Targeting Accuracy and Radiosurgical Dose Tolerance

Jimm Grimm, PhD, DABR
Conflicts of Interest

Dr. Grimm designed and holds intellectual property rights to the DVH Evaluator software tool (www.DiversiLabs.com) which is an FDA-cleared product in commercial use, and which has been used for this analysis

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Introduction and Clinical Overview of the DVH Risk Map
Sucha O Asbell, MD, Jimm Grimm, PhD, Jinyu Xue, PhD, Meng-Sang Chew, PhD, and Tamara A LaCouture, MD

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Jimm Grimm, PhD

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Erasmus MC Data
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David A Clump, MD
John C Flickinger, MD
Ron Lalone, PhD
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MD Anderson at CUH
Duodenum
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Wilco Schellemans, MSc
Joachim G Aerts MD PhD
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Jimm Grimm, PhD, DABR, AAPM 2017
Guest Editor: Jimm Grimm, PhD
One person’s journey from Skeptic to Believer

- **Skeptic**
  - Submillimeter end-to-end
  - Intentional offsets
  - Attenuate Images
  - Patient Accuracy
  - Dosimetric Accuracy

- **Believer**

I had developed my own stereotactic alignment system – why would I need CyberKnife® System? So I was the biggest skeptic – let me show you what I found…

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Daily AQA Phantom

- Skeptic
- **Submillimeter end-to-end**
- Intentional offsets
- Attenuate Images
- Patient Accuracy
- Dosimetric Accuracy
- Believer
What if we intentionally offset the phantom, and instead of moving the couch, make the robot do the corrections?

- Skeptic
- Submillimeter end-to-end
- Intentional offsets
- Attenuate Images
- Patient Accuracy
- Dosimetric Accuracy
- Believer

Alignment QA (AQA) Phantom

AQA Phantom with guides for inducing +/- 10mm offsets

What if we intentionally offset the phantom, and instead of moving the couch, make the robot do the corrections?

- Skeptic
- Submillimeter end-to-end
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- Attenuate Images
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- Believer

- 17 months of Daily AQA data
- Phantom intentionally offset by up to 10mm in x,y,z and 1 degree in roll, pitch, and yaw before irradiation
- The tracking system and robot indeed maintained submillimeter accuracy 99% of the time despite the intentional offsets

What if x-ray images are attenuated due to large patients?

- **Skeptic**
- **Submillimeter end-to-end**
- **Intentional offsets**
- **Attenuate Images**
- **Patient Accuracy**
- **Dosimetric Accuracy**
- **Believer**

- We further studied CyberKnife® System robustness by inducing more challenging patient conditions
  - Intentionally attenuated images
  - Intentionally sub-optimal imaging parameters
  - Intentionally disabled some fiducials

- We could induce and study false locks:
  - With at least 4 fiducials, we could not induce any false lock when reported confidence level was above 40%
  - Regardless of “hostile” conditions, accuracy not degraded except for false locks, and false locks are detectable with sufficient fiducials.

Is it really that accurate for patients?
Logfile analysis of 4824 image pairs from 24 liver patients, 3fx each

• Skeptic
• Submillimeter end-to-end
• Intentional offsets
• Attenuate Images
• Patient Accuracy
• Dosimetric Accuracy
• Believer

Tracked tumor motion:
♦ 6.4 +/- 5.5 mm inf/sup

Without rotations,
♦ 3D residual fiducial offsets looked like up to 3mm (red points), but

With rotational corrections,
♦ 0.2 +/- 0.2 mm (black datapoints)

99% were Submillimeter 3D

But what about dose calculation?

- Skeptic
- Submillimeter end-to-end
- Intentional offsets
- Attenuate Images
- Patient Accuracy
- Dosimetric Accuracy
- Believer


- Standard Imaging
- Stereotactic Dose Validation Phantom (SDVP)
- Lung material insert
- Drilled for microchamber, stereotactic diode, or W1 pinpoint scintillator
Scintillator Matches Monte Carlo within 3% Lung Phantom, 60mm cone to 5mm cone

- Skeptic
- Submillimeter end-to-end
- Intentional offsets
- Attenuate Images
- Patient Accuracy
- **Dosimetric Accuracy**
- Believer

<table>
<thead>
<tr>
<th>detector</th>
<th>cone mm</th>
<th>rdg nC/pC</th>
<th>T/P cor</th>
<th>Gy/C</th>
<th>cGy</th>
<th>MC dose cGy</th>
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<td>1.36%</td>
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<td>238.63</td>
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<td>240.99</td>
<td>-0.77%</td>
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<td></td>
<td>50</td>
<td>0.831</td>
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<td>60</td>
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<td>247.77</td>
<td>0.19%</td>
</tr>
</tbody>
</table>

One person’s journey from Skeptic to Believer

- Skeptic
- Submillimeter end-to-end
- Intentional offsets
- Attenuate Images
- Patient Accuracy
- Dosimetric Accuracy

- Submillimeter end-to-end accuracy,
  - including intentional offsets and attenuations and
  - including patient factors
  - including live tracking for tumor motion

- Dose calculation accurate within 3%

- Many other unpublished testing, still ongoing…

No matter what we believe, the truth is still the same. Seek the truth, and believe it!
• Part II: Radiosurgical Dose Tolerance
Apples to Apples Outcomes Comparisons

CyberKnife® System

versus

CyberKnife® System!!
Dose Tolerance for Stereotactic Body Radiation Therapy (SBRT)  
Seminars in Radiation Oncology, April 2016

Introduction and Clinical Overview of the DVH Risk Map  
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**Duodenum**  
CyberKnife Centre London Data

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Guest Editor: Jimm Grimm, PhD
Is one fiducial enough?


  “Most of our patients with lung cancer were implanted with a fiducial marker located at the center of the tumors.”
Pancreatic cancer: a focus on duodenal dose constraints

- CyberKnife Centre London, at the Harley Street Clinic
- 44 patients with unresectable pancreatic tumours
- 3 or 5 fractions of SBRT, from March 2009 to March 2013

- Forty one patients were prescribed 18-36 Gy in 3 fractions
- Three patients were prescribed 22.5-25 Gy in 5 fractions as re-irradiation for their pancreatic cancer
  - Composite doses were not performed, only the CyberKnife® System dose was analyzed
  - None of these re-irradiation cases had Grade 3 or higher complications

## Duodenal Dose Tolerance Results

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Grade</th>
<th>D&lt;sub&gt;50%&lt;/sub&gt;</th>
<th>D&lt;sub&gt;10%&lt;/sub&gt;</th>
<th>D&lt;sub&gt;30cc&lt;/sub&gt;</th>
<th>D&lt;sub&gt;5cc&lt;/sub&gt;</th>
<th>D&lt;sub&gt;1cc&lt;/sub&gt;</th>
<th>D&lt;sub&gt;0.035cc&lt;/sub&gt;</th>
<th>Number of Fiducials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duodenal Stricture</td>
<td>4</td>
<td>1.8</td>
<td>6.0</td>
<td>4.2</td>
<td>6.8</td>
<td>8.3</td>
<td>11.2</td>
<td>1</td>
</tr>
<tr>
<td>Duodenitis</td>
<td>3</td>
<td>6.4</td>
<td>14.2</td>
<td>8.5</td>
<td>16.5</td>
<td>26.7</td>
<td>34.6</td>
<td>1</td>
</tr>
<tr>
<td>Bleeding</td>
<td>3</td>
<td>8.6</td>
<td>18.5</td>
<td>17.3</td>
<td>26.6</td>
<td>28.3</td>
<td>29.6</td>
<td>1</td>
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<tr>
<td>Obstructive Jaundice</td>
<td>3</td>
<td>9.4</td>
<td>18.3</td>
<td>15.7</td>
<td>21.1</td>
<td>22.6</td>
<td>23.8</td>
<td>4</td>
</tr>
<tr>
<td>Fatigue and Diarrhoea*</td>
<td>3</td>
<td>8.1</td>
<td>17.0</td>
<td>10.7</td>
<td>21.4</td>
<td>29.0</td>
<td>35.9</td>
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<tr>
<td>Duodenal Haemorrhage</td>
<td>3</td>
<td>10.7</td>
<td>21.5</td>
<td>16.5</td>
<td>25.7</td>
<td>27.7</td>
<td>29.4</td>
<td>3</td>
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<td>4</td>
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<td>23.6</td>
<td>13.8</td>
<td>26.0</td>
<td>29.1</td>
<td>31.6</td>
<td>3</td>
</tr>
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</table>

Note: “Incidence of the diarrhoea and obstructive jaundice complications did not exhibit any change as a function of duodenum dose” – SRO 2016 Apr;26(2):149-56.
Duodenal Dose Response

Duodenal Tolerance: Multiple Fiducials, G3+ Duodenal Complications

CyberKnife Centre London, 32 cases

- Cases with AE
- Cases without AE
- logisticExp
- 5%, 10% and 25% Risk
- 68% Confidence Intervals

45% Risk
9% Risk
Apples to Apples Outcomes Comparisons

• To within the degree possible in any study like this, predominantly the:
  - Same institution
  - Same patient population
  - Same clinicians
  - Same treatment machine
  - Same dose calculation
  - Same energy spectrum

• Every patient is unique and we only can treat each patient once, but as far as this type of comparisons go, none of these factors were intentionally varied.

• The main difference:
  - With/without Synchrony® Tracking System
  - 5-fold reduction in risk!
• From the model, estimate the risk level of each selected dose tolerance limit

• Low- and High-Risk groups like the Emami Table
Clinical use must be easy

- DVH Evaluator user interface
- Previously published High-Risk limits may have been too conservative for pancreas cancer
Clinical use must be easy

- DVH Evaluator user interface
- This case is well below the 10% risk level, based on new data from SRO 2016 Apr;26(2):149-56
- Automated reports
- Automated saving of data
- Automated analysis of data
- Known dose tolerance from clinical outcomes studies
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DVH Evaluator Makes it Easy

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Conclusion

• Targeting Accuracy and Radiosurgical Dose Tolerance:
  - Because of the high dose per fraction of SBRT, and the extremely steep dose gradients,
  - Targeting accuracy is of paramount importance to achieve good radiosurgical dose tolerance

• This is not the end, just the beginning!
• If you treat patients, you have data
  - Let’s analyze and publish the outcomes together

• Please come to see our HyTEC session on Thursday:
1. Jimm Grimm, PhD  
   Introduction

2. Moyed Miften, PhD  
   Radiation Dose-Volume Effects for Liver SBRT

3. Brian Kavanagh, MD  
   Clinical Aspects of SBRT in Abdominal Regions

4. Panayiotis Mavroidis, PhD  
   Modelling Radiation Dose-Volume Tolerance based on data from Hypofx Head and Neck ReTx

5. Vitali Moiseenko, PhD  
   Volume Effects and Reporting Standards for SBRT

6. Ellen Yorke, PhD  
   Conclusion