Organ Sparing Marrow-Targeted Irradiation (OSMI) as an Alternative to Traditional Total Body Irradiation (TBI) Methods:

VMAT Treatment Planning and Clinical Implementation

Wesley Zoller, CMD

6/15/16
I have been a medical dosimetrist at the James Cancer Hospital since August 2013
- Graduate of Cleveland Clinic Medical Dosimetry Program

The “New” James began treating patients in December of 2013
- Over 100,000 square feet of space
- 2nd floor of hospital (true 2nd floor shielding)
- 7 Varian™ TrueBeams™ at main campus
- 2 more at our satellite, the Stefanie Spielman Comprehensive Breast Center
- PET/CT, CT, MRI in our department at campus
- We treat 200-250 patients daily
  - 60-70% VMAT/IMRT
- Wide variety of disease sites
  - Pediatrics, HN, Thoracic, Blood-Based, CNS, GYN, GU, Skin, Breast, GI, Sarcomas, Stereotactic and Palliative Care
Disclosures

- I have no conflict of interest with any of the vendors/software/equipment used for this presentation

- This presentation is not a marketing/sales presentation regarding specific products/software

- Any software/trade names mentioned in the presentation are resultants of accurate reporting of methodology

- All patient plans/setups in this study have been performed at the James Cancer Hospital in accordance with OSU protocol 13219

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Special Thank You to our OSMI Team

- Meng Welliver, MD, PhD, Assistant Professor, Radiation Oncology
  - Principal Investigator OSU 13219
  - Lead Attending Physician – Hematologic Cancer

- Michael Weldon, MS, Medical Physicist, Radiation Oncology

- Mark Addington, CMD, Medical Dosimetrist, Radiation Oncology

- Our wonderful therapists in simulation and on the linear accelerator

- Our dedicated physics team involved in QA, 2nd check, and treatment delivery

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Learning Objectives

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Learning Objectives

- To introduce Organ-Sparing Marrow-Targeted Irradiation (OSMI) as an alternative to traditional Total Body Irradiation (TBI) methods from a dosimetric perspective

- To reveal VMAT planning tricks/considerations encountered during the clinical implementation at the Ohio State University

- To diagnose setup requirements/considerations associated with VMAT OSMI treatment delivery

- To differentiation dosimetric differences between planning methods and reveal correlation to the patient experience
Total Body Irradiation (TBI) - Background
Leukemia

- Group of cancers of hematologic cells that generally arise in bone marrow.
  - Commonly characterized by proliferation of abnormal white blood cells.
  - 2nd most common blood cancer.
- According to National Cancer Institute:
  - 60,140 New Cases predicted for 2016
  - 24,400 Deaths (2016)
- Broken down into 4 most common types:
  - Acute Myelogenous Leukemia (AML)
  - Acute Lymphocytic Leukemia (ALL)
  - Chronic Lymphocytic Leukemia (CLL)
  - Chronic Myelogenous Leukemia (CML)
Leukemia

- **Acute Myelogenous Leukemia (AML)**
  - Most common leukemia in adults
  - Quick-onset; Aggressive, Immature myeloblasts

- **Acute Lymphocytic Leukemia (ALL)**
  - Third most common leukemia in adults
  - Most common cancer in children (25%)
  - Quick-onset proliferation of Immature Lymphocytes

- **Chronic Lymphocytic Leukemia (CLL)**
  - 2nd most common adult leukemia, Middle-aged ➔ Elderly
  - Chronic, Slow-Progressing, More Mature Lymphocytes

- **Chronic Myelogenous Leukemia (CML)**
  - Chronic, Slow-Progression, More Mature Myeloblasts
  - Median age at diagnosis – 67, Philadelphia Chromosome (Translocation, 9 and 22)

1 National Cancer Institute
2 American Cancer Society

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History of Total Body Irradiation (TBI)

- Myeloablative ability of radiation has been studied in animals/humans since 1902
- Bone Marrow Transplant (BMT) first used as a rescue therapy for acute radiation exposures in the 1950’s
  - By 1957-59, attempting to use therapeutic BMT/Stem Cell Transplant with prep chemo and radiation regimens for treatment of leukemia
- In 1994, evidence found little difference tumor cell kill of fractionated vs single fx
  - Improved late toxicity and immunosuppressive effects with fractionation – Dr. Cosset
- In 2000, 12 Gy → 2Gy/fx BID (8 hrs apart) with 6MV or Co-60 unit
  - Lungs blocked to ≤ 10Gy to reduce pneumonitis
  - Able to reduce acute/late toxicities (symptom management)
  - Publication, Established this regimen for use for ablative TBI
Traditional Total Body Irradiation (TBI)

- For many patients with AML, ALL, and MDS:
  - Chemo → allogeneic stem cell transplant (HSCT) remains only curative therapy
  - HSCT - Hematopoietic Stem Cell Transplantation
  - Allogeneic – coming from matching donor

- Patients must undergo conditioning prior to stem cell transplant in order to:
  - Prevent relapse
  - Eradicate Residual cancer cells
  - Ensure Engraftment
    - New cells grow, make healthy stem cells
  - Achieve Immunosuppression

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Traditional TBI Continued

- **Goal of TBI** – Achieve Homogeneous dose distribution throughout patient’s body
- **Extended Distance/Opposed Fields**
- **Potential Pulmonary and GI toxicities limiting factors for regimen**
  - TBI conditioning regimen associated with less relapse
- **TBI Toxicity profile:**
  - Fatigue
  - Nausea
  - Emesis
  - Parotid tenderness
  - Pruritus
  - Pneumonitis
  - Early onset cataracts
  - Increased risk for secondary malignancies
Traditional TBI Method at The James

- **12 Gy in 6 fractions BID, 6 MV**
  - Separation measured for:
    - Head, Neck, Thorax, Umbilicus, Upper Arm, Wrist, Thigh, Ankle
  - Dose Prescribed mid-plane
    - Umbilicus (Hand Calculation)
  - 500 cm SSD
    - Both AP and PA
  - Patient on customized cart, laying on side (AP/PA)
  - Gantry Lateral
  - Collimator Setting 40 x 40 cm$^2$
    - Collimator turned to 45 Degrees (pt height)
Traditional TBI Method at The James

- **Beam Spoiler can be used**
  - Decrease skin sparing
  - Generate Electron Contamination
- **Diodes placed by physics for in-vivo dosimetry**
  - Monitor dose to various areas
  - Adjustments if necessary
- **Even dose distribution desirable**
  - Lead Panels placed at 300 cm block screen to achieve homogeneity
- **Limit Lung mean less than 10 Gy**
  - Lung Blocks Used (example right)
  - Lung Blocks/Tray placed at 300cm block screen
  - Image verification prior to treatment
Traditional TBI Method at The James

**AP Field**
- Patient against backstop for stability
- 500 cm SSD to Umbilicus
- Spoiler can be placed front of table

**PA Field**
- 500 cm SSD aligned with back
Organ Sparing Marrow-Targeted Irradiation (OSMI)

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Premise of Organ Sparing Marrow-Targeted Irradiation (OSMI)

- **Contributors (Tech):** MLC’s/Intensity-Modulation, Improved Imaging/IGRT, Improved Setups.

- **Contributors (Field/Study):** Improved understanding of true targets for TBI.
  - Treat Skeletal Bone (Marrow), Lymphatic Chains, Testes, CNS, Extramedullary Organs (if applicable)
  - Limit dose to sensitive organs such as liver, lungs, bowel, kidneys, lenses, and oral cavity

**Potential Benefits of OSMI:**
1. Myeloablative radiation-based conditioning for older patients or patients who otherwise would not be eligible due to other co-morbidities
2. Allows for focal dose escalation in high risk disease areas
3. Patient who can otherwise tolerate full dose TBI, OSMI potentially offers less acute and late toxicities, including secondary malignancies
History of Organ Sparing Marrow-Targeted Irradiation (OSMI)

- Theoretically, OSMI planning can be achieved using several methods:
  - IMRT, Helical Tomotherapy, LINAC-Based VMAT

- Intensity Modulated Total Marrow Irradiation (IM-TMI):
  - 2006-2012 Hypothetical IMRT planning studies, assess technique dosimetrically

Helical Tomotherapy
- Ideal for long volumes, couch motion w/ treatment
- Patient safely treated using Tomo since 2010-11
  - Tomotherapy only available in ≈20% of centers

Linac-Based VMAT – OSMI
- 2011-2012: Hypothetical VMAT planning studies, assess technique dosimetrically, dose verification in phantom
- Linac-based VMAT OSMI more readily available
  - OSU 13219
OSU 13219

A FEASIBILITY STUDY OF ORGAN-SPARING MARROW-TARGETED IRRADIATION (OSMI) TO CONDITION PATIENTS WITH HIGH-RISK HEMATOLOGIC MALIGNANCIES PRIOR TO ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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First patient enrolled completed radiation June 2015

Slides 19-24 reference OSU Protocol 13219, Reference 7
A FEASIBILITY STUDY OF ORGAN-SPARING MARROW-TARGETED IRRADIATION (OSMI) TO CONDITION PATIENTS WITH HIGH-RISK HEMATOLOGIC MALIGNANCIES PRIOR TO ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

**Hypothesis:**
- OSMI can be administered by conventional linear accelerators in a **safe, feasible, well-tolerated manner** to patients with high-risk hematologic malignancies who are not eligible for conventional myeloablative TBI preparative regimens.

**Primary Endpoints:**
- To assess feasibility and tolerability of OSMI based HSCT -- **Transplant-Related Mortality (TRM)** at day 30
- Assess rate of grade II/III organ toxicity attributable to conditioning occurring within D30.
  - >10% Day 30 TRM or any grade III organ toxicity related to OSMI or conditioning at D30 or D100 will be considered unacceptable
    - Trial will be suspended to perform a careful review and to decide next steps. Day 30 TRM will be assessed in each cohort separately.
  - TRM at 10% or less at D30, and 15-20% at D100 consider it feasible and move forward to phase 2.
Hematopoietic Cell Transplantation-Specific Comorbidity Index (HCT-CI)

- Stratification of pts into low, intermediate, and high risk group for non-relapse mortality

High risk AML, ALL and MDS patients

**Cohort 1**: 18-50 years with HCT-CL of 2-4
**Cohort 2**: 51-65 years with HCT-CL of ≤3
**Cohort 3**: 66-75 years with HCT-CL of ≤2

*Organ-Sparing Marrow-targeted Irradiation*
administered 200 cGy x6, bid, with min 6 hrs between fractions
Preparative Regimen Overview:
- OSMI 200 cGy BID Day -6 through Day -4
- Cyclophosphamide 60 mg/kg q24h Day -3 through Day -2
- If unrelated donor, give ATG 2.25 mg/kg q24h Day -3 through Day -2.
- If deemed necessary, sequence of OSMI and cyclophosphamide administration could be reversed

Patient to be consulted in Radiation Oncology a minimum of 3 weeks prior to transplant

Simulation:
- Supine in Treatment Position, Whole-Body Vacbag
- Custom Head Rest
- Head and Shoulder Mask to minimize motion
- 3-mm or less slice thickness from vertex to mid-thigh
- Four sets of appropriately-spaced triangulation skin marks will be placed on the patient to aid in alignment
  - Head (mask), Thorax, Abdomen, Pelvis
OSU 13219

**Radiation Administration:**
- Linacs with energy ≥ 6 MV photons
- IMRT or VMAT radiation
- Phantom study will be carried out to ensure adequate dose to the target areas
- Quality assurance will be performed per department standards

**Radiation Treatment Planning:** 12 Gy, 6 fractions, BID (≥ 6 hours apart)
- **Upper Body: Modulated** → Target all marrow-containing bones and perspective sanctuary sites (if applicable) from vertex through ischial tuberosity/hands
  - This target area will be defined as CTV
- **PTV = CTV + 5-10 mm margin (area dependent)**
- 90% PTV should receive ≥ 90% of 12 Gy prescription dose
- 99% CTV should receive > 10 Gy
- Dose to lung, liver, kidneys, lenses, esophagus, oral cavity, GI will be limited to as low as possible
- Total *mean Lung Dose* should not exceed 10 Gy

- **Lower Body: AP/PA** → Bilateral lower extremities from Isch Tub/Hands Inferiorly
  - Uses intra-fractional feathering technique at junctions with borders
  - No specific radio-sensitive organs to spare

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CT Simulation

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CT Simulation - Overview
CT Simulation - Immobilization
CT Simulation – Vacbag/Stereotactic Board

- Vendor Stereotactic Board Indexed to Table Surface
  - Alpha-Numeric Coordinate System
  - Index Points for additional immobilization

- Vacbag Indexed to Stereotactic Board
  - Includes entire posterior contents of patient from shoulders descending inferiorly

- Knee Sponge indexed to Stereotactic Board
  - Coordinate Recorded/Captured
  - Used for Patient Comfort

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CT Simulation – Creating Vacbag

- **Arm Position:**
  - Posterior, as tightly as possible to the patients body
  - The “narrower” the better
  - Hands in a comfortable fist

- **When creating the Vacbag/BodyLok:**
  - Start Superiorly and work down the body
  - PUSH INWARD for arms/hands
  - Choose appropriate height to hold arms against body
  - Create visible “notch” around fist/hands
  - Notch over Knee Sponge
CT Simulation – Head and Neck Immobilization

- Head-Only Aquaplast/Thermoplast Mask
  - Indexed to Vendor Stereotactic Board using Index Bar
  - Coordinates Recorded/Captured

- Custom HR on top of Clear Vendor HR
  - Patient Comfort
  - Head Rest Indexed

- Tilt Head as anatomically straight as possible when making Mask
  - Use lasers for assistance

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CT Simulation – Fiducial Placement

- Prior to placing Fiducials/Marks:
  - Acquire Topogram to visualize spine alignment as well as anatomical straightness of the body habitus
  - Use Sagittal laser to place anterior marks—same for all origins

- Choose Appropriate Height:
  - Use coronal laser to visualize plane for Head, Thoracic, Abdominal, and Pelvic fiducial placement (4 Total)
  - Make sure isocenter will not fall on forearm
  - Use same height/plane for all origin markings
CT Simulation – Fiducial Placement

- Begin by placing Head Isocenter on Mask
- Move inferiorly (cranio-caudal plane) to place thoracic isocenter
  - Choose Stable location (generally on shoulders)
  - Place “leveling” marks on patient
  - Use whole/round numbers for shift
  - RECORD BOARD NUMBERS
  - Place Sup/Inf Mark on Vacbag at each isocenter for setup assistance/verification

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CT Simulation – Fiducial Placement

- Abdomen origin: Mathematical Division b/w Thorax and Pelvis
  - Equidistant of these 3 is very helpful for setup verification
- Continue to record board numbers
  - Generate marks at each isocenter, and on vacbag for setup purposes
- For placement of Pelvis Isocenter
  - Do not place inferior to your midpoint/limit of linac travel
  - Denoted K0
CT Simulation – Fiducial Placement

- **K0—Board Number**
  - This represents the inferior extent on the stereotactic board that can be achieved in the Head-First Supine Position
  - Based on measurements at the linear accelerator
  - Fiducials placed at this point on the Vacbag for dosimetry purposes
  - For Pelvis isocenter, do not go inferior
CT Simulation

- Simulated on PET/CT Scanner
  - 182 cm Scan Length
  - Approximately 6 feet of dataset

- Extended Field of View
  - eFoV 70 cm
  - To acquire immobilization and extremities

- As mentioned, start with Topogram to validate alignment of spinal column
CT Simulation

- **Free Breathing CT acquired helically with 2.5 mm slice thickness**
  - Reconstructed at 5mm slice thickness
  - Both imported into treatment planning system
    - 5mm used to save time on contouring
    - Planning performed on 2.5mm

- **If we cannot acquire entire patient in dataset due to length maximum:**
  - MUST GET all of HEAD
  - Leave remainder at inferior extent (feet/toes)
    - Example to Left
  - Measure remaining cm to end of toes, this part will be AP/PA

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CT Simulation – Verify Free Breathing

- After Free Breathing Scan has been acquired, review at console:
  - Verify anatomic contents of CT scan with extended field of view
  - Review superior and inferior extents of dataset
  - Verify that all isocenters/fiducials placed can be visualized
  - Verify K0 can be seen on the free breathing CT
    - This will be necessary for planning purposes
    - Fiducials placed on vacbag instead of body to avoid confusion
CT Simulation – Analysis of Breathing

After the free breathing CT has been determined as acceptable:

- Acquisition of motion analysis CT(s) are now necessary using some kind of motion management system

Acceptable Options:

- **4D CT Lungs/Upper Abdomen**
- **Inhalation/Exhalation Breath-Hold CT Scans**

Uses:

- Assess the need for ITV for anterior rib targets
- Determine required margins
- Assess motion of liver/spleen

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Segmentation and Contouring

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Contouring - Overview

<table>
<thead>
<tr>
<th>CTV Ant Ribs/ITV</th>
<th>PTV Ant Ribs</th>
<th>*CTV Liver</th>
<th>*PTV Liver</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ant Ribs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTV Post Ribs</td>
<td>PTV Post Ribs</td>
<td>*CTV Brain</td>
<td>*PTV Brain</td>
</tr>
<tr>
<td>CTV HN</td>
<td>PTV HN</td>
<td>*CTV Testes</td>
<td>*PTV Testes</td>
</tr>
<tr>
<td>CTV Pelvis/Abd</td>
<td>PTV Pelvis/Abd</td>
<td>*CTV Spleen</td>
<td>*PTV Spleen</td>
</tr>
<tr>
<td>CTV Arm L</td>
<td>PTV Arm L</td>
<td>*Only to Extramedullary/Sanctuary if Applicable</td>
<td></td>
</tr>
<tr>
<td>CTV Arm R</td>
<td>PTV Arm R</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTV Total</td>
<td>PTV Total</td>
<td></td>
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</tr>
</tbody>
</table>
CTV Head/Neck

- Includes bony contents of skull, base of skull (Excluding Facial Bones, Mandible, Brain)

PTV Head/Neck

- CTV+0.5 cm
- Cropped 3mm from External (excluding areas where crop brings PTV inside CTV)
CTV Ant Ribs

- Includes bony contents of Anterior Thorax in addition to Ribs (Sternum, Clavicles, etc.)

PTV Ant Ribs

- CTV+0.5 cm (ITV+0.5 if applicable per physician based on analysis of Motion Management)
- Cropped out of Lung Total/3mm skin
**CTV Post Ribs**
- Includes bony contents of Posterior Thorax in addition to Ribs (Scapula, etc.)

**PTV Post Ribs**
- CTV+0.5 cm
- Cropped out of Lung Total/3mm skin
CTV Pelvis/Abd

- Includes inferior to thorax/ribs, including Spinal Column and Pelvic Girdle through sup femur (AP/PA)

PTV Pelvis/Abd

- CTV+0.5 cm
- Cropped 3mm from External
CTV Arms L/R

- Humeral Head superiorly descending through hands/fingers

PTV Arms L/R

- CTV+1.0 cm
- Not cropped from skin, will use Arm Flash structure to account for setup
<table>
<thead>
<tr>
<th>CTV/PTV to Sanctuary/Extramedullary</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CTV Brain</strong></td>
<td><strong>PTV Brain</strong></td>
</tr>
<tr>
<td>• Normal Brain</td>
<td>• CTV + Contents of Bony Skull (Simply Include in Total PTV)</td>
</tr>
<tr>
<td><strong>CTV Testes</strong></td>
<td><strong>PTV Testes</strong></td>
</tr>
<tr>
<td>• Both Testes</td>
<td>• CTV + 1.0 cm</td>
</tr>
<tr>
<td></td>
<td>• Not Cropped, Skin Flash Structure added during planning to account for setup</td>
</tr>
<tr>
<td><strong>CTV Spleen</strong></td>
<td><strong>PTV Spleen</strong></td>
</tr>
<tr>
<td>• ITV of Spleen</td>
<td>• ITV + 0.5 cm</td>
</tr>
<tr>
<td>• Drawn on 4D sets or EBH/IBH and merged)</td>
<td>• Cropped 3mm from Surface</td>
</tr>
<tr>
<td><strong>CTV Liver</strong></td>
<td><strong>PTV Liver</strong></td>
</tr>
<tr>
<td>• ITV of Liver</td>
<td>• ITV + 0.5 cm</td>
</tr>
<tr>
<td>• Drawn on 4D sets or EBH/IBH and merged)</td>
<td>• Cropped 3mm from Surface</td>
</tr>
</tbody>
</table>

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CTV/PTV Liver - Example

Liver Inhalation

Liver Exhalation
CTV/PTV Liver - Example

Liver ITV (GREEN)

- Contoured Liver on Exhalation Breath Hold CT
- Contoured Liver on Inhalation Breath Hold CT
- Contoured Liver on Free Breathing CT

**MERGED ALL THREE ON Free Breathing (Planning) CT**

- Note: 4D CT is ideal method for motion delineation—compared to EBH/IBH
CTV Total

- The Sum of All CTV’s—including sanctuary/risk sites if applicable per physician

PTV Total

- The Sum of All PTV’s—including sanctuary/risk sites if applicable per physician

NOTE: Do not re-expand
## Contouring - Overview

### Normal Structures and Immobilization

<table>
<thead>
<tr>
<th>Normal Structure</th>
<th>Immobilization/ Vacbag/BodyLok</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder</td>
<td>Skin</td>
</tr>
<tr>
<td>Bowel</td>
<td>Rectum</td>
</tr>
<tr>
<td>Lung L</td>
<td>Spinal Cord</td>
</tr>
<tr>
<td>Lung R</td>
<td>Spinal Cord PRV</td>
</tr>
<tr>
<td>Lung Total</td>
<td>Stomach</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Eye R (Globes)</td>
</tr>
<tr>
<td>Esophagus-PTV</td>
<td>Eye L (Globes)</td>
</tr>
<tr>
<td>Body (Eclipse)</td>
<td>Couch (Eclipse)</td>
</tr>
<tr>
<td></td>
<td><strong>Only if Applicable</strong></td>
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<tr>
<td></td>
<td>Immobilization/ Vacbag/BodyLok</td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>Larynx</td>
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<tr>
<td></td>
<td>Oral Cavity</td>
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<tr>
<td></td>
<td>*Brain</td>
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<tr>
<td>Kidney Total</td>
<td>*Liver</td>
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<tr>
<td>*Spleen</td>
<td>*Genitalia</td>
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<tr>
<td>Kidney L</td>
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<tr>
<td>Kidney R</td>
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<td>*Genitalia</td>
<td></td>
</tr>
<tr>
<td>Kidney Total</td>
<td></td>
</tr>
</tbody>
</table>

*Brain, *Liver, *Genitalia, **Only if Applicable
Normal Tissue Contouring - Notes

- Applicable Normal Tissue Structures in chart contoured per RTOG Guidelines
- **Skin Contour** – 5mm rind from surface
- **Spinal Cord PRV** – 5mm expansion on Spinal Cord
- **Brain/Genitalia** contoured as normal structures when applicable per physician
- **Liver/Spleen** – ITV not necessary if non-targets. Normal Tissue contoured on Free Breathing CT
- Correct any artifact

- Carina used for Visualization/Alignment at Linac (as well as specific vertebral body contours)
- Couch/Body Contours exclusive to Vendor Specific TPS
- Override density for objects that won’t be present for treatment (indexing bar)

**Examples to Follow:**
- Stereotactic Board
- Immobilization (Vacbag)
- Bowel

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Stereotactic Board

- **Contour of Stereotactic Board**
  - *To edge unless eFoV produces significant artifact*
Immobilization – Vacbag/BodyLok

- **Contour all Immobilization as accurately as possible**
  - *Lung Window is helpful for visualization*
  - *To edge unless eFoV produces significant artifact*
Bowel

- Entire Bowel Sac included in contour
  - Large Bowel + Small Bowel
Treatment Planning

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Treatment Planning for OSU 13219

**Helpful Tips:**
- Linac with 6MV and higher energy setting (10MV, 15MV, or 18MV)
  - Assists with AP/PA
- Linac with Large Field Size capabilities is preferable
  - 40x40 cm field may be necessary
- Linac with CBCT capability is useful for setup
- *Planning done on 2.5 mm dataset*

**Radiation Treatment Planning:**
- 12 Gy, 6 fractions, BID (≥ 6 hours apart)
- 90% PTV should receive ≥ 90% of 12 Gy prescription dose
- 99% CTV should receive > 10 Gy
- Dose to lung, liver, kidneys, lenses, esophagus, oral cavity, GI will be limited to as low as possible
- Total *mean Lung Dose* should not exceed 10 Gy
- *Upper Body VMAT; Lower Body AP/PA*
All planning isocenters will be placed in the same coronal and sagittal planes

- Superior/Inferior Shift between fields for ease of treatment
- For sagittal placement, choose neutral sagittal plane that mirrors the body, bifurcating vertebral column
- For coronal isocenter placement, choose neutral coronal plane that lies mid-plane ant/post in the thorax.
  - For lung sparing/rib coverage, will need centrally located rotational axis
- For TPS with single origin, place origin at head fiducials
- When placing isocenter, it is often necessary to shift.
  - Do not feel the need to stick with origin as iso
  - The details matter, make it perfect
Treatment Planning (Lower Extremities)

- Begin planning with the Lower Extremities
  - Bilateral Legs in single open fields, AP/PA
    - No radiosensitive avoidances
  - Reminder: ALL isocenters will have same coronal and sagittal planes, even if in space or immobilization for legs
  - 6MV, 10MV, 15MV, or 18MV all acceptable based on necessity/thickness
  - Treated/Planned FEET-FIRST-SUPINE

1) Start with Inferior Portion of Legs
2) Maximize the inferior independent Y jaw so you have 3-5 cm of flash over the toes
   - The upper jaw will be feathered with the superior legs
3) Set width to have margin over lateral aspect of long bones, usually 38-40 cm X collimator
Treatment Planning (Lower Extremities)

- 4) Move to placement of Upper Leg Fields
- 5) Superior field border will be placed inferior to hands or ischial tuberosities (whichever is most inferior)
  - AP/PA not wide enough to treat hands, even stretched at 40cm
  - Bony pelvis will benefit from VMAT due to OAR
- 6) Set width to have margin over lateral aspect of long bones, usually 38-40 cm X collimator
- 7) Find good match location between Upper and Lower Leg Fields
  - Usually equidistant between fields is best
  - Do not maximize adjacent independent jaws to 20cm as we will need to feather the junction
- 8) If patient height does not allow for 2 isocenters for lower body, add 3rd intermediate isocenter equidistant between Upper and Lower
  - Will have additional junction
Lower Extremities (Feathering the Junctions)

- Superior field border of Upper Legs will need to be feathered
  - Create more gradual gradient for VMAT matching
  - This junction entails switching from HFS to FFS
- May be helpful to utilize intra-fractional feathering technique
  - Subfields/control points within a plan stepped back at 0.5-1.0 cm intervals
  - Does not require “shifting the junction” after a set number of fractions
  - Reduces margin for error
- If treatment planning system allows, this upper field border will be used as a “base-dose plan” during optimization of VMAT inferior field

The James
Lower Extremities (Feathering the Junctions)

- Field junctions between Upper/Lower Leg fields will need to be feathered
  - Desirable to match across long bone
- May be helpful to utilize intra-fractional feathering technique
  - Subfields/control points within a plan stepped back at 0.5-1.0 cm intervals
  - When Upper Field’s bottom border shifted superiorly, Lower Field’s top border must be shifted superiorly to match
  - Creates diamond shape centered in spongy bone
Lower Extremities (Feathering the Junctions)

- Easy if bone junction in same coronal plane as TTL
- If bone lies anterior or posterior…

\[ X = \frac{100(D)}{100-H} \]

- \( X \) = collimator setting for independent jaw
- \( H \) = height anterior from TTL to bone match point
- \( D \) = distance sup/inf to match location from iso
- TTL = height of isocenter for entire OSMI

The James
Lower Extremities (Feathering the Junctions)

- Prescribe such that 11-12Gy covers the contents of long bones within the fields
- YOU’RE HALF DONE—KIND OF!!

The James
VMAT Considerations

- **VMAT Considerations (RapidArc\textsuperscript{TM}/TrueBeam\textsuperscript{TM}):**
  - For our linacs at the James, an individual MLC leaf can only travel 15 cm beyond the jaw (X)
    - Treating with a large VMAT field sizes (40cm x 40 cm) is not applicable for OSMI
    - If X jaws are set to 30cm, each leaf bank can only theoretically travel to CAX, no further
  - **Unless Jaw is reduced**
    - This leaves other half of field blocked behind jaw
  - May not run into as many complications with different disease sites (smaller treatment volumes)
  - OSMI requires each arc to be very productive in terms of modulation
    - Large treatment area/volume

The James
VMAT Considerations

- Quick Example: MLC Bank on R side is leaving open to treat chest wall
- MLC Bank on L Side would need to block lung or set vertebral column
VMAT Considerations

- *The MLC cannot travel to block R Lung, or even vertebral column due to large field size*
VMAT Considerations

- *This leads to open sectors/gaps, causing dose to flare out away from target*
- *Take that same 30 cm field, and break it up into an upper field (15 cm) and lower field (15 cm)*
  - *Now MLC can travel completely across the field, allowing blocking where necessary*
VMAT Considerations

- **Planning Arcs: Collimator settings of 90 degrees and 0 degrees**
  - Due to length of target, and placement of multiple isocenters, fields will be overlapping/sharing treatment areas
  - 0/90 degrees produce more predictable dose sharing in overlapping regions based on our experiences thus far
  - Corners create a “shearing effect” dose gradient between fields, especially at superior and inferior border
    - Gradient in an oblique plane
    - Irregular matching in vertebral bodies
    - Larger Margin for Error at delivery

- **MLC Leakage associated with 0 degree Collimator Setting is of minor concern**
  - Often contained in dose calculation in modern TPS; Treating entire body
OSMI VMAT Upper Body—HEAD FIRST SUPINE.

1) Select location of Pelvis Isocenter
   - Lower field can appropriately cover the area being matched by the upper legs with the Y1 jaw
   - Reminder: Do not place pelvis isocenter inferior to K0
   - It may be helpful to contour a single slice for K0 for easy viewing in a BEV

2) Derive 3 other Isocenters locations
   - (4 total) such that the shifts are Equidistant
   - Usually 20-25 cm spaces between each isocenter depending on patient’s height
   - Keep in mind, Head isocenter must have enough range in upper jaw to cover vertex
Helpful tips to help place the pelvis isocenter:

- Convert the 11Gy range from the upper legs into a structure for visualization
  - Ensure that the inferior border covers the gap/junction
- Contour the K0 slice of external to make sure isocenter placement does not extend inferiorly
Preliminary Upper Body Optimization

- We will run an optimization with all isocenters in a single plan/study
- This is to create field sharing between overlapping VMAT fields
  - The goal is to soften the gradient between fields
- Our TPS limits us to 10 VMAT fields in a single plan
  - This plan is INITIAL RUN (PRELIMINRY)
  - The final product will benefit from having a few additional arcs
  - This is based on difficulties created by plan width/organ sparing

ALL FIELDS RUN WITH SAME ENERGY

- TPS Version Requirement
Preliminary Upper Body Optimization

- **Head and Neck Isocenter**
  - *Initial Run – 10X, 2 Full Arcs*
  - *Both at collimator 0*
    - *Arc 1: X1=0; X2=15; Arc 2: X1=15; X2=0 (Y Jaws – Machine Maximum (38-40 cm))

The James
Preliminary Upper Body Optimization

- Chest Isocenter
  - Checkerboard Arrangement
  - Initial Run – 10X, 4 Full Arcs
  - Two at collimator 90
  - Two at collimator 0
    - Arc 1: X1=0; X2=15
    - Arc 2: X1=15; X2=0
    - Arc 3: X1=0; X2=15
    - Arc 4: X1=15; X2=0
  - (Y Jaws – Machine Maximum (38-40 cm))
Preliminary Upper Body Optimization

- **Abdomen Isocenter**
  - *Initial Run – 10X, 2 Full Arcs*
  - *Both at collimator 90*
    - **Arc 1**: $X_1=0; X_2=15$; **Arc 2**: $X_1=15; X_2=0$ (*Y Jaws – Machine Maximum (38-40 cm)*)
Preliminary Upper Body Optimization

- **Pelvis Isocenter**
  - *Initial Run – 10X, 2 Full Arcs*
  - *Both at collimator 90*
    - **Arc 1:** $X_1=0; X_2=15$; **Arc 2:** $X_1=15; X_2=0$ (*Y Jaws – Machine Maximum (38-40 cm)*)
Planning and Optimization Structures

- **Arm Flash**
  - Override Density to Tissue
  - Created as a “Skin Flash” Tool for Arms/Hands
  - 3mm expansion of PTV, Included in BODY/Calculation Region
  - This negates need to crop back PTV from surface, cutting into margin
Planning and Optimization Structures

- **Planning PTV’s based on “SECTORS”**
  - One set for each isocenter
  - PTV’s “cut off” within region of Arcs/Shared Arcs
    - Allows for independent optimization/dose control
  - Extremity and Body Targets broken up into two parts
    - Drive Dose to Arms (Width creates difficulty)
Planning and Optimization Structures

- **OAR “Ramp-Down” Structures**
  - Stair Case fall-off within encased OAR by setting stiffer objectives
  - Primarily use for Brain and Lung Total
Planning and Optimization Structures

- **Various Rings and Avoidances**
  - If pushing 90% Isodose, start Ring/Avoidance 5mm away for HN, 1 cm away for other isocenters
    - Anything closer, difficult to control
  - **Examples:**

---

The James
Optimization of Preliminary

- You will use the “Upper Legs” dose in Optimization of VMAT Upper Body
  - “Base Dose Plan” – Different ways to do this based on TPS
Optimization and Completion of Preliminary

- **Ideal Treatment Goals for Preliminary:**
  - **D99% CTV > 10 Gy**
  - **D90% PTV > 10.8 Gy**
  - Lung Mean < 8 Gy (9 Gy)
  - Kidney Mean < 8 Gy (9 Gy)
  - Bowel Mean < 8 Gy (9 Gy)
  - Heart Mean < 8 Gy (9 Gy)
  - Stomach Mean < 8 Gy (9 Gy)
  - Brain Mean < 10 Gy
  - Liver Mean < 10 Gy
  - Lens < 7 Gy Max (8 Gy)
  - Oral Cavity mean < 8 Gy
  - Esophagus-PTV mean < 10 Gy

- **OAR acceptable if not met on preliminary, same goals for final plan**

The James
Treatment Planning (Final Plans)

- Copy the Preliminary and break it into 3 separate plans
  - HN Isocenter
  - Thorax/Abdomen Isocenters (Same Plan)
  - Pelvis Isocenter

- Note: Record the OAR mean doses for the preliminary plan, you should attempt to improve these with the final draft

- 1) Now re-optimize the Head and Neck Plan alone with 6 MV
  - No change to Fields; 2 full arcs with 0 collimator
  - 6X will help get better dose to periphery of cranium, spare medial brain
  - NOTE: You will use the Preliminary Thorax Plan as a Base Dose Plan to recreate shared field gradient
2) Now re-optimize the **Pelvis** plan alone with **4 Total Arcs** instead of just 2

- Add 2 full arcs with 0 collimator; Keeping 2 full arcs with 90 collimator
- Still use 10 MV; **Checkerboard Arrangement**
- **NOTE:** You will use a **Sum of Upper Legs and the Thorax/Abdomen Isocenters Plan** as a Base Dose Plan to recreate shared field gradients
3) Now re-optimize the **Thorax/Abdomen** plan alone with **4 Total Arcs** each instead of just 2 for the Abdomen (4 for Thorax still)

- **Abdomen**: Add 2 full arcs with 0 collimator; Keeping 2 full arcs with 90 collimator
- **Still use 10 MV; Checkerboard Arrangement**
- **Thorax**: Do not change fields

**NOTE**: You will use a **Sum of Re-Optimized HN and Re-Optimized Pelvis Plan** as a Base Dose Plan to recreate shared field gradients
Final Plans Should Include:

- **Head and Neck**: 2 arcs, 0 collimator; 6X (alternating X1 and X2 with 15 cm/0 cm)

- **Thorax**: 4 full arcs, 2 0 collimator, 2 90 collimator, 10X (alternating X1 and X2 with 15 cm/0 cm)

- **Abdomen**: 4 full arcs, 2 0 collimator, 2 90 collimator, 10X (alternating X1 and X2 with 15 cm/0 cm)

- **Pelvis**: 4 full arcs, 2 0 collimator, 2 90 collimator, 10X (alternating X1 and X2 with 15 cm/0 cm)

- **Sum all plans, Upper Body and Lower Body**
- For imaging/shift purposes, we must break all isocenters into individual plans
Treatment Plan
Treatment Plan
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Treatment Plan
Dose Analysis

The James
Dose Analysis (Summary)

- **Target Coverage Goals Exceeded**
- **Lung, Bowel, Heart, Kidney means 7-8 Gy; Brain/Liver < 10 Gy**

<table>
<thead>
<tr>
<th>Patient</th>
<th>D90% of PTV Total (&gt;10.8 Gy Required)</th>
<th>D99% of CTV Total (&gt;10 Gy Required)</th>
<th>Lung Total Mean (Gy)</th>
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<th>Liver Mean (Gy) (if applicable)</th>
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Dose Analysis (Summary)

- **First patient we planned**
- **Also includes Brain, Liver, Spleen, and Testes in CTV/PTV**

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The James
## Dose Analysis (Summary)

### Dose results without the first patient

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</table>
Treatment Delivery/Setup

The James
Verification Sim

- Each isocenter broken into singular plan so images can be taken/shifted
  - Put in order, HN to Lower Legs
  - Stereotactic board placed flush with superior aspect of treatment table, unindexed for rotation to FFS
  - Aligned using Board #’s/Lasers
  - Isocenter TTL usually falls on bag
    - Use CT origin marks for triangulation/alignment of patient
    - Progress down each site visually to ensure that we are on each -- Bag Marks, Origin Marks
    - Compare with Recorded Sup/Inf Shift to assess compression of pt

The James
Verification Sim

- After getting patient visually aligned based on CT marks, shift to HN Isocenter
  - SSD’s Verified
- Make Shift to Thorax Isocenter
  - Take AP Setup Image
  - Visualize alignment, make adjustments
  - Record table parameters
- Apply measured inferior shift to Pelvis Isocenter
  - Take AP Setup Image
  - Visualize alignment, trends and make adjustments
  - Record table parameters
- **GOAL:** Verify that patient is aligned Cranio-Caudal prior to CBCT/treatment
  - Re-setup if necessary

The James
Verification Sim

- Use table longitudinal coordinates from recorded Pelvis parameters to assess patient compression or extension in the sup/inf direction
  - Ideally, Pelvis longitudinal position differs from planned shift from head isocenter by 3mm or less
  - Maximum allowable – 5mm
- Assess Thorax Isocenter in reference to Head Isocenter
  - Thorax longitudinal position should not differ from planned head isocenter shift (based on TPS) by more than 3mm
- If Patient longitudinal extension or compression exceeds tolerance, adjust/re-setup

Thorax AP Match

The James
Verification Simulation

- **Shift back to Head Isocenter**
  - Acquire CBCT and match
  - MD Approval
  - Capture couch parameters, Mark Isocenter

- **Apply inferior shifts to Thorax Isocenter**
  - Use captured couch parameter to verify
  - Acquire CBCT and match
  - MD Approval, Mark Isocenter

- **Shift to Abdomen Isocenter**
  - **CALCULATED**: Based on longitudinal split of Pelvis Couch Parameter and Thorax Couch parameter
  - Take Orthogonal images
  - CBCT only if necessary
Verification Simulation

- Abdominal Orthog Pictured left
  - Used to save additional CT
  - Verification (Pelvis and Thorax imaged)
- Shift to Pelvis Isocenter
  - Use captured parameters
  - Acquire CBCT and match
  - MD Approval
  - Mark Isocenter

- Verify that all isocenters are marked
- Check SSD’s at all isocenters
- Take plenty of photos
- Getting ready to flip to Feet-First Supine
  - Mark Inferior Match Field on Skin
  - Mark K0 on bag

The James
Verification Simulation (Match on skin)

- **Setup field created for Pelvis field called “LB Skin Match”**
  - This field is created to match most superior field (1st field) of Upper Legs
  - Make 40 cm wide

- **Before rotating to Feet-First, project this Field HFS at Pelvis iso and mark on the vacbag (and/or patient)**
  - Used as a verification of positioning after rotation

- **K0 will also be marked on the vacbag**
  - From Pelvis Isocenter, shifts to K0 will be calculated, with remainder from K0 to Upper Leg Isocenter. Once patient is moved from HFS to FFS, this remainder will be applied
Verification Sim (Lower Body, Feet-First)

- **Rotate un-indexed stereotactic board to feet first supine**
  - Use lasers to straighten board, verify alignment
  - Bottom of board flush with superior aspect of table
- **Apply shift remainder from K0 to Upper Legs isocenter**
  - Verify position using SSD and SETUP SKIN MATCH
- **Acquire AP/Lateral images at upper leg isocenter**
  - MV port field, larger (helps to get pelvis or knee)
  - Apply necessary shifts (mark)
- **Shift inferiorly to lower leg isocenter**
  - Repeat imaging/mark process
Treatment Delivery

- Same procedure as verification simulation
  - Begin Head-First Supine (VMAT)
  - Triangulation based on CT marks
  - Use isocenter marks from v-sim
  - Thoracic and Pelvic AP images

- Begin treatment after CBCT and continue inferiorly

- Same setup rules apply
  - 5mm maximum difference pelvis iso to head iso compared to planned value

Entire Verification Plan Process
- 2-3 hours

Treatment Delivery
- 1.5-2 hours each session (BID)
- Based on setup, Imaging
Setup Analysis

The James

The Ohio State University
Wexner Medical Center
Setup Analysis (Treatment Plan)

- By having overlapping fields (with base dose planning), dose sharing/fall-off between fields is not as steep

- Abdominal Total: Plan Dose falls from 12 Gy to 6.4 Gy in 2.5 cm
  - Fall-off Rate = 22.4 cGy/mm

- Thoracic Total: Plan Dose falls from 11.8Gy to 6.4 Gy in 3.5 cm
  - Fall-off Rate = 15.4 cGy/mm
<table>
<thead>
<tr>
<th>TABLE</th>
<th>AP FILM THORAX</th>
<th>AP FILM PELVIS</th>
<th>ESTIMATED ABDOMEN SETUP</th>
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<td>-0.42</td>
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<td>0.16</td>
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<td>LAT 0.45</td>
<td>LAT 999.24</td>
<td>0.65</td>
<td>999.89</td>
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</tbody>
</table>

**Notes:**
- Setup HN Table Positions
- AP Film Thorax
- AP Film Pelvis
- Estimated Abdomen Setup
- Final positions are in red.
Setup Analysis

- **Based on couch longitudinal coordinates, we are able to assess the degree of compression or extension**
  - Sup/Inf plane
  - This has the ability to derail a plan with multiple isocenters

- **Coordinates acquired from AP setup fields of Thorax and Pelvis**
  - Compared to Superior/Inferior distance between isocenter in the treatment plan

- **If difference is >5mm, we will adjust setup**

- **Our patients have been very consistent in length, as seen to left**

<table>
<thead>
<tr>
<th>Thorax to Pelvis separation</th>
<th>Separation (cm)</th>
<th>Difference (cm)</th>
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</thead>
<tbody>
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<td></td>
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<tr>
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<td>44.12</td>
<td>0.12</td>
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<tr>
<td>Thorax to Pelvis separation:</td>
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<td>-0.07</td>
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<tr>
<td>Thorax to Pelvis separation:</td>
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Results/Discussion with the Principal Investigator

The James

THE OHIO STATE UNIVERSITY
WEXNER MEDICAL CENTER
Ongoing Study → Results Pending
- 5 of desired 25 patients accrued and treated at time of this presentation

Words from Meng Xu Welliver, MD, PhD
- Principal Investigator for OSU 13219
- Dr. Welliver consented to interview regarding our experiences thus far

How are patients tolerating radiation thus far—specifically compared to traditional TBI?

“Patients tend to have less GI toxicities—nausea, vomiting, poor appetite—which are the most acute toxicities (associated with TBI).”

Have there been any complications thus far? What could be the cause of this?

“We’ve seen mucositis from esophagitis in the neck region. We try to limit the dose in the esophagus but it is difficult since it is close to the cervical spine target.”
Words from the PI (continued)

- What have you done for side effect management for these patients?

- “All patients have needed IV pain medication for esophagitis/mucositis.”

- Does this study open an option to those with none previously?

- “Yes, those who are more elderly and sicker patients can now undergo myeloablative RT (as opposed to RIC methods).”

- When might Reduced Intensity Conditioning (RIC) methods be used, such as a “mini-TBI”, and how does this compare to myeloablative conditioning such as TBI/OSMI?

- “RIC methods, including mini-TBI, have been successfully used for lower risk patients, and may be used for the elderly or those who have a co-morbidity. For high risk patients, recurrence of disease can be roughly 50% with RIC, compared to about 25% with TBI.”

  - Note: “Mini-TBI” traditionally 2Gy in 1 fraction, conditioning method
Words from the PI (continued)

- **What is the criteria to treat sanctuary/extramedullary sites in addition to bone marrow, versus marrow only?**

  “We would only treat these sites if they are at high risk of relapse. This would include: 1) ALL and 2) If there is CNS or testicular involvement prior to chemotherapy. As for Liver and Spleen—if they are suspicious or biopsy proven to have disease, then we will treat them.”

- **How satisfied have you been with treatment setup and delivery thus far?**

  “Very satisfied. As you know, we have modified set-up and delivery quite a bit—like removing the mask after finishing treatment of the head/neck region, and limiting the number of CBCT, etc.”
Would you say that OSMI has been more or less labor intensive for the care team when compared to traditional TBI?

“No, not for the care team, but definitely more labor intensive from the treatment planning team.”

What have you learned so far as a result of this study?

“4 out of 5 high risk patients are disease free thus far. The remaining 1 out of 5 patients (has since) died from infection—not likely from OSMI.”

- Note: All 5 received OSMI RT from June-October 2015
Recommendations and Tips

The James
I know, this was my reaction, too.
Recommendations/Tips

- **Training/Stability is vital:** Get a physicist, dosimetrist and therapist dedicated to the physician’s OSMI team—responsibility generates ownership
  - Communicate to make sure the details are covered for each step of the process, Consult -> Simulation -> Planning -> Physics Review -> Delivery
  - Experts in each modality throughout the process
  - Lean on each other through implementation

- **Due to size, structure set may be too large for treatment console**
  - Delete optimization/unnecessary structures after plan approval

- **Reproducibility has been very good, helps to take AP images first**
  - Leads to smaller corrections for CBCT; Verification of length/compression
  - Arms most difficult to reproduce (use 1 cm margin, can use 1.5 cm if necessary—no OAR)

- **Trying to plan “predictable’ shared fall-off between fields is difficult**
  - Collimator 0 or 90 degrees improved this
Recommendations/Tips

- **The narrower the patient, the better the plan is going to be**
  - Arms, width beyond 50cm is very difficult to drive dose

- **6X creates a diamond shape for body VMAT, large hot spots >25-30%**
  - 10X helped alleviate this (< 20% hotspots)
  - Trying to pump dose to arms at oblique angles

- **Order fields superior -> inferior for treatment machine**
  - Progress down the line at the machine, avoid confusion

- **Verification day is crucial**
  - Time consuming, but table parameters can be saved and images taken
  - Good idea of what setup will be like daily for particular patient

- **Plenty of Photos at every stage!**

- **Each step is very time-consuming and labor intensive**
  - Give plenty of time for contouring, planning, setup on these cases

- **IMRT QA can be tedious due to 14 VMAT arcs**
  - Portal Dosimetry at James
Equipment Disclosure - Methodology

- Varian™ Eclipse™
- Varian™ RapidArc™
- Varian™ TrueBeam™
- GE™ PET/CT
- Civco™ Stereotactic Board
- Civco™ Body Pro-Lok™ System
- Q-Fix™ 3-Chamber Vac-Q-Fix™ Cushion
- Civco™ Knee Sponge

- Q-Fix™ Aquaplast U-Frame Mask - Standard
- Q-Fix™ U-Frame
- Q-Fix™ Q2 Silverman HR
- Q-Fix™ Moldcare ® 20x35 cm Cushion
- Varian™ Real-time Position Management (RPM)™ System
References


Thank You!

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(614) 293-5747

To learn more about Ohio State’s cancer program, please visit cancer.osu.edu or follow us in social media: