Risk Analysis and Risk Management in Cancer Therapy:

*It’s not as simple as we first thought.*

Robert C. Lee
Assistant Professor
Departments of Community Health Sciences and Oncology
Director
Calgary Health Technology Implementation Unit
University of Calgary, Alberta, Canada
What’s the Problem?

"All right, so he dropped the heart. The floor is clean."

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What’s the Problem?

- “Do no harm”, yet harm is done. . .
- “Doctors are godlike”, or, “Let’s just let insurance cover it”
- The Leape of faith: 1,000,000 injured, 100,000 deaths per year in the US!
- 185,000 serious adverse events per year in Canadian health care-- 7.5% of hospital admissions!

Medical care is one of the leading causes of death!
Sources of Incidents

Organization

Individuals

Equipment

Software

Information Flow

INCIDENTS
Challenges in Health Care

**Industry**
- Line management control
- Production pressure
- Customers external to the risk system
- Objective measures of outputs
- Profits motivate resource allocation
- Bound by common values and corporate mission statement

**Health Care**
- Doctor control
- Demand pressure
- “Customers” (patients) internal to the system
- Subjective measures of outputs
- Politics (often) motivate resource allocation
- Conflicting demands from multiple stakeholders
- **COMPLEXITY!**
Managerialism vs. Systems Approach

<table>
<thead>
<tr>
<th>Issue</th>
<th>Managerialism</th>
<th>Systems Approach</th>
</tr>
</thead>
<tbody>
<tr>
<td>Defining Problem</td>
<td>Symptoms, “self-evident” definition</td>
<td>Approached carefully and systematically</td>
</tr>
<tr>
<td>Defining Solution</td>
<td>Immediately evident alternatives, “cost-effectiveness”</td>
<td>Objectives determined first, alternatives chosen after careful analysis</td>
</tr>
<tr>
<td>Type of Solution</td>
<td>Framed by “goals”, “targets”, “one-offs”</td>
<td>Framed by fundamental objectives, operational/process considerations</td>
</tr>
<tr>
<td>Outcomes Assessment</td>
<td>Simplistic cause-and-effect (or simply not done. . .)</td>
<td>Analysis of whole system</td>
</tr>
<tr>
<td>Underlying principles</td>
<td>Linear thinking, qualitative approaches, compliance</td>
<td>Systematic/holistic/quantitative thinking, innovative solutions, iterative process</td>
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</table>
Cancer treatment often involves exposing patients to potentially risky (and costly!) scenarios, including surgery, powerful drugs, radiation.

About half of all cancer patients receive ionizing radiation (radiation therapy, or RT) as part of their treatment.

In Alberta (pop. 3,000,000), about 11,000 patients receive RT per year, rate of incidents unclear.

Appreciable resources are expended for quality assurance/quality control (QA/QC), but no systematic process for resource allocation considering constraints.

And, in many cases, we are talking about some very complex systems...
Radiation Therapy

- RT entails the accurate irradiation of a limited area of the body which contains the tumour
- Most radiotherapy is delivered with high energy x-rays generated by a linear accelerator
- Small deviations from the prescribed dose or location can not only compromise the treatment but also seriously injure or kill the patient
- Small probability of serious systematic incidents that can affect multiple patients (sometimes hundreds...)
- Complex technology and operational system that is constantly evolving = need for innovative assessment
Research Program

- Novel approach to informing decisions regarding safety of patients undergoing radiation therapy for cancer, as well as addressing resource allocation questions.
- Objective is to develop an integrated probabilistic risk and decision analysis framework for the evaluation of uncertainties and process errors in a complex healthcare delivery system.
- Intent is to inform quality control decisions (e.g. which quality control procedures are most cost-effective in terms of improving patient safety?), and to improve incident reporting systems and organizational learning.
Team

- Robert Lee (PI: risk and decision analyst)
- Dr. Peter Dunscombe (co-I: medical physicist)
- Edidiong Ekaette (RA: engineer)
- Dr. David Cooke (post-doc: engineer, operations researcher)
- Dr. Karie-Lynn Kelly (collaborator: radiation oncologist)
The Problem as a Graph

- **Catastrophic Range (Underdose)**
- **Catastrophic Range (Overdose)**

Typical Tolerance

Administered/Prescribed Dose
(1.0 = “correct” dose)

Probability (log scale)
System Map

PATIENT ENTERS SYSTEM

External patient information

PATIENT DECISION: Cease process?

FOLLOW UP

PATIENT DECISION: Cease process?

TREATMENT

Veriﬁcation

PREPARATION

Patient setup

Equipment setup and dose delivery

TREATMENT

Patient setup

Equipment setup and dose delivery

FOLLOW UP

Clinical examination of patient response

Treating side effects of radiotherapy

FOLLOW UP

DECISION: Radiotherapy?

If yes, which technique?

PRESCRIPTION

Dose fractionation, protraction

Target volume localization

PRESCRIPTION

Dose fractionation, protraction

Target volume localization

VERIFICATION

Univariate distribution computation

Simulation verification

Treatment aid preparation and verification

ASSESSMENT

History and physical examination

Imaging and biochemical imaging

Pathology review

ASSESSMENT

History and physical examination

Imaging and biochemical imaging

Pathology review

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The Physician’s Brain...
Uncertainty Analysis: Diagnostic and Staging Decisions

- History and physical exam
- Mammography
- Biopsy

Cancer state

Diagnostic decision

- Patient has cancer
- Patient has no cancer
- More tests required

Testing threshold

Treatment threshold
## Uncertainty Analysis: Results

<table>
<thead>
<tr>
<th>True stage of cancer</th>
<th>Physician’s diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>‘Stage X’</td>
</tr>
<tr>
<td>Stage X</td>
<td>0.9935</td>
</tr>
<tr>
<td>Stage 0</td>
<td>0.0034</td>
</tr>
<tr>
<td>Stage I</td>
<td>0.0031</td>
</tr>
<tr>
<td>Stage II</td>
<td>&lt;1E-06</td>
</tr>
<tr>
<td>Stage III</td>
<td>&lt;1E-06</td>
</tr>
<tr>
<td>Stage IV</td>
<td>&lt;1E-06</td>
</tr>
</tbody>
</table>
## Uncertainty Analysis: Results

<table>
<thead>
<tr>
<th>Required treatment</th>
<th>Prescribed treatment</th>
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<tbody>
<tr>
<td></td>
<td>‘none’</td>
</tr>
<tr>
<td>none</td>
<td>0.9934</td>
</tr>
<tr>
<td>2-field</td>
<td>0.0066</td>
</tr>
<tr>
<td>4-field</td>
<td>&lt;1E-06</td>
</tr>
<tr>
<td>palliative</td>
<td>&lt;1E-06</td>
</tr>
</tbody>
</table>

System Analysis: Fault Trees

- A fault tree considers all the possible ways a treatment could go wrong and traces the problems backwards to all possible initiating errors or conditions.
- Unlike root cause analysis (RCA), a fault tree applies to a process, not a particular event.
- Unlike failure mode and effect analysis (FMEA), a fault tree allows for the modeling of the causal interactions.
- Can be updated with probabilistic values for estimation of the probability of “top” and/or “intermediate events”.

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Probabilistic Risk and Decision Analysis (PRADA)

Start

System definition

Elicitation of possible faults

Qualitative fault tree analysis

Determination of severity of faults

Quantitative fault tree analysis

Risk estimation

Acceptable risk?

Multi-attribute risk management

Stop

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The Bayesian Approach

- Identify tasks
- Identify task components
- Collect empirical performance data
- Establish time dependent error rate in subtasks - $\lambda(t)$
- Calculate the subtask reliability $R(t)$: the probability that a task will be accomplished successfully by an individual within a specified minimum time $t$, (i.e. if the time requirement exists).

$$R(t) = e^{-\int_0^t \lambda(t) dt}$$

- When a back-up person is available, the overall reliability of two individuals working together to accomplish a task is given by:

$$R_D = \frac{(1-(1-R_S)^2)P_a + R_SP_u}{P_a + P_u}$$

, where $R_S$ is the reliability of a single individual, $P_a$ is the percentage of time the backup individual is available, and $P_u$ is the percentage of time the backup individual is unavailable.
The Bayesian Approach

- Calculate the task reliability of the entire task (using a Bayesian network or fault tree).
- Bayesian networks allow us to model both deterministic and non-deterministic relationships between subtasks.
- Bayesian networks handle uncertainty and allow the integration of subjective expert knowledge with objective data analysis results during inference.
Bayesian networks are graphical models. The nodes on the network represent random variables representing variables of interest, and the arcs indicate dependencies between nodes.

The strength of the relationship between a “parent” node and its “child” is captured in a conditional probability or distribution stored at the child node.
Estimated error rates without QC measures
Estimated error rates with QC measures
Consequence metric

- Severity of error quantified using a function of equivalent uniform dose to the target \( (\text{EUD}_{\text{target}}) \), equivalent uniform dose to critical organs \( (\text{EUD}_{\text{organs\_at\_risk}}) \), and a scaling factor \( (\gamma) \), the value of which is dependent on whether the error is a systematic error or a random error.

\[
\text{severity}(\varepsilon_i) = \varphi(\text{EUD}_{\text{Tumor}}, \text{EUD}_{\text{organs\_at\_risk}}, \gamma)
\]

- Difference in EUD can be mapped into clinical measures of morbidity or quality-of-life measures based on expected side-effects of treatment.
- Consequence will then be estimated based on a scale (e.g. 1-10) or a class (e.g. critical, major, average, minor)
Role of PRADA in health care

- **Formality/Objectivity:**
  - Provides a formal systematic way to identify and represent the causal relationship between events

- **Logic**
  - Provides a logical basis to explore interventions and barriers that could improve patient safety

- **Structure**
  - Provides a framework for incident reporting requirements and guides the processing and interpretation of incident reports

- **Prioritization**
  - Provides an objective means of prioritizing resource allocation
Ongoing Work

- Roll-out of integrated incident tracking system
- Complete the risk analysis
- Define severity and net-benefit metrics
- Determine multi-attribute tradeoffs associated with quality control alternatives: financial cost (fixed budget), human resources, acceptability; incorporate into PRADA model to rank alternatives
- Build prioritization and planning model
Thorny Issues. . .

- How does an organization decide on the level of analysis needed; e.g. rigorous analysis vs. pragmatic, rapid approaches?
- Once a rational risk analytic/risk management/priority-setting framework has been developed, is there management support?
- Given frequent changes in management and staff, how can sustainability be built into such a framework?
- How do political decisions affect implementation of such a framework? How can the risk of such political decisions be managed?
- How do rare, high-consequence events (disasters, etc.) affect the system, and how can they be managed?
Yet Another Monkey-Wrench in the Works... 

- Medical technology (including drugs, devices, procedures, etc.) is advancing at a super-exponential rate, and costs rarely (if ever...) go down
- Patients demanding new technologies, and are increasing empowered
- The field of health technology assessment seems to be largely divorced from operations research, risk management, etc.
- The result is an overwhelmed technology assessment and appraisal system...
Constraints and Safety...
The Risk Manager in Action (or, Look Ma, No Hands!)

Aha! I’ll have you in my hands soon!