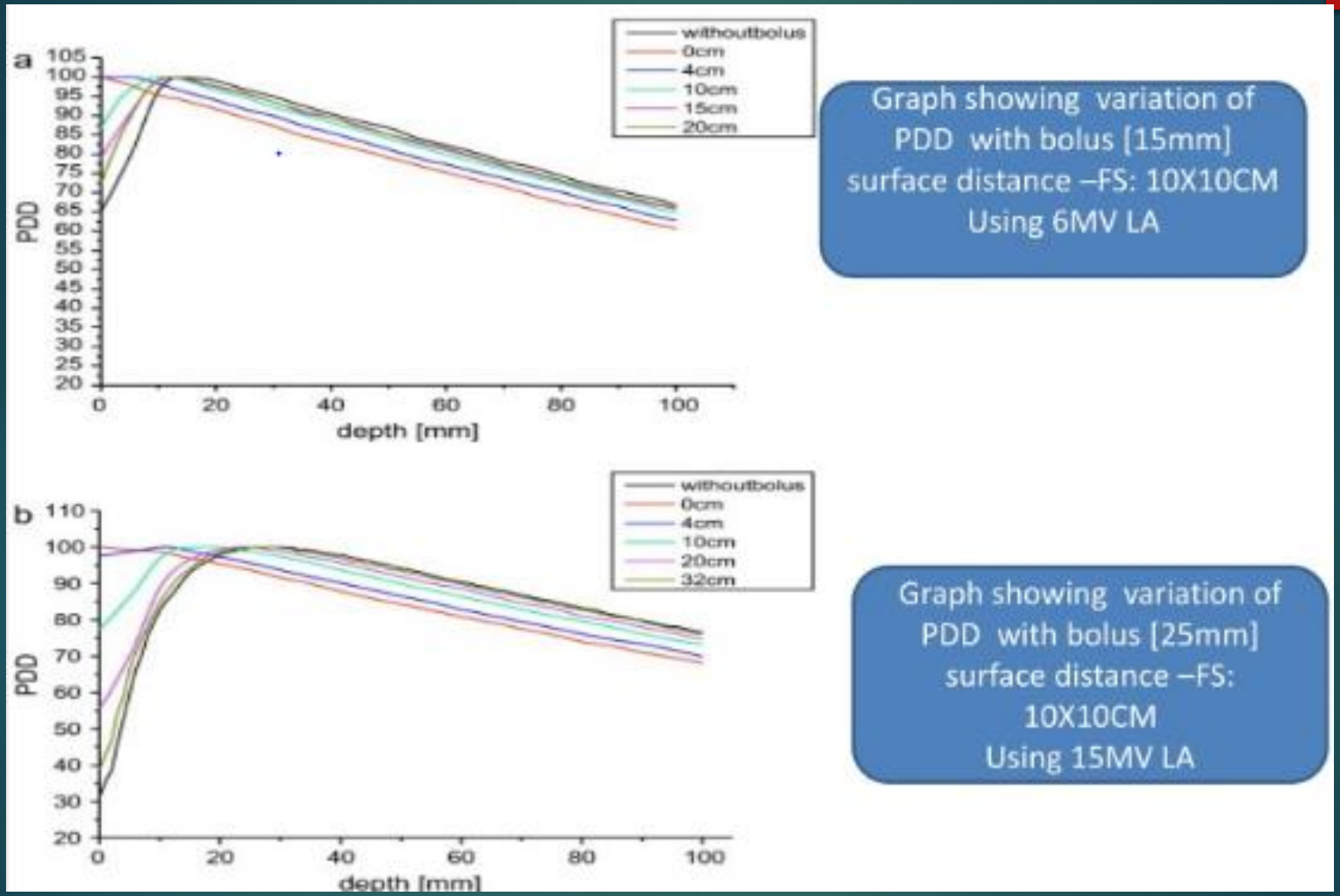
- **Special TBI stands or tables are often used to aid in immobilization, placement of organ shields, and patient support and comfort**



Beam Spoiler

Plexiglas beam spoiler is used .

- **For cobalt : 2mm thickness ,placed at a distance of 20cm from the patient.**
- **For LA : 1.5cm thickness ,at a distance of 34cm from the patient.**
- **USE- Increases the surface dose to 90% of prescribed dose**
- **To produce scattered electrons, which deposit most of the energy at shallow depth near the surface**



Graph showing variation of PDD with bolus [15mm] surface distance –FS: 10X10CM Using 6MV LA

Graph showing variation of PDD with bolus [25mm] surface distance –FS: 10X10CM Using 15MV LA

Compensating contour variations

1. Tissue equivalent bolus –

   a. Rice flour + $NaHCO_3$ --- not in much use because control of thickness is very difficult.

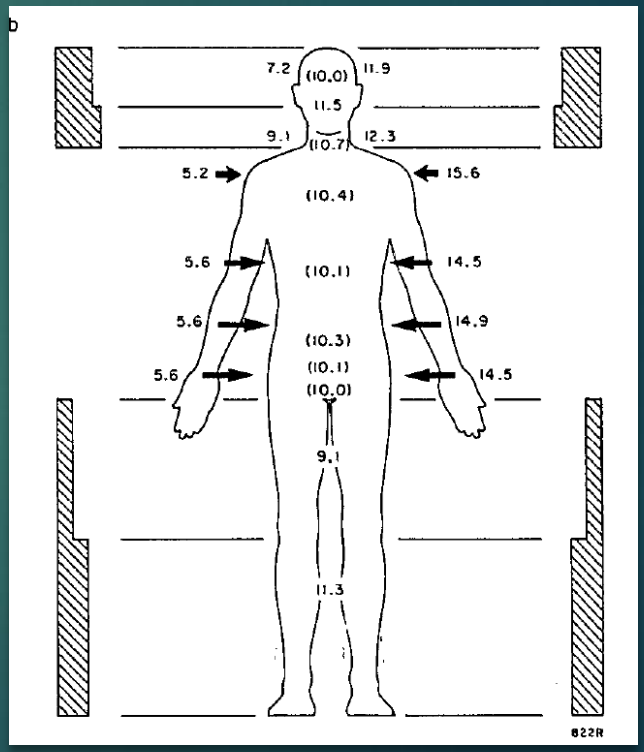
   b. Superflab --- semiflexible material

2. Missing tissue compensators –

   a. Large SSD makes miniature compensators placed on the treatment head difficult.

   b. Lack of adequate immobilisation makes its use uncertain.

Simple one dimensional compensator made of Pb or Cu strips can be used.



Patient Position

- Comfortable to the patient
- Reproducible
- Stability
- T/t geometry that allows accurate calculation & delivery of dose in accordance with TBI protocol

Premedication

- Pre-treatment- Inj Ondensetron 16 mg i.v.

  -Inj dexamethasone 16 mg i.v.

  -Inj Ranitidine 50 mg i.v.

- Post-treatment - T. Lomotil 5 mg TDS

  -T. Ondansetron 8 mg TDS

  -T. Ranitidine 150 mg BD

Simulation of patient for Lung block

- Patient is made to sit straight & comfortable on couch facing the gantry, kept at 270 degree.
- Field size -30x30cm2 at 100cm SSD is opened .
- Patients midline is alligned to the central axis of the beam .
- Fluroscopic images are taken with normal breathing ,then printed using 1:1 magnification

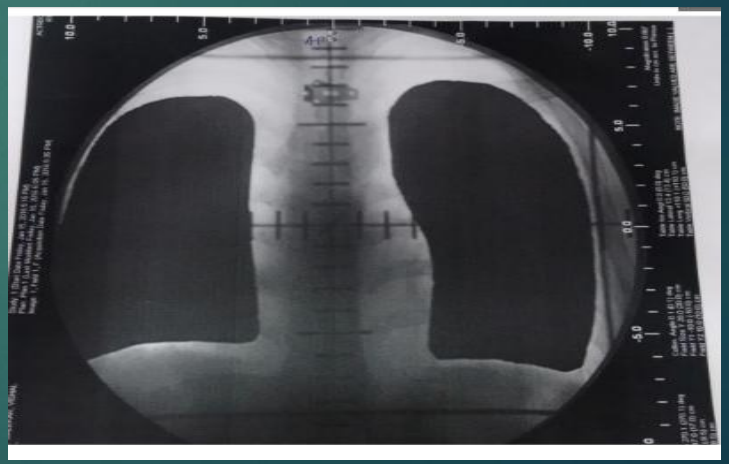
Delineation & fabrication-

- Done on simulator –transferred to graph paper with a 1cm grid size.
- Apex : at the level of clavicle
- Lateral border :1cm medial to inner chest wall
- Medial border :1cm off the lateral border of vertebral body

  [Right lung block & upper half for Left lung block]
- Lower half of medial border of Left lung block-drawn along cardiac shadow
- Inferior border: At the level of diaphragm

Verification of lung block on simulator

- **Customized lung blocks are housed inside a customised block holder with straps ,which is positioned on the patients chest wall.**
- **Position of lung blocks in relation to the lungs are verified by fluoroscopic images .**
- **Upper centre, mid-centre & lower centre tattooed on the patient skin.**
- **For reproducibility, horizontal & vertical distances of both lung blocks relative to these centres are measured .**



Treatment delivery- AAPM Guidelines

TBI containing myeloablative transplant programs typically utilize fractionated or hyperfractionated regimens (twice a day or three times a day) over several days -to minimize both acute and chronic toxicities and to 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, where total doses are typically only 200 cGy, organ shielding is not utilized.**
- **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**
- **A physician should be in close proximity to manage any problems related to treatment.**
- **Medications that may cause orthostatic hypotension (such as phenothiazines) should be avoided .**
- **Administration of intravenous fluids for hydration or transfusions for anemia may help to prevent syncope or near-syncopal episodes when the patient is treated in the standing position.**

AP/PA Technique

- **The most common irradiation technique.**
- **Patient in standing position.**
- **PRINCIPLE: Standing TBI allows shielding of certain organs such as lungs, brain, kidneys from photons & boosting of superficial tissues in the shadow of blocks with electrons.**
- **This technique requires a source to surface distance (SSD) in excess of 3 m to encompass the patient within the large beams.**
- **Sickness and fatigue associated with chemotherapy makes it difficult for many patients to hold a standing position during the prolonged radiation time, resulting in poor reproducibility in setup.**
- **The shielding blocks are placed on top of acrylic box tray at short distance from pt's surface.**
- **The tray (1cm thick) also act as beam spoiler to build up skin dose at least 90% of the prescription dose.**

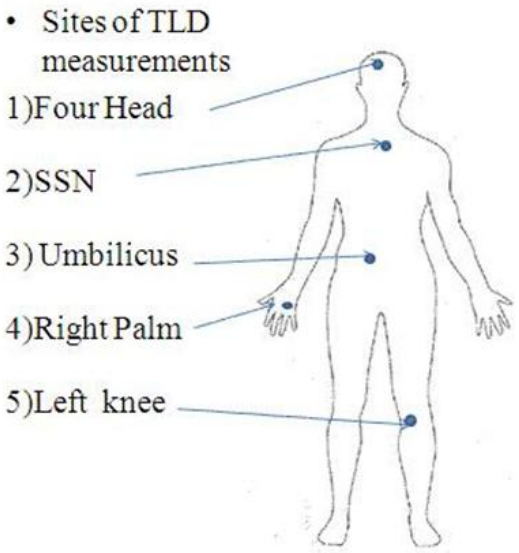
- Treated with anterior and posterior fields in a supported, standing position.
- A 2 cm PMMA (Perspex) screen used to provide radiation build-up.
- Individualized lead lung compensators designed and supported on the screen.
- Patients stands facing the machine for anterior fields and facing the wall for posterior fields, with their arms held by their sides.

Dosimetry

- Doses are measured using TLDs/MOSFET during the first fraction.
- TLD measurements are made of the doses to the head, neck, abdomen, right hip, right ankle and four positions on the chest (superior and inferior for each lung).
- The TLDs are placed on the anterior and posterior surfaces of the patient under 1 cm wax build up.
- With the exception of the chest points, the TLDs remain in place for both the anterior and posterior fields, to give the sum of the entry and exit doses.
- For the chest measurements, separate dosimeters are used for the two fields, to give separate readings of entry and exit doses.
- The positions of the chest TLDs are determined from measurements taken from the planning films.
- Patient separations are measured at the TLD sites.

Patient Dosimetry TLD positions

- Axilla
- Neck- Overlying the thyroid
- Bladder – in the midline just above the pubic symphysis
- Ovary- mid pt between pelvis & bladder dosimeters
- Parotid- over parotid gland at level of tragus
- Eye- on closed eyelid



Dose Prescription

- **Average dose- By averaging the calculated integral dose**

  Disadvantage- Difficult to perform & tedious dose calculation

  Doses not identify high & low dose region
- **Limited Average- Includes are of high & low dose**

  Disadvantage- Difference can cancel & leave the average unchanged
- **Minimum tumour dose at the midpoint of maximum separation**

  Disadvantage- Does not tell where the minimum dose occurs
- **Single point prescription- It specifies limit for highest & lowest dose acceptable for any point in the body**

  Dose limit are set for certain specific tissue e.g- Lung

Advantages of prescribing dose at umbilicus

- **Symmetric coverage of the head & feet**
- **Less contour variation**
- **Absence of low density tissue**
- **Dose calculation is straightforward**

Dose Prescription

- •High dose TBI : 1200cGY/6#[Dose ranges from 3-10Gy]
- Low dose TBI : 10-15cGY in 10-15#

-Dose is prescribed at the level of umbilicus .[ACR guidelines : suggest umbilicus]

- Treatment is given twice daily with a minimum of 6 hr between fractions.

Myeloablative TBI	**Age group**	**TBI dose/No of fractions***
ALL	Paediatric	14.4/8Fractions
	Adult	13.2/8 Fractions
AML	Paediatric	13.2 /8 Fractions
	Adult	12/8 Fractions
Non Myeloablative TBI	**Age group**	**TBI dose/No of fractions**
Myelofibrosis	Adult	2Gy/1Fraction
Aplastic Anemia	Paediatric	2Gy/1Fraction

*hyperfractionated radiation doses given twice daily with a gap of 6-8 hours between two fractions of radiation

Toxicity

- **Low Dose TBI**
  - **Nausea, vomiting**
  - **Thrombocytopenia (occurs after doses exceeding after 1 to 1.5 Gy)**
- **High dose TBI**
  - **Nausea/ vomiting (few hrs after TBI)**
  - **Oral mucositis, diarrhea (4-5 days)**
  - **Parotiditis (within 24hrs, subsides spontaneously)**
  - **Transient xerostomia**
  - **Dental caries**
  - **Fatigue**
  - **Skin erythema**
  - **Veno-occlusive disease**
  - **Prolonged pancytopenia**
  - **Reversible Hair loss (10-14 days)**

Graft versus Host Reaction (GVHD)

- **Acute – within 100 days of allogenic transplant**
  - **dermatitis, hepatitis,**
- **Chronic- more than 100 days after allogenic transplant**
  - **Rx – methotrexate, cyclosporin, combination of both, Prednisolone**

Pneumopathy

- **Occurs in 10-26% patients**
- **Fatal in 2/3rd patients**
- **Increased incidence :**
  - Old age
  - Increased body wt,BSA
  - CML
  - Underlying lung condition
  - Age of donor & recipient
  - Type of regimen used
  - Genetic predisposition

Cont...

- **Randomized trial has shown that TBI with dose 15.75Gy vs 12Gy – increased mortality due to lung toxicities .**
- **Retrospective study –mean dose >9.4Gy –an independent risk factor.**
- **Lowering the dose rate [0.025-0.09Gy/min] –reduces the incidence of pneumopathy.**
- **Fractionated TBI & use of Lung shielding –Reduces the complications .**

- **Cataract**
  - **Single dose (80-100%) pts developes cataracts in 8-10 yrs**
  - **Less (20 %) in fractionated TBI**
  - **High dose rate (>0.035-0.048 Gy/min)**

- **Hepatic dysfunction**
  - **Veno- occlusive disease of liver- Can occur in 70% patients (at dose >13.2Gy higher incidence)**
  - **Fractionated regimen decreases incidence of VOD**
  - **Hepatitis**

- **Renal dysfunction**
  - **In Approximately 17% of HSCT survivors**

- **Endocrine dysfunction**
  - **Hypothyroidism**
  - **Growth deficits**
  - **Impaired sexual development**
  - **Infertility**

Thank You