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 - Aldrich 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
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)
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

- High Dose Chemotherapy
- Total Body Irradiation
- Bone Marrow Transplant
- Reverse Isolation For Bone Marrow Recovery
- 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 immunosuppressive 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 coronal and mid axial planes
TBI Requirements - Clinical

- Required dose uniformity $\pm$ 5%
- Realistic $\pm$ 10%
- Low dose rate
- Less dose to Lung
  - $< 700$ cGy for single fraction of 900cGy
  - $< 950$ cGy for 2 fractions of 600cGy (1200cGy)
  - $< 14$ Gy 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 cm²
• 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 & multiple sources
- Track mounted mobile sources
- Specially designed flattening filter
- Max. field size of $75 \times 210 \text{cm}^2$
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

- 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
- i) Half body, direct and oblique fields
- j) Half body, adjacent direct fields
Princess Margaret Hospital (PMH), Toronto - Hemitron
Princess Margaret Hospital, Toronto

Hemitron

- Cobalt-60
- $80 \times 250 \text{ cm}^2$
  @ 150 cm
McGill University
Sweeping Beam Technique
TBI: McGill Technique
Translational Couch

Computer controlled
The Utrecht TBI Chair

- Developed at the University Hospital of Utrecht
- To have equal sagittal thickness both in trunk and legs
- Perspex attenuators to guarantee maximum skin dose
Iso-centrically 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 $D_{\text{max}}$)

- **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
Calibration of Diodes for In vivo-Dosimetry

- PTW diodes were placed at the middle of the phantom
- Exposed to known dose at $D_{\text{max}}$
- 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

<table>
<thead>
<tr>
<th>Patient Name:</th>
<th>Patient No:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Position the height of linac couch</td>
<td>121 cm</td>
</tr>
<tr>
<td>Collimator angle</td>
<td>45°</td>
</tr>
<tr>
<td>Gantry angle</td>
<td>90°</td>
</tr>
<tr>
<td>Measure patient length</td>
<td>135 cm</td>
</tr>
<tr>
<td>Fix source to surface distance (SSD)</td>
<td>285 cm</td>
</tr>
<tr>
<td>Check the patient with light beam</td>
<td></td>
</tr>
<tr>
<td>Place the Diodes</td>
<td></td>
</tr>
<tr>
<td>Measure the distance</td>
<td></td>
</tr>
<tr>
<td>I EAM level</td>
<td>298 cm</td>
</tr>
<tr>
<td>II Centre level</td>
<td>285 cm</td>
</tr>
<tr>
<td>III Knee level</td>
<td>294.4 cm</td>
</tr>
<tr>
<td>IV Ankle level</td>
<td>298.5 cm</td>
</tr>
<tr>
<td>Distance between beam spoiler and isocenter</td>
<td>254 cm</td>
</tr>
</tbody>
</table>
# Measurement of Separations

**Day – 5**

<table>
<thead>
<tr>
<th>Regions</th>
<th>Separation (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skull</td>
<td>15.50</td>
</tr>
<tr>
<td>Neck</td>
<td>11.00</td>
</tr>
<tr>
<td>Shoulder</td>
<td>45.00</td>
</tr>
<tr>
<td>Chest</td>
<td>31.00</td>
</tr>
<tr>
<td>Center</td>
<td>35.00</td>
</tr>
<tr>
<td>Thigh</td>
<td>32.00</td>
</tr>
<tr>
<td>Knee</td>
<td>21.00</td>
</tr>
<tr>
<td>Calf</td>
<td>20.50</td>
</tr>
<tr>
<td>Ankle</td>
<td>13.50</td>
</tr>
</tbody>
</table>

![Anatomical diagram]
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
- \( \mu \) - Linear attenuation coefficient
- \( t \) - Compensator thickness
## Calculation of Compensator Thickness

### Day – 4

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

## Day – 3

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

Day – 3

- 40 x 40 cm Field Size, Gantry 90°
- 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

<table>
<thead>
<tr>
<th>REGION</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skull</td>
<td>92.5</td>
<td>102.7</td>
<td>90.8</td>
<td>99.3</td>
<td>97.0</td>
</tr>
<tr>
<td>Neck</td>
<td>102.2</td>
<td>97.7</td>
<td>93.7</td>
<td>87.6 +</td>
<td>101.1</td>
</tr>
<tr>
<td>Chest</td>
<td>104.9</td>
<td>98.6</td>
<td>98.0</td>
<td>100.6</td>
<td>89.6</td>
</tr>
<tr>
<td>Umbilicus</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Thigh</td>
<td>98.4</td>
<td>104.4</td>
<td>106.6</td>
<td>98.5</td>
<td>102.2</td>
</tr>
<tr>
<td>Knee</td>
<td>90.7</td>
<td>94.9</td>
<td>91.9</td>
<td>94.5</td>
<td>95.7</td>
</tr>
<tr>
<td>Calf</td>
<td>93.1</td>
<td>91.2</td>
<td>95.4</td>
<td>92.3</td>
<td>91.9</td>
</tr>
<tr>
<td>Ankle</td>
<td>109.6</td>
<td>100.8</td>
<td>95.4</td>
<td>101.1</td>
<td>98.0</td>
</tr>
</tbody>
</table>
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
Acknowledgements

- Dr Paul Ravindran
- Dr Rajesh B
- Dr Rajesh I