Current Status of Clinical Tomotherapy at the University of Wisconsin

Valle d'Aosta Conference, 20 November 2010

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THANKS

Grazie to Professor Tofani and Professora Peroni for the invitation to this beautiful country to be part of this exciting conference.

2. UW Tomotherapy Lung Clinical Program (Bin protocol and SBRT)

3. UW Tomotherapy WBHA Brain treatments (WBRT with SIB and HA-SRS)
History of Tomotherapy at UW

- 1988 – First ideas at the University of Wisconsin.
- 1993 – First paper of tomotherapy published.
- 1994 – GE Radiotherapy (Buc, France) funds UW research project.
- 1997 – GE gets out of radiotherapy.
- 1997 – Mackie and Reckwerdt found TomoTherapy Inc.
- 2002 – Received FDA 510(k) to market.
- 2002 – First patient treated at UW.
- 2003 – First deliveries of HI-ART units.
- 2006 – Second UW machine commissioned in Madison.
UW Benchtop unit

Orion 4 MV linac, GE detectors, rotating stage.

First experiments were on this unit with canine cadavers.
UW Clinical Helical Tomotherapy Unit

May 2000 at UW Physical Sciences Laboratory, Stoughton WI
FDA Approval Celebrations, 2002

Julie Zachman
Ken Ruchala
Guang Fang
Paul Reckwerdt
Gustavo Olivera
Jeff Kapatoes
August 2002 at UW Radiotherapy Clinic, notice the very small room, used to house a Varian 4 MV linac.
% Tomotherapy Treatments at UW (2005-2010)

2010: ~ 9000 tomo treatments so far
Current Tomotherapy Special Procedures

- Clinical objective: To utilize the Tomotherapy system’s integrated helical IMRT delivery and daily in-room image guidance to improve outcomes...not just “pretty pictures.”
- Today’s talk focuses on 2 current UW clinical programs:
  - Lung – dose escalation and SBRT
  - Brain WBRT-HA, SRS and WBRT with SIB and HA
I. 2007 Dose escalation
   A. “Bin Protocol” (RO 04502), 79 enrolled, closed and now will we begin enrolling patients on RTOG 0617 (dose escalation and chemotherapy trial)
   B. Initial results of bin protocol.

II. SBRT
   A. 2006 Radiosurgery paper: “How can tumor effect and normal tissue effect be balanced in SBRT” *
   B. 2006 Feasibility Study for SBRT using TomoTherapy
   C. 2007 IG–SBRT Protocol, peripheral (RO 05503)
   D. SBRT data: Preliminary SBRT results

* Quite a bit of radiobiology, since we are dealing with dose escalation. So I added a box with definitions of the acronyms on some slides.
• 75-80 % lung cancer
• With conventional dose schemes (50-66 Gy, 1.8-2.5 Gy/fxn), 5 yr survival < 20-30%
• Martel et al. (1999) set ground work for dose escalation to improve local-progression free survival.


85 Gy for 50 % ! Impossible/not feasible with standard fractionation and conventional XRT.
I. “Bin Protocol”

- “The Use of Helical Tomotherapy to Achieve Dose-per-fraction Escalation in Lung Cancer” Study Chair, Minesh Mehta M.D.
- **Purpose:** determine maximum tolerated dose with helical Tomotherapy.
- Clinical endpoint: grade 3 pneumonitis lasting > 2 weeks.
- Always 25 fractions, dose per fraction varied in each bin.
- Fractional dose bins based on tumor size and volume of residual lung. *(bins are based on ratio of doses, RNTD_{mean})*
- Fractionation scheme set by % NTCP (keep risk of grade 2 pneumonitis < 20%) which is represented as a function of RNTD_{mean}
- Esophagus dose is often limiting factor.

**NTCP:** Normal Tissue Control Probability
**NTD:** Normalized tissue dose, in 2 Gy fractions
**RNTD:** ratio of NTD of tumor to residual lung
Precise Immobilization and Motion Management

- Reduce INTRA-fraction motion by inhibiting breathing motion
- Easy to ensure set-up reproducibility
- No need for external coordinate system with MVCT
UW “Bin Protocol” How high can we go?

- Calculate the ratio of the $\text{NTD}_{\text{mean}}$ (Normalized total dose in 2 Gy fractions) of the residual lungs to that of the tumor

- Risk stratified bins: If RAR are within tolerance, stay in bin. If not, we drop a bin.

- Check that the $\text{NTD}_{\text{Esophagus}} < 64\text{Gy}$ and $\text{NTD}_{\text{cord}} < 50 \text{ Gy}$

- Continual reassessment of bins (over 5 yrs)

\[
R_{\text{NTD}}_{\text{mean}} = \frac{\text{NTD}^{\text{residLung}}_{\text{mean}}}{\text{NTD}^{\text{PTV}}_{\text{mean}}}, \text{ all doses are normalized to 2 Gy/fraction dose level.}
\]

<table>
<thead>
<tr>
<th>Bin</th>
<th>$R_{\text{NTD}}_{\text{mean}}$</th>
<th>Dose schedule (2007)</th>
<th>5/09 Dose schedule ($\text{BED}_{2\text{Gy}}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.00-0.119</td>
<td>3.22 Gy</td>
<td>3.42 Gy (110 Gy)</td>
</tr>
<tr>
<td>2</td>
<td>0.12-0.179</td>
<td>3.00 Gy</td>
<td>3.22 (100)</td>
</tr>
<tr>
<td>3</td>
<td>0.18-0.239</td>
<td>2.77 Gy</td>
<td>3.22 (100)</td>
</tr>
<tr>
<td>4</td>
<td>0.24-0.309</td>
<td>2.53 Gy</td>
<td>3.42 Gy (70)</td>
</tr>
<tr>
<td>5</td>
<td>0.31-0.41</td>
<td>2.28 Gy</td>
<td>2.28 Gy (60)</td>
</tr>
</tbody>
</table>

All bins are 25 fractions
• Stage: IIIB
• PTV vol: 481 cc
• Res lung vol: 3062
• 2.5 FW, P 0.287, MF 2
• Direction block of L brach. plex.
Recent Bin protocol patient (PTV 481 cc)

- Res lung NTD_{\text{Mean}} (<32 Gy_3)= 15.06 Gy_3
- PTV NTD_{\text{Mean}}= 82.70 Gy_{10}
- RNTD_{\text{Mean}}: 0.18, place in Bin 3 (which used to be 3.00 Gy)
- Tumor NTD_{\text{Mean}}: 82.70 Gy_{10}
- Max dose to 5 cc of eso. (<64 Gy_3)= 50.35 (NTD:50.49)
- Max dose to cord – 44.05 Gy (NTD: 41.95 Gy_3)

<table>
<thead>
<tr>
<th>Bin</th>
<th>RNTD_{\text{mean}}</th>
<th>Current bins</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.00-0.119</td>
<td>3.42 Gy x25 fxn</td>
</tr>
<tr>
<td>2</td>
<td>0.12-0.179</td>
<td>3.22 Gy x25 fxn</td>
</tr>
<tr>
<td>3</td>
<td>0.18-0.239</td>
<td>3.22 Gy x25 fxn ** at time of this patient – 3.0 Gy</td>
</tr>
<tr>
<td>4</td>
<td>0.24-0.309</td>
<td>2.53 Gy x25 fxn</td>
</tr>
<tr>
<td>5</td>
<td>0.31-0.41</td>
<td>2.28 Gy x25 fxn</td>
</tr>
</tbody>
</table>

Note: Bin 3 had the maximum and most frequent change because most patients fell into that bin and the dose could be escalated.
3.00 Gy x 25 = 75 Gy, RBE dose of 100 Gy
Max dose to 5 cc of eso. ($<\text{64 Gy}_3$) = 50.35 Gy (NTD: 50.49 Gy)
2008 results: Better Survival and lower than expected toxicities, max dose has yet to be reached.

46 % As Compared to 21 %
Two Year Survival, with conventional fractionation

<table>
<thead>
<tr>
<th>Grade 2 Pneumonitis</th>
<th>13 %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 2 Esophagitis</td>
<td>15 %</td>
</tr>
<tr>
<td>Grade 3 Pneumonitis</td>
<td>0 %</td>
</tr>
<tr>
<td>Grade 3 Esophagitis</td>
<td>0 %</td>
</tr>
<tr>
<td>2 year Survival</td>
<td>47%</td>
</tr>
<tr>
<td>Median Survival</td>
<td>18 months</td>
</tr>
</tbody>
</table>

Double the comparable data for 2 yr survival (46 vs 21%) with no Grade 3 lung toxicity on hypofractionated, typically Stage 3 lung cancer (46 pts)

2010: Interim Results Summary

- Median follow-up: 13.3 months (71 patients)
- No grade 3 or greater pneumonitis or esophagitis
- Overall survival (2 yr): 44%
- Local control (2 yr): 52%

Enrolled Patients by Stage

- 76% IB - IIB
- 7% III
- 7% IV
- 10% Recurrent

Percentage of patients with toxicity

- Acute esophagitis, grade 1-2: 50%
- Late esophageal toxicity, grade 2: 10%
- Grade 2 pneumonitis: 5%

Chemotherapy:
- None: 23 (32%)
- Adjuvant: 30 (42%)
- Neoadjuvant: 16 (23%)
- Other: 2 (3%)

Presented by Dr. Don Cannon at ASTRO 2010
Interim Results: Local (in-field) Control

$p = 0.1968$

Presented by Dr. Don Cannon at ASTRO 2010
II. Beyond dose escalation...SBRT

- Next step is extreme hypo-fractionation: radio-ablative doses delivered using stereotactic localization, conformal delivery and PTV accounting for accurate tumor motion = SBRT (Stereotactic Body Radiotherapy)
- Timmerman, 2006: SBRT effective, but very toxic to central tumors.
- What about the Radiobiology? Choosing total dose and fractionation schedule for an optimal balance between TCP and NTCP

TCP: Tissue Control Probability, NTCP: Normal Tissue complication Probability

Timmerman et al, J Clin Onc, 24(30) 2006
Total dose should be $NTD_{10} \geq 84$ Gy to achieve 80% progression free survival. Since accelerated repopulation is avoided with the short delivery schedules (< 2 weeks).

Graph based on normal fractionation, not SBRT.

TCP curve excluding the effect of proliferation as recalculated by Fowler, Tomé, Fenwick and Mehta [10]. $D_{50} = 70$ Gy and $\gamma_{50} = 1.94$.

TCP curve including the effect of proliferation as published by Martel, Haken, Hazuka et al. [11]. $D_{50} = 84$ Gy and $\gamma_{50} = 1.5$.
Radiobiology: Patient Specific Fractionation Scheme

• Model based, patient specific methodology to select appropriate dose fractionation for radio-ablation SBRT (TFM model):
  – Progression Free Survival at 30 months ≥ 80%
  – Risk of significant pneumonitis (grade 2 or above) < 20%

• Fractionation schedule depends on RATIO of VOLUMES:
  – Prescription Isodose Volume (PIV): volume actually irradiated to at least the prescription dose
  – The NTD_{mean} received by the residual healthy lung
  – The volume of the residual healthy lung
  – Minimal peripheral late local damage NTD_{3} around the high dose volume

Tomé, Fenwick, Mehta, Radiosurgery, 2006:6;87-98
Is this Feasible with Helical Tomotherapy?

- Report on technical feasibility, dosimetric aspects and daily image guidance with MVCT for 9 early stage, medically inoperable patients treated with SBRT on Tomotherapy at UW between Nov 2004-April 2006.

- 60 Gy total (12 Gy x 5) to a motion defined PTV + 6 mm margin, average delivery time of 22 minutes.

- **Primary endpoint:** Tomotherapy SBRT is feasible and well tolerated.

- **Secondary endpoint:** assessing acute and sub-acute toxicity and tumor response.
  - Mean NTD_{tumor}=117 Gy_{10} and Mean NTD_{res lung}=9 Gy_{3}
  - No patients had grade ≥2 pulmonary toxicity
  - Mean tumor regression as seen on MVCT 72%

Hodge et al., *Acta Oncologica* 2006 (45), 890-896
• Phase I Study of Image Guided Stereotactic Radiotherapy for Small Lung Malignancies (RO 05503, Study chairs: Drs. Mehta and Khuntia.)

• Primary objectives:
  1. Verify TFM model’s prediction for 80% or higher 3 year tumor control
  2. Verify TFM model's prediction of < 10% grade II radiation pneumonitis rates at 6 months.

• Peripheral tumors of any T stage (NO), ≤ 6 cm, no concomitant chemo, may not be on > 2L oxygen (refer to protocol for other criteria)

• Must be able to tolerate BodyFix immobilization device.
UW SBRT Protocol: PTV definition

- Target delineated using FDG-PET and 4DCT. GTV includes all areas of SUV ≥ 4 and final GTV based in clinical judgment.
- Motion defined envelope (MDE) of GTV position (with immobilization device in place) during respiration course.
- PTV = MDE + 5 mm (10 mm SI direction)
1. Use Body-Fix or other immobilization system, ideally, need to keep motion under 5mm.

2. Contour ITV on 4D CT scan, Expand ITV by 5 (axial) – 10 (longitudinally) mm to account for CTV margin and setup variation = PiTV

3. Contour OAR (Brachial plexus, spinal cord, normal lung, ribs, trachea, heart, esophagus…). Create a 2 cm ring to keep dose homogeneous.

4. Choose total dose (ie 70 Gy) and plan:
   1. Use smaller pitch (0.143) to allow for delivery of larger fractional dose avoid multiple fields (usually need 2 “passes”)
   2. Keep mod factor low to minimize treatment time (1.82)
   3. Often will be able to get away with a field size of 2.5

5. Pick fraction size based on patient specific model
Sample SBRT protocol patient

- Stage IA(T1,N0,M0)
- PTV volume: 122 cc
- Residual Lung: 5381 cc
- Green is the 98% ID Volume
- Direction block of cord
- Minimize dose to ribs
- FW = 1, P 0.215, MF 2.67
- 1636 sec for each & 7 Gy pass
- First MD has to choose Total dose. (usually pick 60 or 70)
- How was fraction size chosen?
Each curve represents different fractionation schemes and what the NTD to residual lung would be for a given ratio of volumes. Red line represents 20% risk of > grade 3 pneumonitis.
Example: RL vol. = 5381 cc and PIV 141 cc = ratio 3 %, bottom 6 fractionation schemes are ok, but if ratio is 7 only bottom 2 curves are ok.
Step 2. Based on the NTD$_3$(mp) determined in step 1, select # of fractions and dose/fxn such that the expected NTD$_{10}$ > 84 Gy$_{10}$ and its expected local damage NTD$_3$ ≤ NTD$_3^{MP}$ as selected in step 1.

3 - 9 fractions 5 is common
Back to sample SBRT patient

Note directional cord block
Back to sample SBRT patient

esophagus - green
Res lungs - turquoise

Cord - yellow
ribs

Brachy plex - purple

PTV
SBRT – Restrictions on Sensitive Structures

- Once you pick your fractionation scheme you need to confirm your other RAR are acceptable
- Use concept of FED to convert back to doses delivered at standard fractionation at which the tolerance tables are listed.

Patient Name: SW.txt
MR Number: 14Gyx5
RNTD Mean = 0.10 (not used for SBRT)
Residual Lung NTDMean (<18.5 Gy3) = 14.64
Tumor NTDMean = 145.04
Max FED Dose to Esophagus (<27 Gy3): 3.79
Max FED dose to cord (<18 Gy3) = 9.75
Max FED dose to Heart (<30 Gy3) = 6.15
Max FED dose to Trachea (<30 Gy3) = 0.13
Max FED dose to BP (<30 Gy3) = 0.04

We run a simple MatLab script to calculate FED. (max tolerable doses are in parenthesis.)

\[
FED^{fs}_{\alpha/\beta} = \frac{D(1+d/\alpha/\beta)}{(1+fs/\alpha/\beta)}
\]
Initial staging was IA- 78% and IB- 22%
Follow-up: Median 20.8 months (all patients) and 30.6 months (living)
In-field recurrence 1/23 pts all 12Gy x5 (linac and tomo)

Courtesy of Dr. Wolfgang Tomé
Disease Free Survival – UW Experience II

- 2-yr DFS 75%
- 2-yr CCS 79%

Courtesy of Dr. Wolfgang Tomé
Grade 2+ acute toxicity is 9%.
Grade 3 chronic toxicity is 13%.

Also note: only 4 (17%) had rib fractures, no Grade 2+ skin, esophageal or cardiac toxicities reported.

Courtesy of Dr. Wolfgang Tomé
Summary of Current NSCL UW “Algorithm” (inoperable patients)

- **Early stage (I/II): SBRT**
  - Peripheral – RO 05503 SBRT protocol
    - If ineligible: many still can get SBRT off protocol
  - Central – UW will start enrolling patients in RTOG 0813 SBRT protocol in January 2011
    - If ineligible: standard 3D or IMRT with possible dose escalation, non-SBRT

- **Stage IIIA/IIIB: Dose Escalation**
  - Any location – RTOG 0617 – dose escalation and chemo (Bin Protocol, RO 05503 is ending)
    - If ineligible for RTOG 0617, standard fractionation or some escalation based on our bin protocol (which will be closed)
Outline of topics to discuss regarding UW Brain Program

I. Whole Brain Radiotherapy with Hippocampal Avoidance (WBRT-HA)
   A. Why avoid Hippocampus?
   B. 2007 Planning study by Gutierrez et al.
   C. “How to” (tomo or linac) precursor to RTOG 0933

II. SRS –
   A. Planning technique
   B. 9 met palliative patient example

III. Whole brain with Simultaneous Integrated Boost (WB-SIB)
Why avoid hippocampus when treating WBRT?

- Hippocampus involved with learning, memory and spatial information processing.
- Dr. Khuntia et al proposed a potential benefit of hippocampal avoidance (HA) during WBRT.
- Monje et al. showed radiosensitivity of hippocampal-dependent functions in rats.
- Late effects (necrosis, memory changes and neurocognitive deficits observed in long term WBRT survivors.)

Khuntia et J. Of Clin Onc 24(8) 2006
Monje et al. al.Curr Opin Neurol 16 2003
2007 Planning Study

- Retrospective planning study on 10 patients who received SRS or WB
- Limit dose to hippocampus < 6 Gy
- Analyzed “goodness of plans” using different planning parameters (FW: 2.5 and 1.0, P of 0.215, 0.289 and 0.433)

Conclusions: Helical Tomo can deliver:
- Homogeneous WB dose distribution
- Conformal Hippocampal avoidance (NTD\textsubscript{mean} of 5.8.Gy\textsuperscript{2} with 1.0 cm FW)
- Radiosurgically equivalent dose distribution to individual mets
- PiTV, CN and HI for mets and homogeneity of WB dose was improved with 1.0 cm FW but at a cost of more than double the treatment time.

- Created a “how to” document
- Whether the HA delivers low enough dose to have a clinical benefit while maintaining TCP is the next question....

Gutierrez et al Int J Rad Onc Biol Phys 69(20) 2007
WBRT with HA: a “How to technique”

- A clear and consistent method is described to deliver WBRT-HA with either helical tomotherapy or linac IMRT.
- Contouring – important to minimize avoidance region (ave. volume of 3.3 cm$^3$)
- Treatment parameters: for both tomo or linac
- **Next step is a phase II Cooperative trail (RTOG 0933, opening in 2011.)** Contouring will be reviewed by UW team.
First Address the Contouring

- Semi-automatic fusion of CT (non contrast) and MRI (gadolinium contrast-enhanced T1-weighted) images (1.25 mm slice thickness)
- Target and avoidance structures were contoured using the Phillips Pinnacle\textsuperscript{3} version 8.0m treatment planning software.
- Hippocampus avoidance region (green) is a 5 mm expansion of hippocampus and had an average volume $3.3 \text{ cm}^3$

Gondi, Tolakanahalli, et.al, I.J. Radiation Oncology Biol Phys 2010
### Tomo Planning Parameters

- Prescription: 30 Gy in 10 fractions
- 1.05 cm field width, Pitch = 0.215 and Modulation < 3.0
- * Eyes and lenses are directionally blocked
- Linac parameters are in paper

<table>
<thead>
<tr>
<th>Structure</th>
<th>Helical Tomotherapy Plan Criteria</th>
<th>Penalty</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Brain PTV</td>
<td>Max Dose: 30 Gy</td>
<td>100</td>
<td>200</td>
</tr>
<tr>
<td></td>
<td>30 Gy to ≥96%</td>
<td></td>
<td></td>
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<tr>
<td>Hippocampus</td>
<td>Max Dose: 6 Gy</td>
<td>100</td>
<td>500</td>
</tr>
<tr>
<td></td>
<td>3 Gy to ≤20%</td>
<td>20</td>
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<td>Hippocampal Avoidance Volume</td>
<td>Max Dose: 30 Gy</td>
<td>1</td>
<td>5</td>
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<tr>
<td></td>
<td>20 Gy to ≤20%</td>
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<td>Eyes*</td>
<td>Max Dose: 8 Gy</td>
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<td>20</td>
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<td>5 Gy to ≤20%</td>
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<td>Lenses*</td>
<td>Max Dose: 3 Gy</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>2 Gy to ≤20%</td>
<td>10</td>
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</tbody>
</table>

*Gondi et al Int J Rad Onc Biol Phys 78(4) 2010*
DVH for five patients on Tomotherapy

Gondi, Tolakanahalli, et.al, I..J. Radiation Oncology Biol Phys 2010
P3 IMRT DVH – Linac based

[Graph showing dose-volume histograms for different structures: PTV, Eyes, Hippocampus, Lenses]
Acceptable TC and HI with Tomo and Linac

- Target Coverage (TC) = 1 means perfect coverage
- Homogeneity Index (HI) = 0 means totally homogenous dose.

\[ TC = \frac{\text{fraction of PTV receiving } D_{Rx}}{\text{volume of target PTV}} \]

\[ HI = \frac{D_{2\%} - D_{98\%}}{D_{\text{median}}} \]

<table>
<thead>
<tr>
<th>Patient</th>
<th>Target coverage</th>
<th>Homogeneity index</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>HT</td>
<td>LINAC</td>
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<tr>
<td>1</td>
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<td>0.92</td>
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<td>0.92</td>
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<td>0.95</td>
<td>0.93</td>
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<tr>
<td>Mean</td>
<td>0.95</td>
<td>0.93</td>
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</table>

Gondi et al Int J Rad Onc Biol Phys 78(4) 2010
Acceptable TC and HI with Tomo and Linac

- Normalized Mean Tissue Dose to hippocampus < 8 Gy

<table>
<thead>
<tr>
<th>Patient</th>
<th>HT</th>
<th>LINAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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<td>7.2</td>
</tr>
<tr>
<td>2</td>
<td>4.8</td>
<td>7.3</td>
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<tr>
<td>3</td>
<td>4.6</td>
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<tr>
<td>4</td>
<td>4.8</td>
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<tr>
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<td>7.2</td>
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<tr>
<td>Mean</td>
<td>4.9</td>
<td>7.3</td>
</tr>
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</table>

Gondi et al Int J Rad Onc Biol Phys 78(4) 2010
WBRT HA Current case

- Rx: WB – HA 95% will receive 37.5 Gy
- 2.5 Gy/fraction
- Note protocol study is 30Gy/3 Gy fxn
- FW 1.0, P 0.215, MF 2.9
- Direction blocking of both eyes
- Complete blocking of both lenses

<table>
<thead>
<tr>
<th></th>
<th>Hippocampus</th>
<th>Hippocampus avoidance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume (cc)</td>
<td>3.25</td>
<td>25.09</td>
</tr>
<tr>
<td>Max dose (Gy)</td>
<td>16.84</td>
<td>33.7</td>
</tr>
<tr>
<td>Median</td>
<td>9.64</td>
<td>15.28</td>
</tr>
</tbody>
</table>

\[(30/37.5)\text{Gy} \times 9.64 \text{ Gy} = 7.7 \text{ Gy}\]
DVH for WBHA

- L (green) & R optic nerve
- Brain stem
- WB CTV
- eyes
- lenses
- HA avoidance
- HA
Note blocking of eyes and lens
Whole Brain with Hippocampal Avoidance and Simultaneous Integrated Boost

- **WBRT** – sterilize microscopic disease
- **SIB** – improve local control which has been shown to correlate with improved survival
- **HA** – preserve post WBRT hippocampal neurogenesis
- Tomotherapy makes this dose distribution possible
- Daily (or more) imaging ensures boost and avoidance regions are covered as planned

• Minimizing avoidance volume is critical to avoid a clinically unacceptable risk of disease progression.

• By analyzing location of mets (Gondi et al. Radiother Oncol 2010) and assuming that risk of developing subsequent mets scale with risk at presentation, WBRT-HA patients derives 91.4% of the relative benefit.

• Postulate: either helical tomo or linac bases IMRT will sufficiently spare hippocampus to yield a clinically significant neurocognitive benefit

• RTOG 0933 will open in early 2011
In Conclusion

• The research and development of tomotherapy at the University of Wisconsin has been a wonderful and enriching experience for all of us. I was privileged to be involved in the earlier years and it is exciting to present to you some of the new ways in which we clinically use tomotherapy to improve patient care.

• We have had great success on treating for 5 years on two tomotherapy units at the UW Main Campus Hospital.

• I shared with you two examples of advanced applications of tomotherapy: lung cancer and WBRT-HA with proven successes whose potential is still being developed.

• Thank you to Profesor Tofani and Professora Peroni again for the extraordinary invitation to this scientific conference.

• I, and my colleagues in Madison look forward to learn from you and collaborate with you in the near future.
SRS... 9 mets example
I am using her slides and illustrating the method with the first case recently treated at UW. A palliative 9 met case with only mask for localization.
9 Met “SRS” case

- Mask only,
- Created 2 plan (one for inferior mets and one for superior mets) 2 plans
- 37.5 Gy (7.5 Gy X 5 fractions)
- Highest Rx was to PTV 2 and it is 37.5 Gy

<table>
<thead>
<tr>
<th>PTV</th>
<th>Vol (cc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23.97</td>
</tr>
<tr>
<td>2</td>
<td>5.38</td>
</tr>
<tr>
<td>3</td>
<td>1.3</td>
</tr>
<tr>
<td>4</td>
<td>5.24</td>
</tr>
<tr>
<td>5</td>
<td>1.64</td>
</tr>
<tr>
<td>6</td>
<td>1.3</td>
</tr>
<tr>
<td>7</td>
<td>3.19</td>
</tr>
<tr>
<td>8</td>
<td>3.91</td>
</tr>
<tr>
<td>9</td>
<td>1.07</td>
</tr>
</tbody>
</table>
Plan 1: Superior Lesions

- Rx: CSV2 100% to 37.5 Gy/5 fxn
- PTVs 1-5, no RAR
Contouring for the PTVs

- All targets should be modified with the following planning structures
  - 3mm ring (not an expansion)
  - Create a small central subvolume at the center of the tumor, use paint brush with 2.5mm diameter and place one contour at the point center as determined by the point placed previously
  - For targets over 2cc ONLY, add a 2mm Inner Ring at the periphery of the target
  - For targets over 2cc ONLY, add a larger contracted subvolume (SV) that is 2cc or less around the CSV.
  - Keep or create the PITV structure (2cm expansion) used in conventional SRS planning for data analysis
Small Lesion Helper Contours

CSV

3mmRing

Target
Large lesion helper contours
LARGE Target Planning Volumes

CSV

3mmRing

SV

2mmOuterRing

3mmRing

2mmOuterRing
DVH plan 1
Plan 2 inferior PTVs

- Rx 7.5 Gy x 5 = 37.5 Gy
- PTV 6-9
- RAR: R L Lens, Optic chiasm, retina, brain stem
- 1.0 cm FW
- MF= 1.8
- P= 0.287
Plan Settings

Start with the following plan parameters:

- Field Width – 1.0cm
- Dose Grid - Fine
- Modulation Factor – 1.7

<table>
<thead>
<tr>
<th>Highest Target Prescription</th>
<th>Pitch</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 Gy</td>
<td>0.13</td>
</tr>
<tr>
<td>21 Gy</td>
<td>0.13-0.14</td>
</tr>
<tr>
<td>20 Gy</td>
<td>0.14</td>
</tr>
<tr>
<td>18 Gy</td>
<td>0.17</td>
</tr>
<tr>
<td>15 Gy</td>
<td>0.18</td>
</tr>
</tbody>
</table>
• The CSV structure for the largest target should initially be used for the prescription

• Prescription type is "%Vol"

• 100% of the volume should receive the prescribed dose to the target divided by the desired prescription isodose line. For example to match conventional SRS, this would be (Prescribed Dose)/0.80
Planning Objectives I

- Tumor Settings
  - Voxels
    - Importance and all penalties = 1
    - Max Dose = Min Dose = 100% DVH = Rx/0.8
  - Targets
    - Importance = 1
    - Max Dose = 120Gy
    - Max Dose Penalty = 1
    - DVH Point = 100% at Rx
    - Min Dose = Rx
    - Min Dose Penalty = 100
Planning Objectives II

- Sensitive Structure Settings
  - 3mm Ring Structures
    - Importance = 1
    - Max Dose = Rx Dose
    - Max Dose Penalty = 100
    - DVH Point – 50% at ½ Rx Dose
    - DVH Penalty = 1
Planning objectives III

• Alterations for large (>2cc) metastases
  – Use one of the contracted subvolumes, choose the largest one that is less than 2cc
  – Type is RAR and overlap priority should be higher (lower number) than the 3mm ring for the same target
    – Importance and all penalties are 1
    – Max = Min = 50% DVH = Rx/0.8

• Alterations for very large (>4cc) volumes and peripheral hot spots
  – Reduce the modulation factor from 1.7 to 1.4
Plan Optimization

- Setting up the plan as described in the preceding slides and allow beamlets to run (add slide for estimation of beamlet comp time)
- Let the plan run 20 iterations
- Evaluate plan with respect to planning goals
- Make appropriate changes as described on the following slides
- Run 20 iterations
- Repeat until goals achieved
- If plan change is too big, cancel the plan and start over instead of trying to bring it back.
Plan at 20 Iterations

- Should see that the dose across the targets are inhomogenous.
- Amount of inhomogeneity at this stage will vary with target volume (i.e. large targets will be less homogeneous than small targets).
- The minimum dose to the target will likely not be at exactly the prescription dose but should be close.