Image-guidance vs Adaptive Radiotherapy

- **Image-guidance radiotherapy (IGRT)**
  - Goal: Stay a pre-determined course
  - Different imaging modalities (CT/PET/MRI) are used to guide planning (target definition) and delivery (localization)

- **Adaptive radiotherapy (ART)**
  - Goal: Make changes in the face of evolving information
  - Repeated measurements of the patient’s geometry (imaging) and/or physiology (biomarkers) during the treatment so that a more patient-specific treatment can be delivered.
ART Principles

Example: patient-specific margins

Some ART Examples I

Head & Neck case

Some ART Examples II
Some ART Examples III

Late mucosal ulcers in dose-escalated adaptive dose-painting treatments for head-and-neck cancer
Leda-Ane Marie Orleans, Robert Cuyts, Vitalie de Nova, Dierk Bantjes, Tom Verhaegen, Werner Baerts, Philippe Desru
Walker Huxanas, Katrien Borrs, Ingelborg Coenhav, Julie Schreiber & Werner De Cremers, *JNC (2020)"(2)
Page 26/34) Revised 15 May 2017, Accepted 09 Aug 2017, Published online 09 Aug 2017

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>52</td>
<td>55</td>
<td>60</td>
<td>58</td>
<td>59</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Laryngeal Carcinoma</td>
<td>Laryngeal Carcinoma</td>
<td>Laryngeal Carcinoma</td>
<td>Laryngeal Carcinoma</td>
<td>Laryngeal Carcinoma</td>
</tr>
<tr>
<td>Dose (Gy)</td>
<td>70</td>
<td>70</td>
<td>70</td>
<td>70</td>
<td>70</td>
</tr>
<tr>
<td>Tumor Size (cm)</td>
<td>4.5</td>
<td>4.5</td>
<td>4.5</td>
<td>4.5</td>
<td>4.5</td>
</tr>
</tbody>
</table>

ART Evolution

What? - ART in era of -omics

El Naqa et al., PMB (journal highlights), 2017
Radiation response is multi-factorial and depend on: radiation dose and patients' physical, clinical, biological and genomic characteristics before and during the course of radiotherapy.

\[ f \{ \text{TCP/NTCP} \} \]

Outcome modeling schemes:
- TCP/NTCP modeling
- Analytical
- Data-driven
  - Mechanistic (LQ)
  - Phenomenological (EUD)
  - Linear (Logistic regression)
  - Non-Linear (Neural networks)

How? - optimize RT adaptation decision?
- Agent (Beam team)
- Radiotherapy Environment
- Markov Decision Process (MDP)
- Action (adapt?)
Precision Radiation Oncology (Personalized decision support system)

Machine learning for ART

- Supervised learning
  - Source: input → output pairs
  - Learning: Training + testing phases
  - Applications: Classification, regression
- Reinforcement learning
  - Source: input data + agent (critic)
  - Learning: exploration (environment) and exploitation (action)
  - Applications: optimizing decision making

Example: Adaptive Decision Making in Liver Cancer

- Dataset
  - 183 HCC liver SBRT tumors (10 Gyx5) from 120 patients
  - 45 cases on non-adaptive
  - 137 cases on adaptive protocols
    - Adaptation was based on liver function using a split-course of 3+2 fractions with a month break

- Candidate variables
  - Clinical (age, gender, stage, etc)
  - Dosimetric (Bio-corrected gEUD of tumor/liver, fx, etc)
  - Plasma biomarkers (cytokines, miRNA)
**RL Application to ART**

- **RT environment**
  - Patient’s clinical, dosimetric, and biological covariates
- **RL objective (reward)**
  - Complication-free tumor control ($P^+$)
    - $P^+ = \text{TCP} \times (1 - \text{NTCP})$
  - NTCP change in ALBI score by 1 point
- **Optimization algorithm: Q-Learning**
  - Greedy search approach to solve Bellman’s principle of optimality with:
    - A simple regression model of state-action mapping

**Dosimetric NTCP modeling using LKB**

**Dose modifying effect of cytokines on LKB-ALBI**

El Naqa et al, IJROBP, 2018
Dose modifying effect of cytokines + imaging

\[ \text{Damage Fraction} \]

\[ \begin{align*}
0 & \quad 0.2 & \quad 0.4 & \quad 0.6 & \quad 0.8 & \quad 1 \\
0 & \quad 0.2 & \quad 0.4 & \quad 0.6 & \quad 0.8 & \quad 1 \\
\end{align*} \]

\[ \text{NTCP} \]

\[ f_{50} = 0.515 \ (0.459, 0.571) \]

\[ f_{50} = 1.05 \ (0.0564, 2.05) \]

\[ f_{50} = 0.217 \ (-0.275, 0.709) \]

\[ f_{50} = 0.651 \ (-0.998, 2.3) \]

\[ f_{50} = 0.959 \ (-2, 3.92) \]

with TGF

El Naqa et al, IJROBP, 2018

\[ \text{MRI} \]

\[ \text{DCE perfusion} \]

**P** Estimation

Retrospective RL analysis

- Adaptation recommendation:
  - 71% for split courses
  - 70% for continuous courses
- Average adaptation probability:
  - Amplitude=0.59 ± 0.16

- Adaptation recommendation:
  - 64% for split courses
  - 67% for continuous courses
- Average adaptation probability:
  - Amplitude=0.64 ± 0.26
Prospective RL analysis

- Adaptation recommendation:
  - 90% for split courses
  - 100% for continuous courses

- Average adaptation probability:
  - Amplitude = 0.67 ± 0.17

Example II: ART in lung cancer

- Multi-Objective Generative Models

Luo et al, Med Phys, 2018 (Editor’s Choice)
Adaptive Decision Making with Deep Learning I

Adaptive Decision Making with Deep Learning II—Need more data?

Adaptive Decision Making with Deep Learning III—Transition probability
Conclusions

- Artificial intelligence/machine learning offers new opportunities to develop better understanding of medical physics/radiation oncology processes and improve their workflow.
- AI/ML approaches are uniquely positioned to improve adaptation in radiotherapy from heuristics to data driven realm.
- Adaptive radiotherapy implies improved outcome prediction (e.g., supervised learning) and optimizing decision making (reinforcement learning).
- Larger and multi-institutional datasets are necessary to realize the potential of AI in ART.

Thank You!