Automating Treatment Planning Process: Stanford Experience

Nataliya Kovalchuk, PhD, Yong Yang, PhD, and Eric Simiele, PhD

Stanford University School of Medicine
Disclosures

- None
Stanford’s Path to Auto-Planning

- **2017**: prostate and HN RapidPlan models, 3D FiF automation with EZFluence
- **2018**: AI-based 3D-dose prediction models based on PTV-only plans
- **2019**: auto-planning Eclipse API-based scripts for HN, prostate, prostate+nodes
- **2020**: auto-planning Eclipse API-based scripts for VMAT TBI
- **2022**: auto-planning Eclipse API-based scripts for HN protocols (NRG HN001, HN005, HN006, HN009), GYN, rectum
- **Work in progress**: auto-planning for CSI, lung, HN auto-planning for RefleXion X1, and GYN brachy
Automating Prostate/HN/GYN/Rectum Planning
3D Dose Prediction using Deep CNN

Physics in Medicine & Biology

PAPER
Incorporating dosimetric features into the prediction of 3D VMAT dose distributions using deep convolutional neural network

Ming Ma¹, Nataliya Kovalchuk¹, Mark K Buuyounouski¹, Lei Xing¹ and Yong Yang¹
Published 20 June 2019 • © 2019 Institute of Physics and Engineering in Medicine

Physics in Medicine & Biology, Volume 64, Number 12

Citation Ming Ma et al 2019 Phys. Med. Biol. 64 125017
3D Dose Prediction using Deep CNN

Contours | Clinical dose | Contour-based prediction | Contour+PTV only prediction
--- | --- | --- | ---

Mean Sum of Absolute Residuals (SARs) for DVHs

<table>
<thead>
<tr>
<th>Organ</th>
<th>Contour-based prediction</th>
<th>Contour+PTV only prediction</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV</td>
<td>0.036</td>
<td>0.007</td>
</tr>
<tr>
<td>Bladder</td>
<td>0.047</td>
<td>0.035</td>
</tr>
<tr>
<td>Rectum</td>
<td>0.068</td>
<td>0.067</td>
</tr>
</tbody>
</table>

Ma et al, (PMB 2019)
Stanford Auto-planning Solution

Preparation for optimization
- Generate optimization structures
- Generate beams
- Run PTV-only plan to predict dose

Optimization
- Create/update optimization parameters

Evaluation
- Evaluate plan
- Create new optimization volumes (hot/cold spots)

Auto-plan

a few iterations
Auto-planning Script GUI
Head and Neck Plan Example

Isodose improvements with successive iterations

DVH (top) and isodose comparison between initial and final optimization results
Prostate Plan Comparison: Auto vs Manual Clinical

Auto Plan vs Clinical Plan

Square: Clinical plan; Triangle: Auto plan
HN Plan Comparison: Auto vs Manual Clinical

Square: Clinical plan; Triangle: Auto plan
Evaluation of Prostate Auto-plans

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Evaluation of HN Auto-plans

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Physicians HN Plan Evaluation Results

- 20 anonymized HN plans (10 auto-planned and 10 manually planned) were evaluated by 5 physicians for 10 patients

- Clinical Acceptability:
  - Auto-plans: 47 (94%) – yes, 3 – no
  - Manual clinical plans: 43 (86%) – yes, 4 – no, 3 - borderline

- Preference to use for treatment:
  - 7 auto-plans
  - 1 equivalent
  - 2 manual clinical plans
Updating Auto-planning Scripts following Physician/Dosimetrist Feedback
Incorporated All MDs Requests into One Approach

Physician 1: posterior neck sparing

Physician 2: no 30 Gy dose “bridging”

Physician 3: CTV V100%=99-100%
NRG HN Trials Auto-planning: HN001, HN005, HN006, HN009
Automating VMAT TBI
Children’s Oncology Group (COG) survey

- In 2020-2021, COG TBI workgroup conducted survey of 152 institutions on TBI techniques for physicists and physicians
- 100% of physicians would like to reduce the lung dose for myeloablative regimens
- 75% of physicians (n=85) would like to introduce VMAT or Tomo TBI in their clinics
- Only 7 US institutions adapted VMAT TBI and 3 institutions adapted Tomo TBI

![Bar chart showing TBI techniques and % institutions](chart.png)
Stanford VMAT TBI Experience

- Introduced VMAT TBI in Oct 2019
- In 2020 created automated planning scripts and shared with the public
- Treated >50 VMAT TBI patients to date
Stanford VMAT TBI: SIM

- Full body scan in whole body bag on Siemens PET/CT scanner with 4-5 mm slice thickness
- Knee fix, foot fix, arms tight to the body
- Matchline b/w HFS and FFS determined at SIM:
  - Patient height ≤ 115 cm – VMAT only (3 isocenters)
  - Patient height > 115 cm – VMAT (3 isocenters) + AP/PA (1-2 isocenters) on Spinning Manny

Figure 1. In-house developed rotational couch-top enabling patient position transition from HFS to FFS.
Stanford VMAT TBI: Contouring

- **Myeloablative regimen (12-13.2Gy):** sparing lungs, kidneys, lenses
- **Reduced Intensity Conditioning (2-4Gy):** sparing lungs, kidneys, lenses, brain, thyroid, ovaries/testes
- **PTV_Body = (Body-3 mm) – (Lungs+3 mm) – Kidneys – [other OARs]**
- **5 mm flash/bolus is added during optimization**

### Table: Structures and Descriptions

<table>
<thead>
<tr>
<th>Name of Structure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human_Body</td>
<td>Search BODY in Eclipse</td>
</tr>
<tr>
<td>Human_Body-0.3cm</td>
<td>0.3 cm inner margin</td>
</tr>
<tr>
<td>Lungs</td>
<td>Lungs, remove tiny islands</td>
</tr>
<tr>
<td>Lungs_Eval</td>
<td>Lungs – 1 cm</td>
</tr>
<tr>
<td>Lungs-2cm</td>
<td>Lungs – 2 cm</td>
</tr>
<tr>
<td>Kidney_R/L, Kidneys</td>
<td>Kidneys, remove tiny islands</td>
</tr>
<tr>
<td>Kidneys-1cm</td>
<td>Kidneys-1 cm</td>
</tr>
<tr>
<td>Ovary_R/L</td>
<td>Ovaries</td>
</tr>
<tr>
<td>Scrotum, Testes</td>
<td>Scrotum, testes</td>
</tr>
<tr>
<td>Brain</td>
<td>Brain, remove tiny islands</td>
</tr>
<tr>
<td>Brain-0.5cm</td>
<td>Brain-0.5cm</td>
</tr>
<tr>
<td>Brain_Eval</td>
<td>Brain-1 cm</td>
</tr>
<tr>
<td>Brain-2cm</td>
<td>Brain-2cm</td>
</tr>
<tr>
<td>Brain-3cm</td>
<td>Brain-3cm</td>
</tr>
<tr>
<td>PTV_Body</td>
<td>(Human_Body-0.3cm) – (Kidneys- (Lungs+0.3cm) – (Ovaries+1 cm include bone) or (Scrotum+2cm) – (Brain-0.5cm)</td>
</tr>
<tr>
<td>Matchline</td>
<td>Plane at the level of pivot bolt center</td>
</tr>
<tr>
<td>TS_PTV_VMAT</td>
<td>Cut PTV_Body at matchline, crop 0.5cm from skin</td>
</tr>
<tr>
<td>Bowel</td>
<td>Bowel bag</td>
</tr>
<tr>
<td>Lens_R/L</td>
<td>Lenses</td>
</tr>
<tr>
<td>Skin</td>
<td>3mm from Human Body</td>
</tr>
</tbody>
</table>
Stanford VMAT TBI: Beam Placement

- 3 VMAT isocenters in HFS – 6MV/10MV (head, chest, pelvis)
- 1-2 AP/PA isocenters in FFS – 6MV (upper legs, lower legs)
- Pelvis VMAT iso and Upper Leg AP/PA iso’s are equidistant from matchline
- >=2-5 cm overlap in junctions for VMAT
- Head iso (3-4 arcs)
- Chest iso (3-4 arcs)
- Pelvis iso (2-4 arcs)
- Skin match for AP/PA
- AP/PA fields have 90° coll for FiF
## Stanford VMAT TBI: Optimization

- **FiF for AP/PA**
- **Set AP/PA dose as base for VMAT optimization**
- **Optimizer auto-feathers beam junctions in VMAT**
- **Dose rate at 100-200 MU/min for Head/Chest iso to keep average dose rate <20 cGy/min for lungs**
- **AAA v15.6, 2.5mm dose grid**

<table>
<thead>
<tr>
<th>Structure</th>
<th>Dosimetric parameter</th>
<th>Limit (2 Gy Rx)</th>
<th>Limit (12 Gy Rx)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTV Body</td>
<td>D90%&gt;=</td>
<td>200 cGy (100%)</td>
<td>1200 cGy (100%)</td>
</tr>
<tr>
<td></td>
<td>Dmax&lt;=</td>
<td>240 cGy (120%)</td>
<td>1440 cGy (120%)</td>
</tr>
<tr>
<td></td>
<td>V110%&lt;=</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td>Lungs Eval (Lungs-1cm)</td>
<td>Dmean&lt;=</td>
<td>80 cGy (40%)</td>
<td>480 cGy (40%)</td>
</tr>
<tr>
<td>Lungs</td>
<td>Dmean&lt;=</td>
<td>110 cGy (55%)</td>
<td>660 cGy (55%)</td>
</tr>
<tr>
<td>Kidneys</td>
<td>Dmax&lt;=</td>
<td>210 cGy (105%)</td>
<td>1260 cGy (105%)</td>
</tr>
<tr>
<td></td>
<td>Dmean&lt;=</td>
<td>120 cGy (60%)</td>
<td>720 cGy (60%)</td>
</tr>
<tr>
<td>Bowel</td>
<td>Dmax&lt;=</td>
<td>210 cGy (105%)</td>
<td>1260 cGy (105%)</td>
</tr>
<tr>
<td>Lenses</td>
<td>Dmax&lt;=</td>
<td>180 cGy (90%)</td>
<td>1080 cGy (90%)</td>
</tr>
<tr>
<td>Testes/ovaries</td>
<td>Dmax&lt;=</td>
<td>50 cGy (25%)</td>
<td>ALARA (required &lt;100 cGy)</td>
</tr>
<tr>
<td></td>
<td>Dmean&lt;=</td>
<td>ALARA (required &lt;100 cGy)</td>
<td></td>
</tr>
<tr>
<td>Brain Eval (Brain-1cm)</td>
<td>Dmean&lt;=</td>
<td>150 cGy (75%)</td>
<td></td>
</tr>
<tr>
<td>Thyroid</td>
<td>Dmean&lt;=</td>
<td>150 cGy (75%)</td>
<td></td>
</tr>
</tbody>
</table>
Stanford VMAT TBI: Dose Distribution

- PTV D90% = 100%
- PTV Dmax = 114.6%
- PTV D1cc = 111.5%
- Lungs Dmean = 41.8%
- Ovaries Dmean = 30%
- Kidneys Dmean = 64.1%
- Brain Dmean = 74.9%

Figure 2: Dose volume histogram (upper right) and dose distribution in coronal (left) and axial (lower right) planes for pediatric VMAT TBI patient diagnosed with congenital agranulocytosis and treated to 2 Gy.
Automation of the treatment planning process for VMAT TBI using the Eclipse API framework

https://github.com/esimiele/VMAT-TBI
Plan comparison

Planned 10 VMAT TBI cases manually and with developed scripts:

- Dosimetric indices:
  - Global $D_{\text{max}}$, PTV V110%, lungs and lungs-1cm $D_{\text{mean}}$, kidneys $D_{\text{mean}}$, and bowel $D_{\text{max}}$
  - Paired t-test
  - Approximate planning time
  - Blinded physician review (60 total responses)

Table 1: Achieved plan quality for each metric considered in this work for the a) manual and b) auto treatment plans. All dose and volume values in a) and b) are expressed as a percentage of the prescription dose and PTV volume, respectively. A plan quality value of $N/A$ indicates that this organ was not considered for sparing in this patient.

(a) Manual treatment plans

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>$D_{\text{max}}$</th>
<th>V110%</th>
<th>Lungs $D_{\text{mean}}$</th>
<th>Lungs-1cm $D_{\text{mean}}$</th>
<th>Kidneys $D_{\text{mean}}$</th>
<th>Bowel $D_{\text{max}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>114.5% 0.2%</td>
<td>55.7% 31.8%</td>
<td>67.6% 111.9%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>121.0% 1.4%</td>
<td>56.7% 41.2%</td>
<td>65.0% 106.1%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>119.5% 6.2%</td>
<td>55.0% 45.7%</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>116.5% 0.1%</td>
<td>60.0% 44.6%</td>
<td>N/A</td>
<td>N/A</td>
<td>110.3%</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>114.0% 0.0%</td>
<td>75.0% 60.6%</td>
<td>N/A</td>
<td>108.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>122.5% 2.5%</td>
<td>65.0% 42.8%</td>
<td>60.0% 111.5%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>128.5% 4.5%</td>
<td>60.4% 45.4%</td>
<td>66.3% 110.6%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>121.5% 1.0%</td>
<td>62.5% 40.0%</td>
<td>72.5% 111.2%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>110.0% 0.0%</td>
<td>65.0% 47.0%</td>
<td>70.0% 112.8%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>113.0% 0.0%</td>
<td>58.3% 36.5%</td>
<td>65.0% 110.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(b) Auto treatment plans

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>$D_{\text{max}}$</th>
<th>V110%</th>
<th>Lungs $D_{\text{mean}}$</th>
<th>Lungs-1cm $D_{\text{mean}}$</th>
<th>Kidneys $D_{\text{mean}}$</th>
<th>Bowel $D_{\text{max}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>114.6% 0.1%</td>
<td>41.8% 26.6%</td>
<td>64.1% 110.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>120.5% 2.2%</td>
<td>58.3% 37.3%</td>
<td>64.2% 111.2%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>120.5% 2.0%</td>
<td>52.5% 40.5%</td>
<td>N/A</td>
<td>N/A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>114.7% 0.3%</td>
<td>54.4% 34.1%</td>
<td>N/A</td>
<td>102.5%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>117.5% 0.7%</td>
<td>54.6% 35.8%</td>
<td>N/A</td>
<td>N/A</td>
<td>112.4%</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>121.0% 0.9%</td>
<td>59.4% 36.5%</td>
<td>65.3% 111.6%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>127.3% 5.3%</td>
<td>59.8% 45.7%</td>
<td>73.3% 114.2%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>120.4% 1.0%</td>
<td>59.0% 37.5%</td>
<td>72.6% 115.0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>112.2% 1.8%</td>
<td>53.4% 35.8%</td>
<td>64.9% 112.3%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>114.2% 0.1%</td>
<td>56.4% 35.3%</td>
<td>68.4% 103.3%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Mean and standard deviation, $\sigma$, of the difference in percent between the auto and manual treatment plans. In addition, the calculated p-value from a one-sided t-test is shown for each evaluated metric. A p-value < 0.05 was considered to be statistically significant in this study.

<table>
<thead>
<tr>
<th>Difference</th>
<th>$D_{\text{max}}$</th>
<th>V110%</th>
<th>Lungs $D_{\text{mean}}$</th>
<th>Lungs-1cm $D_{\text{mean}}$</th>
<th>Kidneys $D_{\text{mean}}$</th>
<th>Bowel $D_{\text{max}}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>0.0% -0.1%</td>
<td>-6.3% -7.1%</td>
<td>0.6% -0.5%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\sigma$</td>
<td>1.6% 1.3%</td>
<td>6.9% 7.2%</td>
<td>3.7% 4.3%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p-value</td>
<td>0.969 0.750</td>
<td>0.018 0.013</td>
<td>0.508 0.703</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 3: Resulting dosimetric distributions for patient 1 for the a) manual plan and b) autoplan. The prescription for this patient was 2 Gy in one fraction where lungs, kidneys, bowel, gonads, brain, and lesions were selected for sparing.
Plan comparison

- 20 plans for 10 patients were reviewed by 3 physicians.
- Overall, the autoplan were marked as equivalent or superior to the manual plans 77% of the time.

Stanford University School of Medicine

Simiele et al, PRO 2021
Plan preparation

- Another script – Automated Plan Checker – automates the physics plan check by inspecting >150 plan elements and outputs the DVH constraints metrics.
Comparison between 2D and VMAT TBI

- For 10 patients treated with VMAT TBI conventional 2D TBI plans were created

Ngo et al, (under review, Advances in RO)
Comparison between 2D and VMAT TBI

- Overall, the coverage was compromised for 2D plans
- On average, mean lung dose with 2D plans was $25.6\% \pm 11.5\%$ higher than that with VMAT TBI plans
- Additionally, VMAT TBI plans spared kidneys, brain, thyroid, testes/ovaries where 2D plans delivered prescription dose

<table>
<thead>
<tr>
<th>Patient</th>
<th>PTV D90</th>
<th>PTV Dmax</th>
<th>PTV V100%</th>
<th>Lungs Dmean</th>
<th>Lungs-1cm Dmean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>6.2%</td>
<td>-7.4%</td>
<td>-1.3%</td>
<td>-48.2%</td>
<td>-49.3%</td>
</tr>
<tr>
<td>Patient 2</td>
<td>8.8%</td>
<td>-2.0%</td>
<td>1.5%</td>
<td>-28.4%</td>
<td>-44.8%</td>
</tr>
<tr>
<td>Patient 3</td>
<td>4.7%</td>
<td>-2.9%</td>
<td>2.4%</td>
<td>-36.5%</td>
<td>-43.7%</td>
</tr>
<tr>
<td>Patient 4</td>
<td>10.0%</td>
<td>-3.8%</td>
<td>-0.1%</td>
<td>-27.5%</td>
<td>-38.9%</td>
</tr>
<tr>
<td>Patient 5</td>
<td>6.6%</td>
<td>4.8%</td>
<td>-1.4%</td>
<td>-26.2%</td>
<td>-34.6%</td>
</tr>
<tr>
<td>Patient 6</td>
<td>4.3%</td>
<td>5.4%</td>
<td>0.7%</td>
<td>-16.0%</td>
<td>-26.1%</td>
</tr>
<tr>
<td>Patient 7</td>
<td>5.0%</td>
<td>14.5%</td>
<td>3.5%</td>
<td>-12.2%</td>
<td>-18.4%</td>
</tr>
<tr>
<td>Patient 8</td>
<td>7.4%</td>
<td>9.4%</td>
<td>1.6%</td>
<td>-12.1%</td>
<td>-23.7%</td>
</tr>
<tr>
<td>Patient 9</td>
<td>1.5%</td>
<td>-1.0%</td>
<td>-6.8%</td>
<td>-30.8%</td>
<td>-33.6%</td>
</tr>
<tr>
<td>Patient 10</td>
<td>6.6%</td>
<td>3.1%</td>
<td>0.1%</td>
<td>-17.8%</td>
<td>-28.1%</td>
</tr>
</tbody>
</table>

- Mean $6.1\%$ $2.0\%$ $0.0\%$ $25.6\%$ $34.1\%$
- $\sigma$ $2.4\%$ $6.7\%$ $2.9\%$ $11.5\%$ $10.1\%$
- p-value $8.11E-06^*$ $0.226$ $0.444$ $2.96E-05^*$ $1.02E-06^*$

Ngo et al, (under review, Advances in RO)
Comparison between 2D and VMAT TBI

Stanford University School of Medicine

Blomain, Kovalchuk et al, PRO 2020
Gonadal sparing: 2D vs VMAT

Blomain, Kovalchuk et al, PRO 2020
Patient Outcomes

- 38 ped/young adult patients treated with VMAT TBI from Oct 2019 to Dec 2021
- 38 ped/young adult patients had follow-up 3-20 mo (mean of 10.3 mo):
  - Age: 1 yr – 27 yr (mean of 7.2 yr)
  - Non-myeloablative – 56%; Myeloablative – 44%
- Overall survival at last follow-up: **89.5%**
- Relapse-free survival at last follow-up: **94.7%**
- Toxicity:
  - Pneumonitis (1 (4%); Grade 2; present before RT)
  - Nephrotoxicity (1 (4%); Grade 1; present before RT)
  - Diarrhea - 40%; Grade 3: 1 (2.6%)
  - Fatigue – 55%; Grade 3: 0 (0%)
  - Nausea – 68%; Grade 3: 1 (2.6%)
  - Mucositis - 84%; Grade 3+: 15 (39.5%)
  - Skin Toxicity - 16%; Grade 2: 0 (0%)

O. Marquez, C. Hui, Ped Blood Cancer, 2022
Conclusions

- Auto-planning scripts are loved in the clinic. They reduce treatment planning time and improve the quality of plans. VMAT TBI scripts are shared with the public at https://github.com/esimiele/VMAT-TBI

- Automating treatment planning for VMAT TBI enabled us to switch to more modern TBI technique which offers:
  - possibility of organ sparing (lungs, kidneys, gonads, brain, thyroid, lenses) and SIB boosts
  - accurate dose calculation and image-guided delivery
  - more comfortable patient positioning
  - ability to treat TBI patient is small size vaults
Future Directions

- Children Oncology Group is interested in setting up a multi-institutional trial to show the efficacy of VMAT TBI technique; We are planning on investigating the use of the auto-planning scripts as explorative objective.

- Expanding the auto-planning scripts to other sites: CSI, lung, GYN brachy, HN for RefleXion X1

- Planning on implementing reinforcement learning plan optimizer.
Acknowledgements

- **Physicians:**
  - Susan Hiniker, MD
  - Richard Hoppe, MD
  - Erik Blomain, MD
  - Caressa Hui, MD
  - Beth Beadle, MD
  - Quynh Le, MD
  - Michael Gensheimer, MD

- **Physicists:**
  - Yong Yang, PhD
  - Nataliya Kovalchuk, PhD
  - Eric Simiele, PhD
  - Peng Dong, PhD
  - Lawrie Skinner, PhD

- **Dosimetrists:**
  - Nic Ngo, CMD
  - Jonathan Lewis, CMD
  - Nicole Howell, CMD
  - Daniel Pham, CMD

- **Engineer:**
  - Manny Villegas

- **All Stanford RTTs**
Thank you!

The scripts are shared with the public at https://github.com/esimiele/VMAT-TBI