RadOnc & AI methods in the real-world: *new lessons, new challenges*

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Disclosures

I have no personal disclosures or conflicts of interest to declare

The AI method for auto planning has been licensed to RaySearch Laboratories
(*Drs. Purdie and McIntosh*)

RaySearch Laboratories

(thought from today)

Whatchamacallit?

- keeps the fibres of the lace from unraveling
- firmness and narrow profile that makes easier: i) to hold; ii) to feed through eyelets

(thought from today)

Whatchamacallit?

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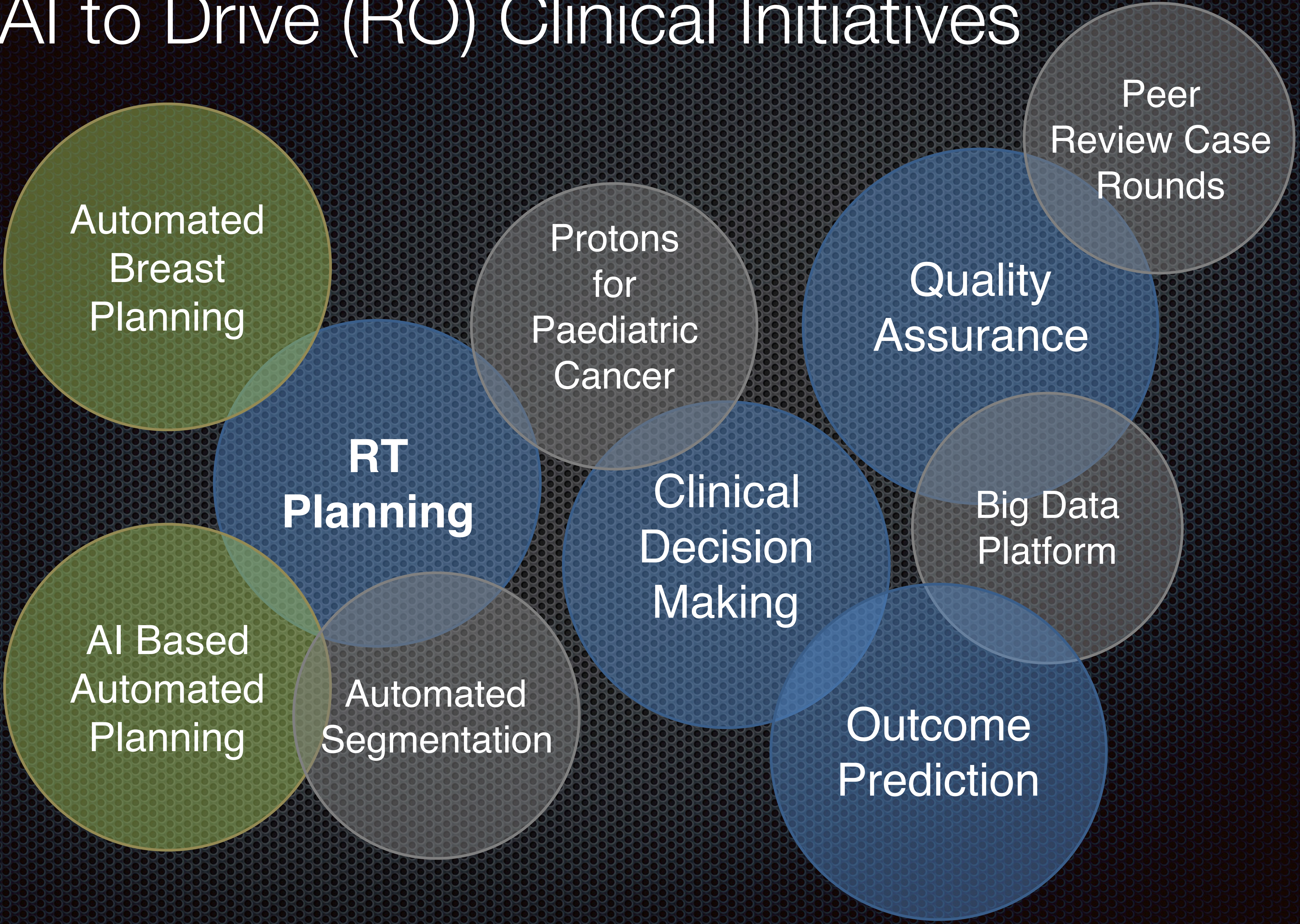
Rumpelstiltskin Principle

Naming something **gives you power** over it.

Vocabulary / taxonomy / ontology are more **fundamental** than we appreciate.

AI to Drive (RO) Clinical Initiatives



AI to Drive (RO) Clinical Initiatives

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

FRONTIERS IN MEDICINE

Machine Learning in Medicine

Alvin Rajkomar, M.D., Jeffrey Dean, Ph.D., and Isaac Kohane, M.D., Ph.D.

nature biomedical engineering

REVIEW ARTICLE

https://doi.org/10.1038/s41551-018-0305-z

Artificial intelligence in healthcare

Kun-Hsing Yu[1], Andrew L. Beam[1] and Isaac S. Kohane[1,2]*

Artificial intelligence (AI) is gradually changing medical practice. With recent progress in digitized data acquisition, machine learning and computing infrastructure, AI applications are expanding into areas that were previously thought to be only the province of human experts. In this Review Article, we outline recent breakthroughs in AI technologies and their biomedical applications, identify the challenges for further progress in medical AI systems, and summarize the economic, legal and social implications of AI in healthcare.

REVIEW ARTICLE | FOCUS

https://doi.org/10.1038/s41591-018-0300-7

nature medicine

High-performance medicine: the convergence of human and artificial intelligence

Eric J. Topol

The use of artificial intelligence, and the deep-learning subtype in particular, has been enabled by the use of labeled big data, along with markedly enhanced computing power and cloud storage, across all sectors. In medicine, this is beginning to have an impact at three levels: for clinicians, predominantly via rapid, accurate image interpretation; for health systems, by improving workflow and the potential for reducing medical errors; and for patients, by enabling them to process their own data to promote health. The current limitations, including bias, privacy and security, and lack of transparency, along with the future directions of these applications will be discussed in this article. Over time, marked improvements in accuracy, productivity, and workflow will likely be actualized, but whether that will be used to improve the patient-doctor relationship or facilitate its erosion remains to be seen.

Main take home messages

Still far from clinical realm
(many retrospective/simulation approaches)

Unquantified value/impact

Simple (and biased) RadOnc view

Statistics

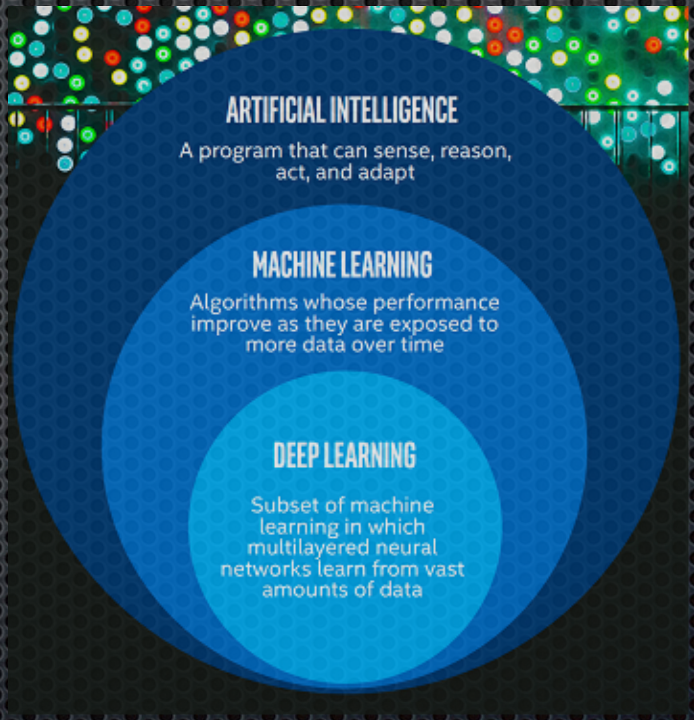
+

Computer Science

+

Data Science

= AI, ML …



→

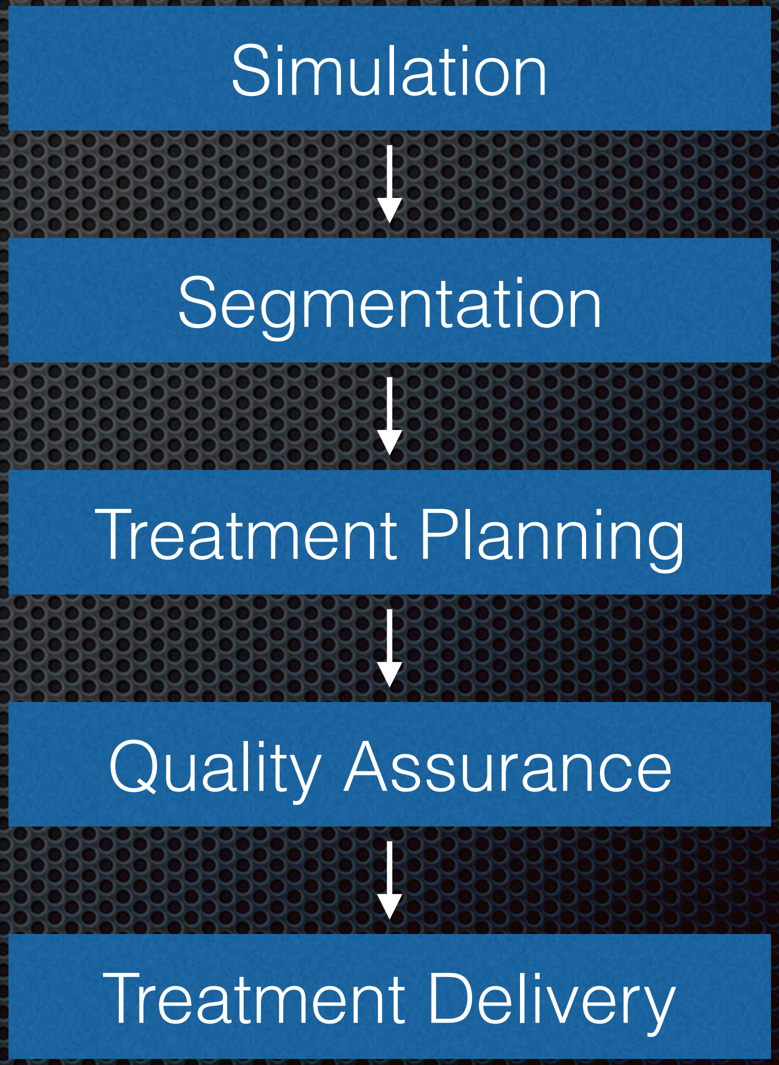
Automation

Support

Enhancement

Why aiming for automation in RO ?

- We are **nerds obsessed** with Tech
- Limited (RT) **resources**, various (RT) tasks are quite resource intensive
- Operator's **time and expertise impact** quality
- Many processes are **not 'standard'**(izable?)
- The **value of good radiotherapy**
- **Moore's Law**
- **Global impact**, can we (practically) share expertise?
- AI is a **sexy topic** = Automatic Investment



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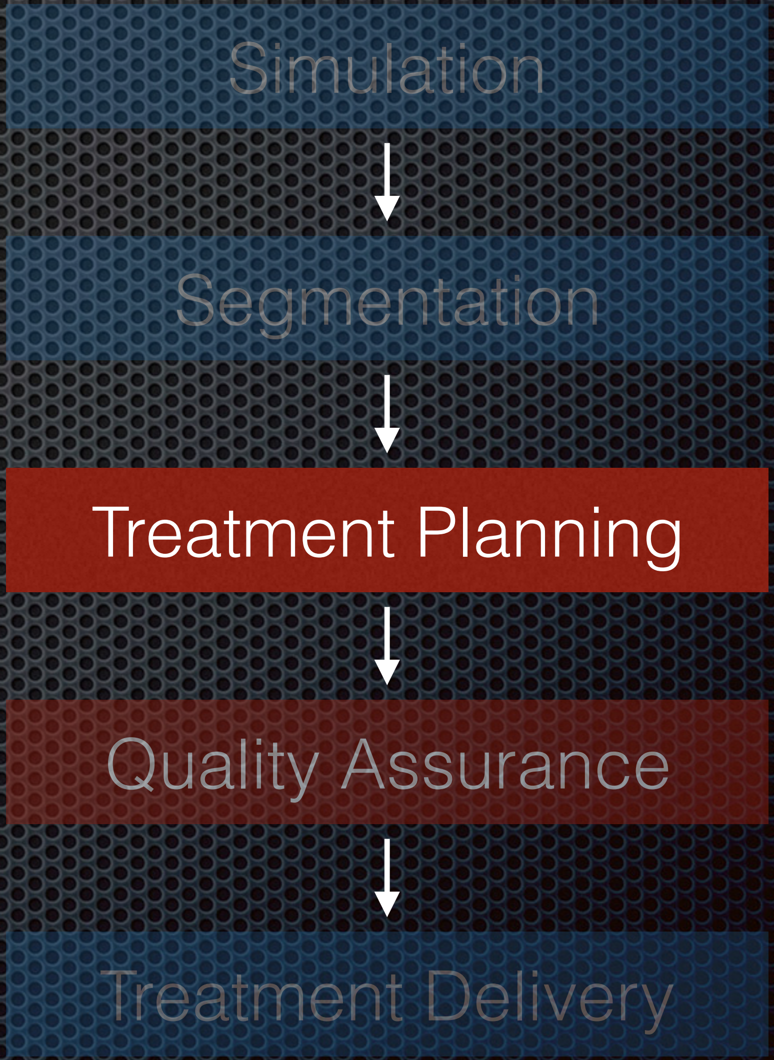
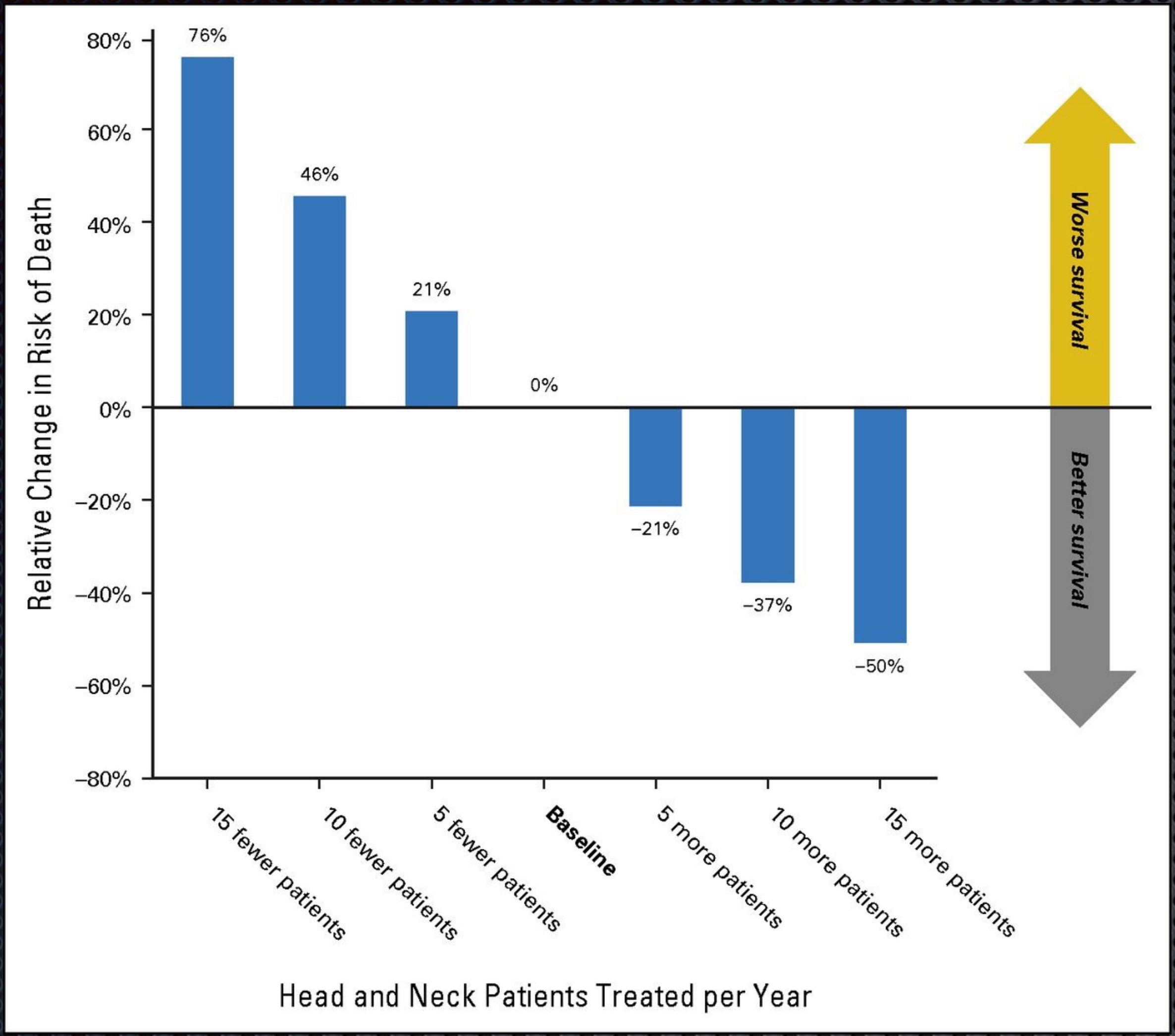
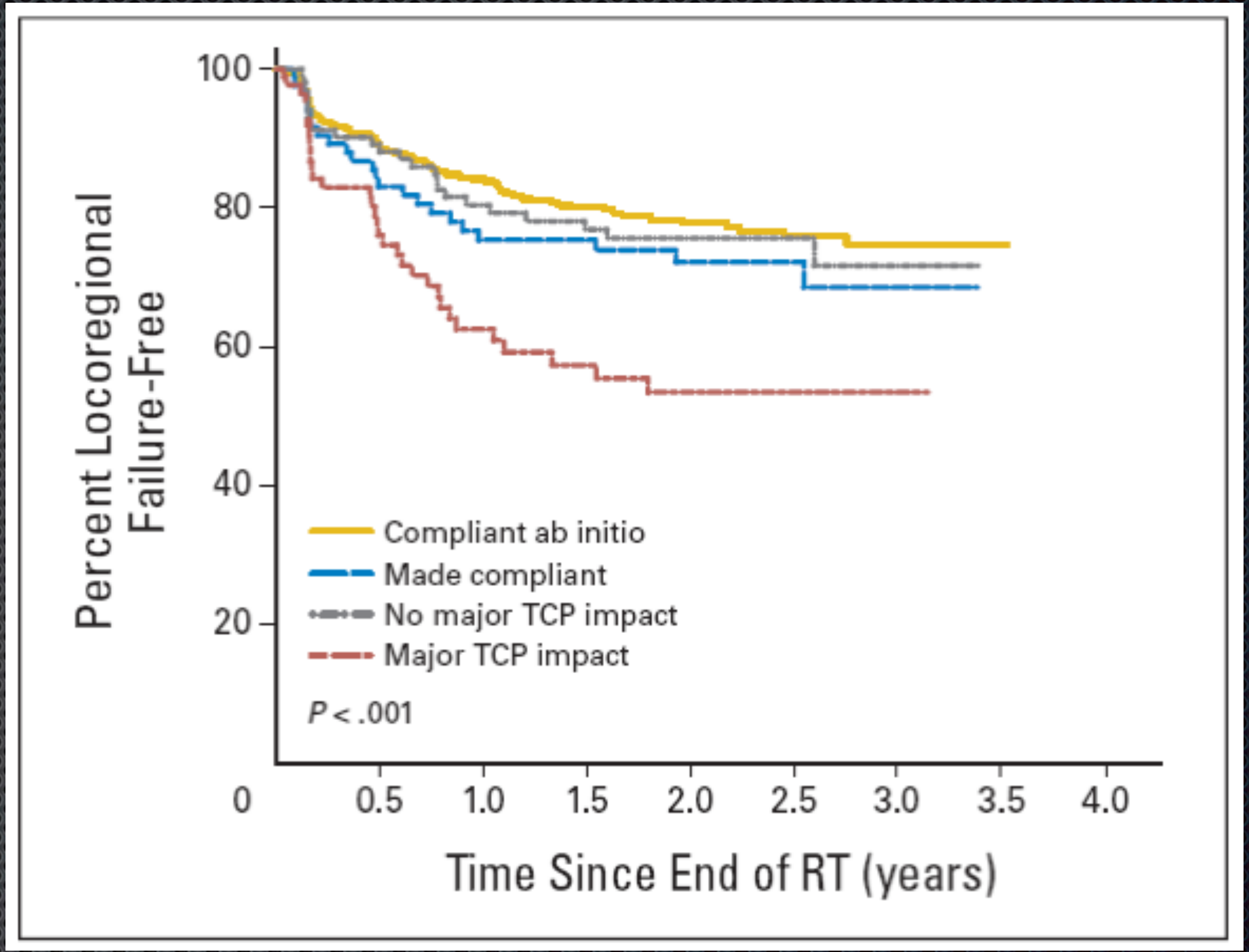


Will automation have good ROI ?



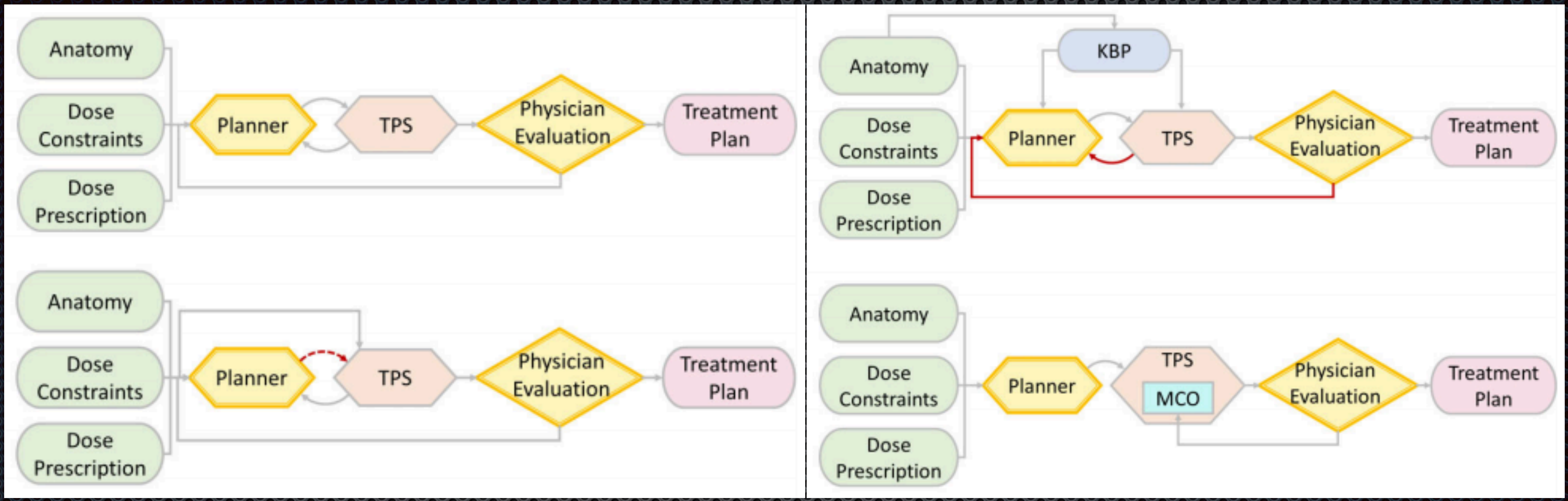


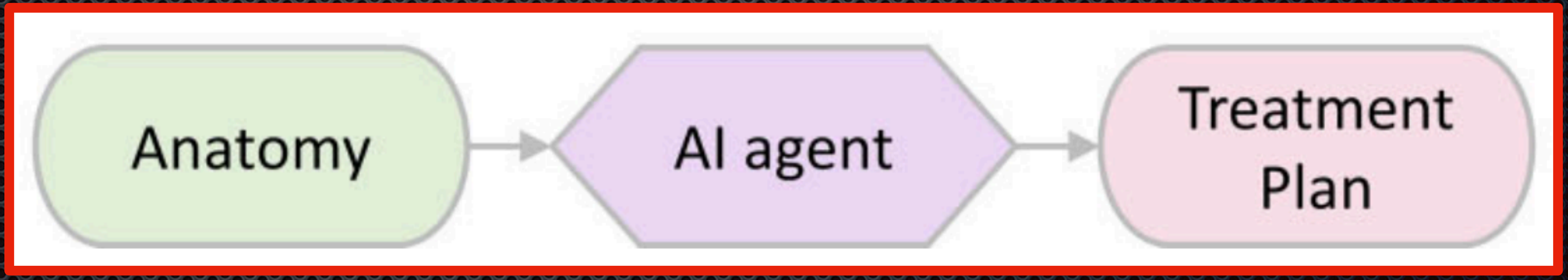
Experience, consistency and quality matter → **impact clinical outcomes**

"The value of good radiotherapy is substantially greater that the incremental gains that have been achieved with new drugs and/or biologics"

Boero et al. *JCO* 2016; Peters et al. *JCO* 2010

Autoplanning approaches



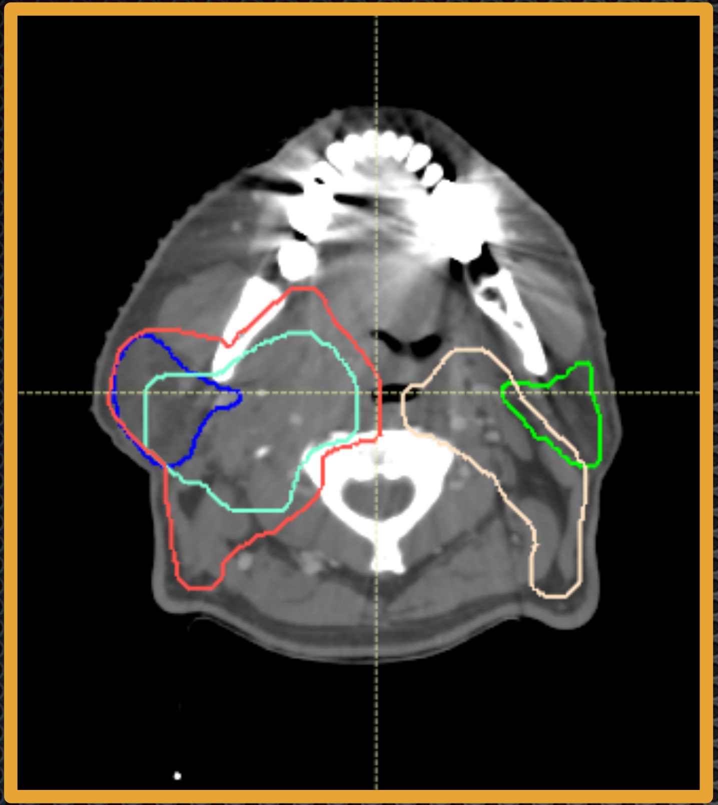


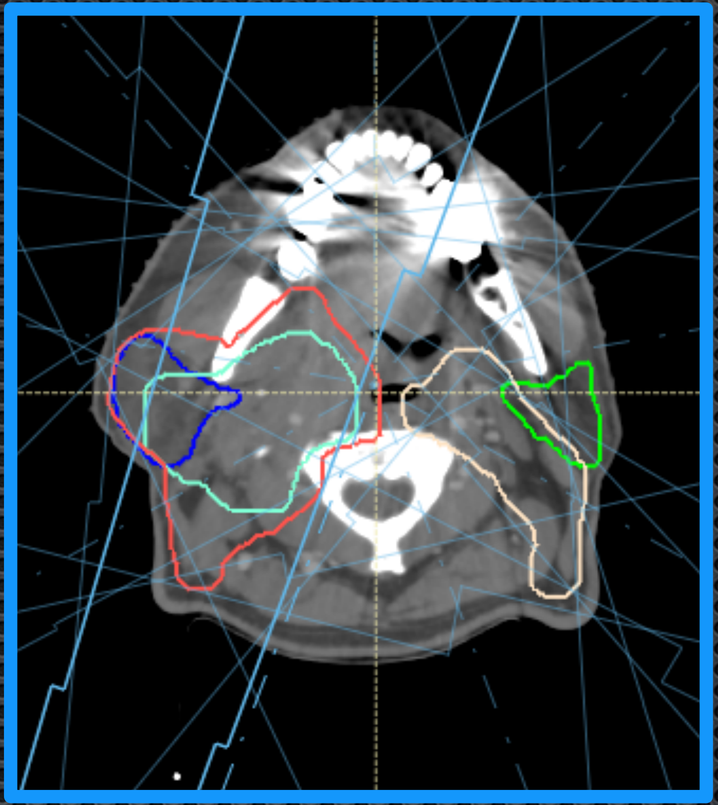
Wang et al. *Tech in Ca Res & Treat 2019*

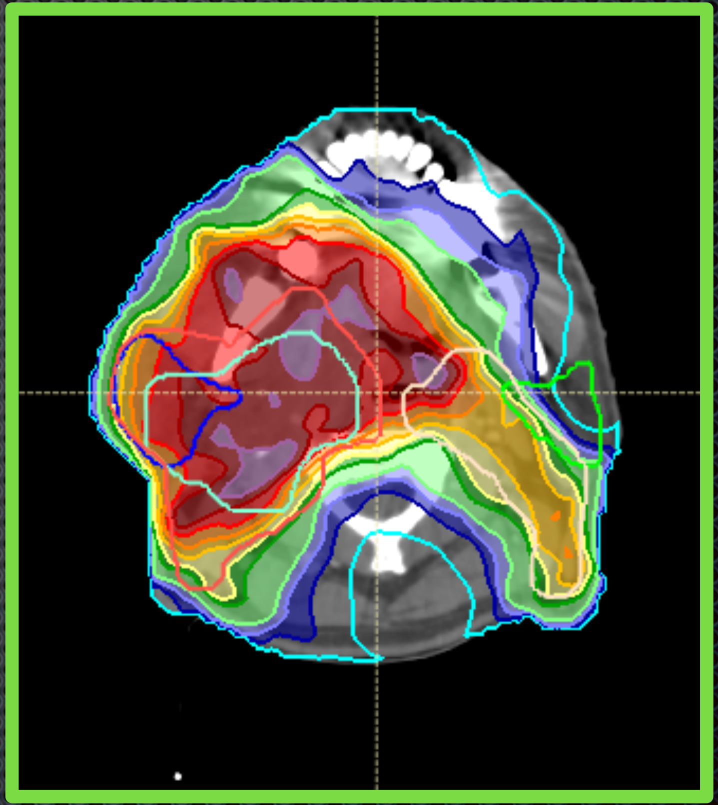
AI Planning Framework

Conventional planning pipeline:

Image → Contour → Beams → Optimize → Dose





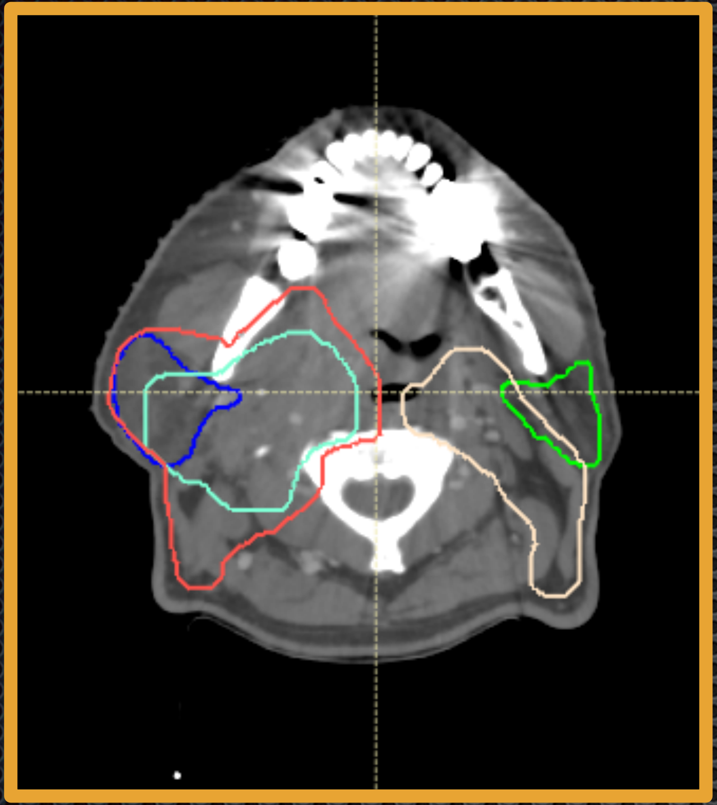


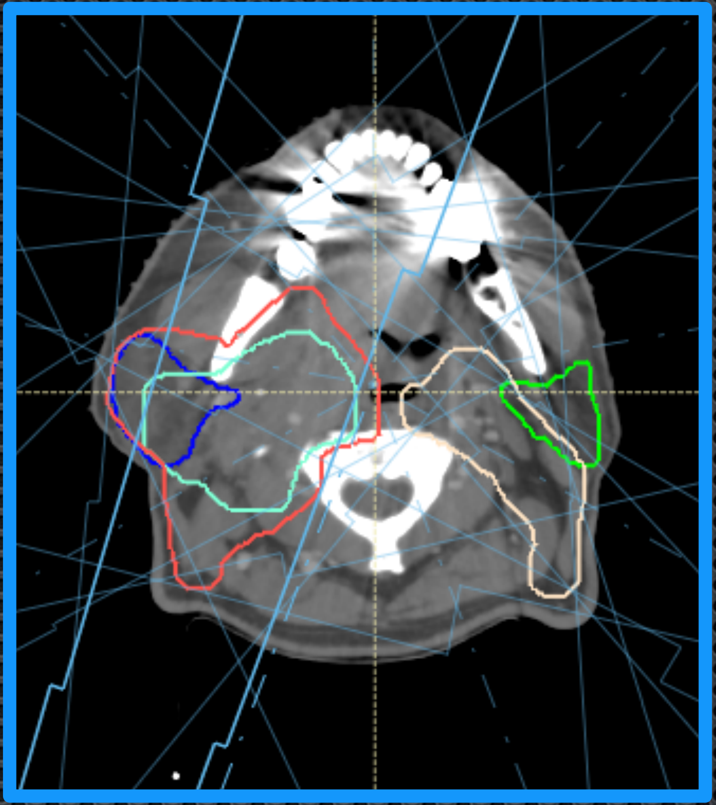
McIntosh C, Purdie TG. *IEEE TMI 2015*

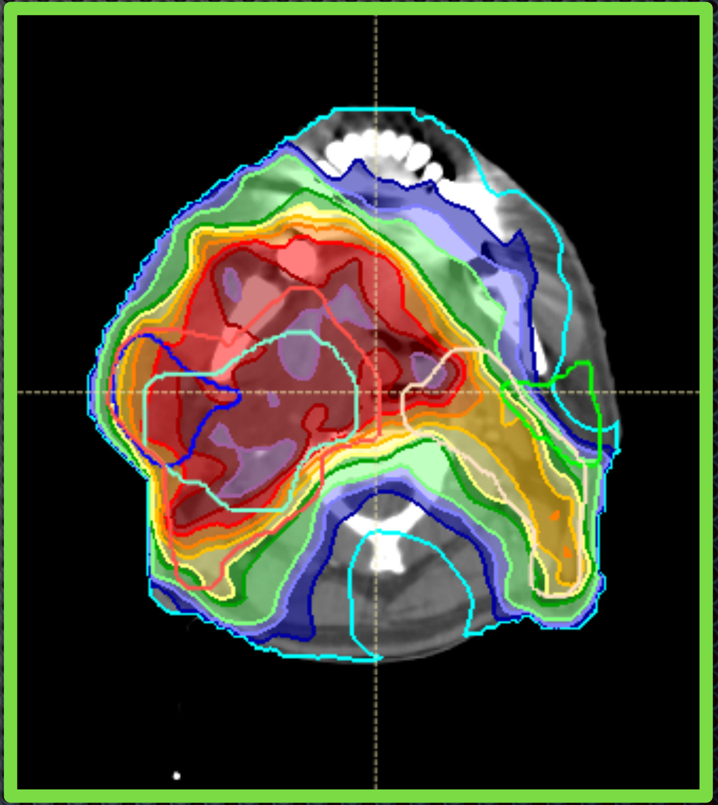
AI Planning Framework

Automated planning pipeline:

Image → Contour → Beams → Optimize → Mimic Dose







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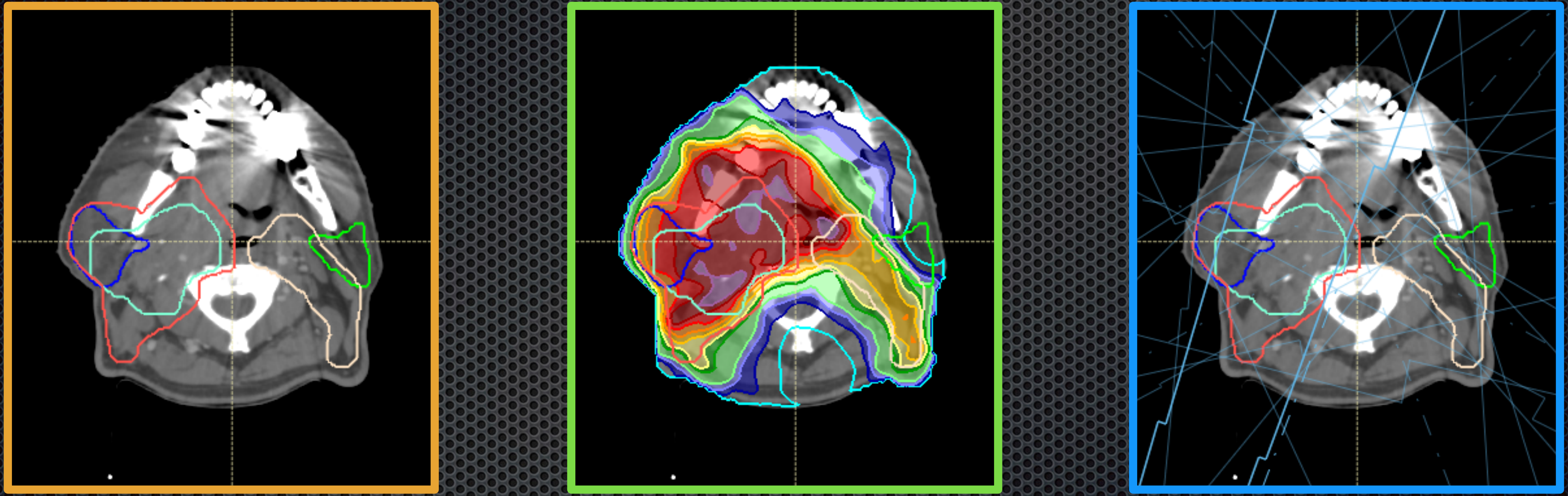
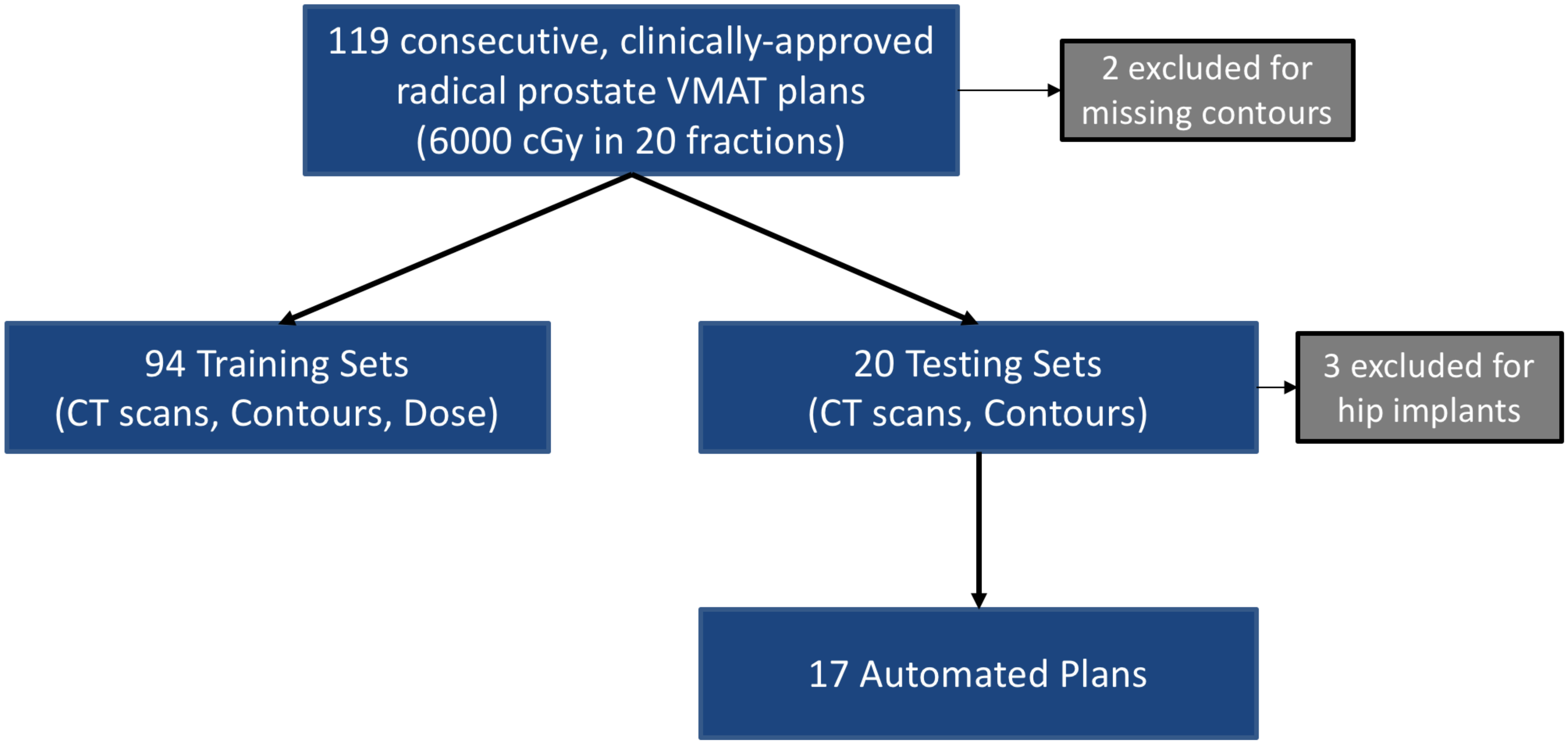


- Learn relationship of image features and patient geometry to infer dose distributions ➔ Spatial Dose Objective
- Complete and deliverable treatment plans without:
  - defining or specifying optimization objectives
  - iterative (manual or automatic) planning steps

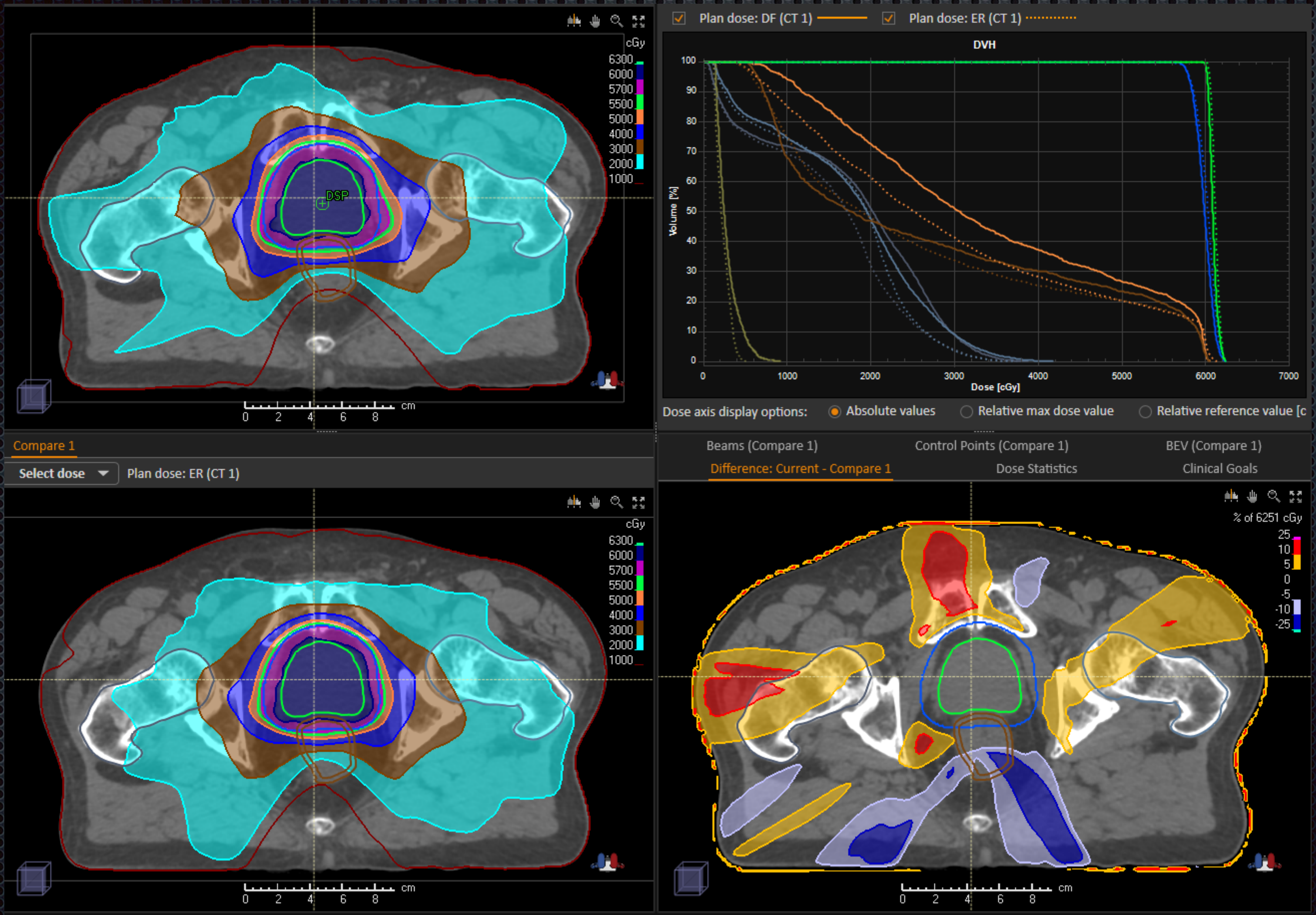
McIntosh C, Purdie TG. *IEEE TMI 2015*

Evaluation of (clinical) performance: Step 1

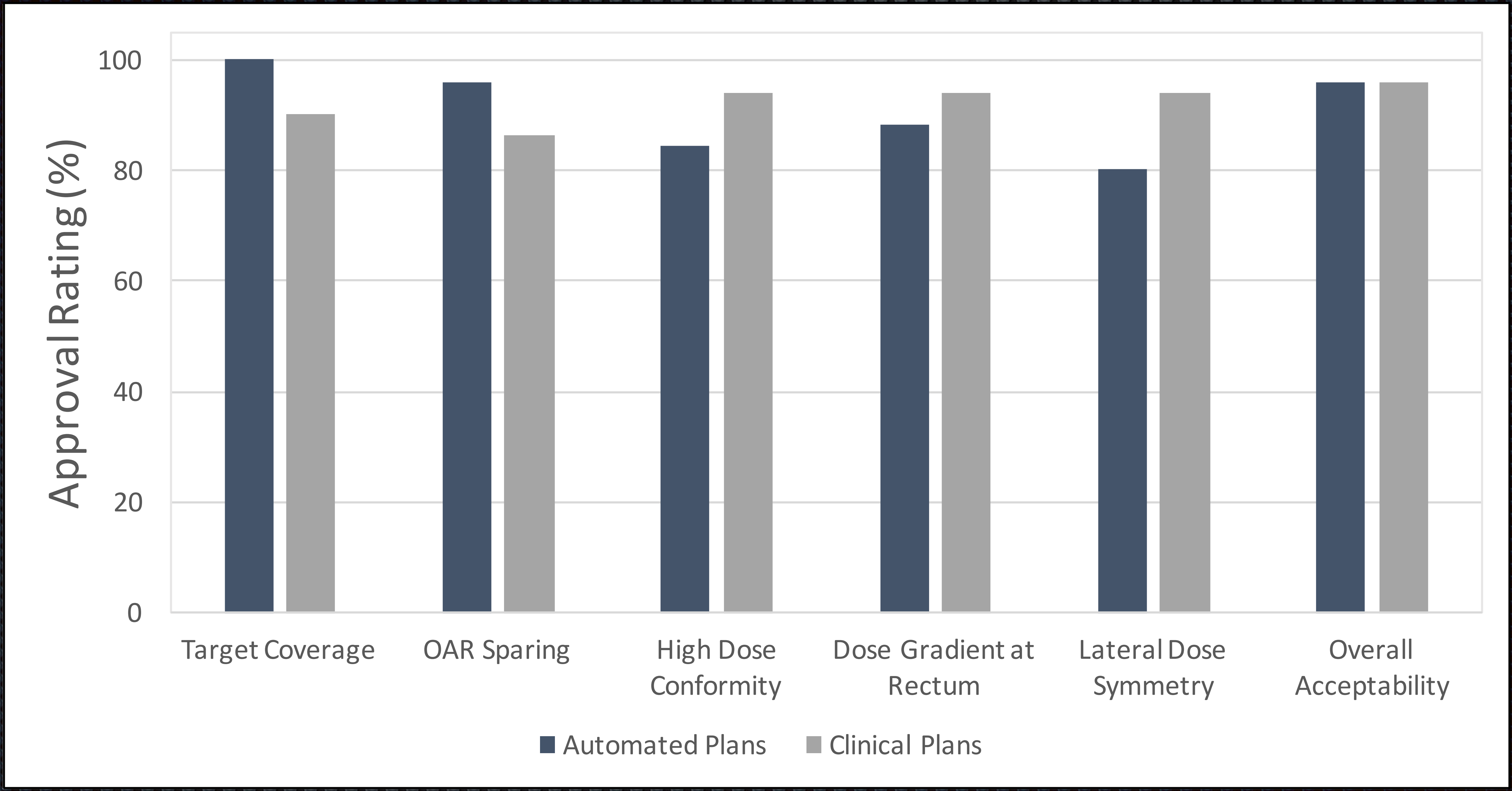


- Reviewed by three expert reviewers.
- Compared directly to clinical patient plan.

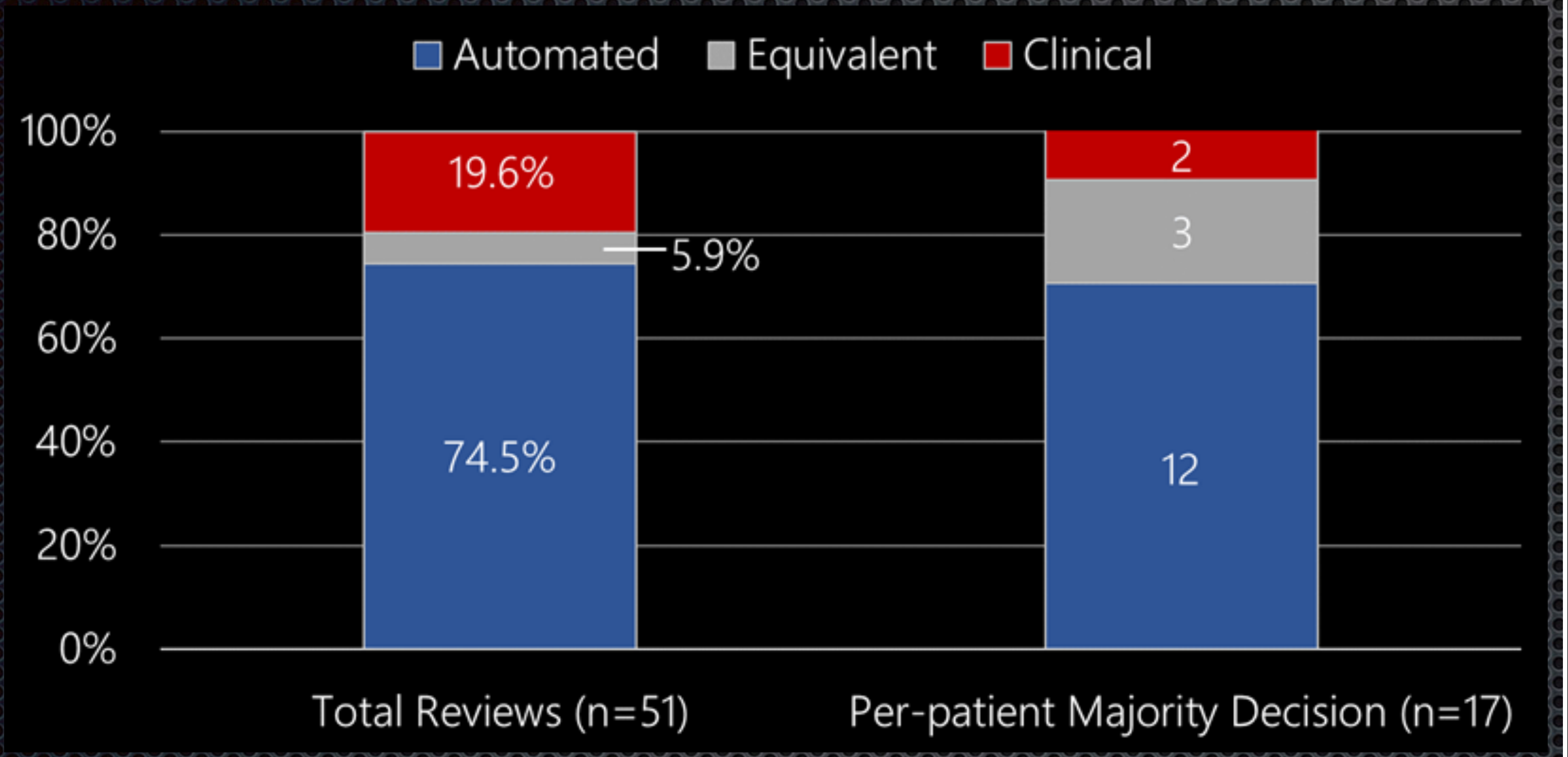
The AI method output



Passing the (high) bar



The exciting result of Step 1



Patient	Reviewer			Majority Decision
	1	2	3	
A	ML	Equivalent	Clinical	Equivalent
B	ML	ML	Clinical	ML
C	ML	ML	ML	ML
D	Equivalent	Clinical	ML	Equivalent
E	ML	ML	Clinical	ML
F	ML	Clinical	Clinical	Clinical
G	ML	ML	ML	ML
H	ML	ML	ML	ML
I	ML	ML	ML	ML
J	ML	Equivalent	Clinical	Equivalent
K	ML	ML	ML	ML
L	ML	ML	ML	ML
M	ML	ML	ML	ML
N	ML	ML	ML	ML
O	Clinical	Clinical	Clinical	Clinical
P	ML	ML	ML	ML
Q	ML	ML	ML	ML

Step 1 - Lesson 1

Thank you for submitting your manuscript to the Red Journal. It has been read and discussed by the senior editorial team who, unfortunately, did not feel it met our criteria for publication and their thoughts are appended below. They did, however, think that it may be a good fit for our sister publication "Practical Radiation Oncology". If you are interested, we would like to suggest that you take advantage of the article transfer service that both journals participate in. This gives you the option to have your manuscript files transferred directly, and removes the need for you to resubmit and reformat your manuscript.

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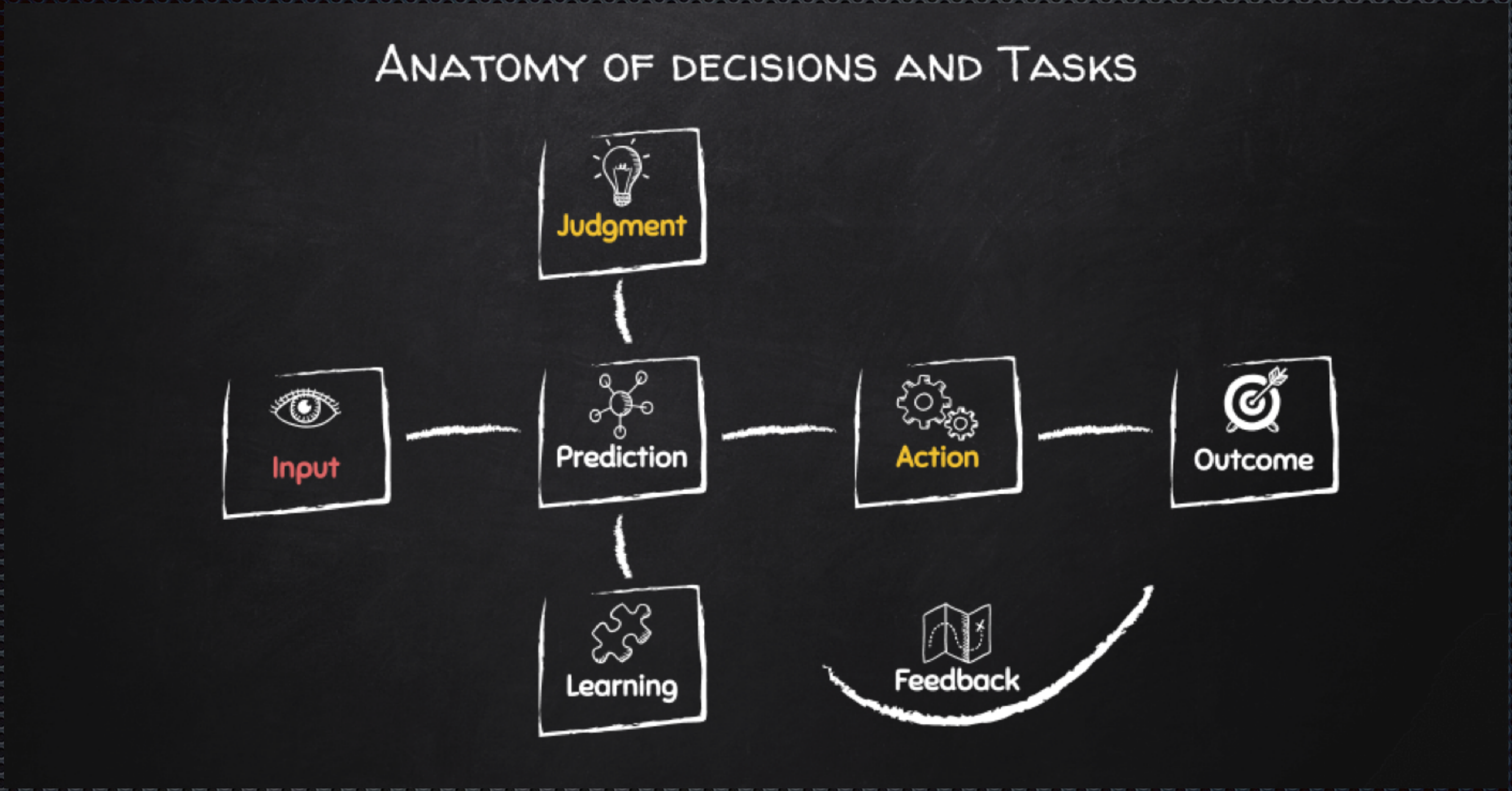
Yours sincerely,

Anthony L. Zietman, MD
Editor-in-Chief
International Journal of Radiation Oncology*Biology*Physics

Value-proposition (was) unclear

What we want (should!) evaluate ?



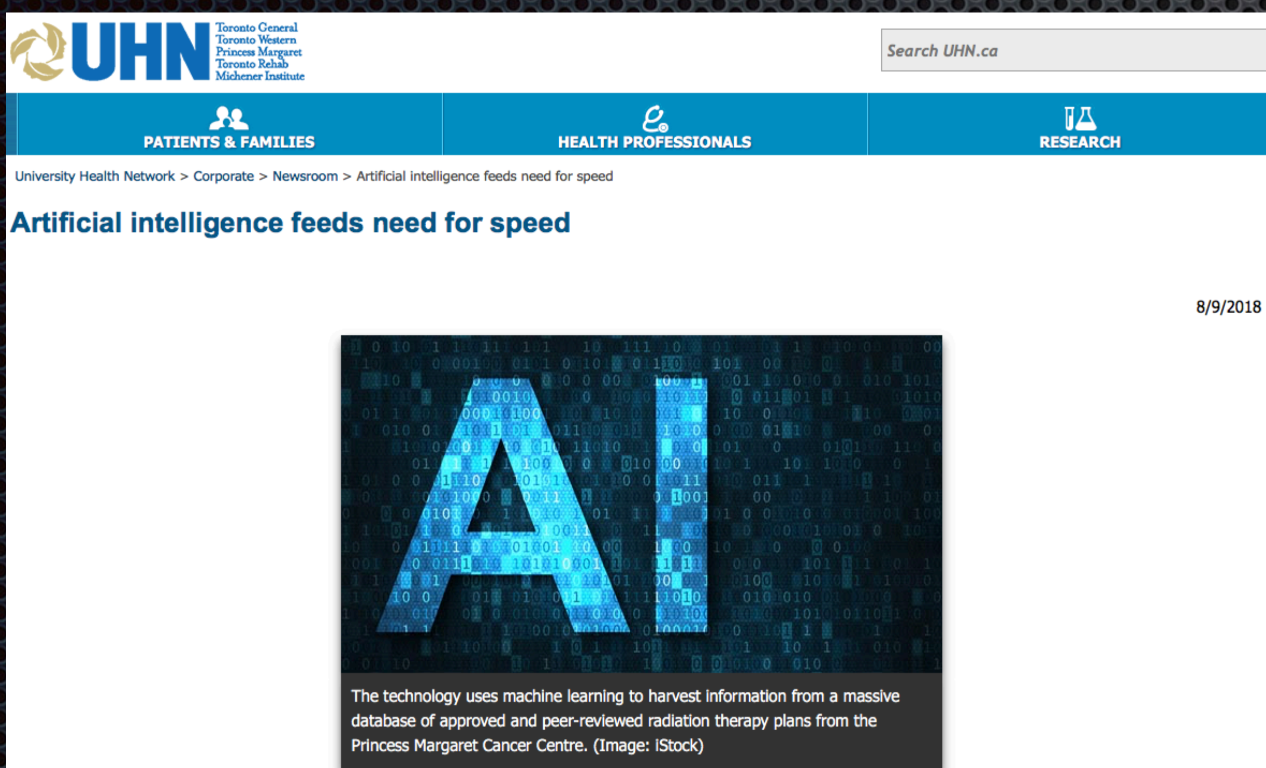
Predict a dose distribution expected to be **judged** favourably (e.g. approved/liked) by treatment team experts

Adapted from 'Prediction Machines' - Agrawal, Gans, Goldfarb

Step 2 - Real World

Magic ingredienTs: Team & Trust (...and Tenacity)

GU group



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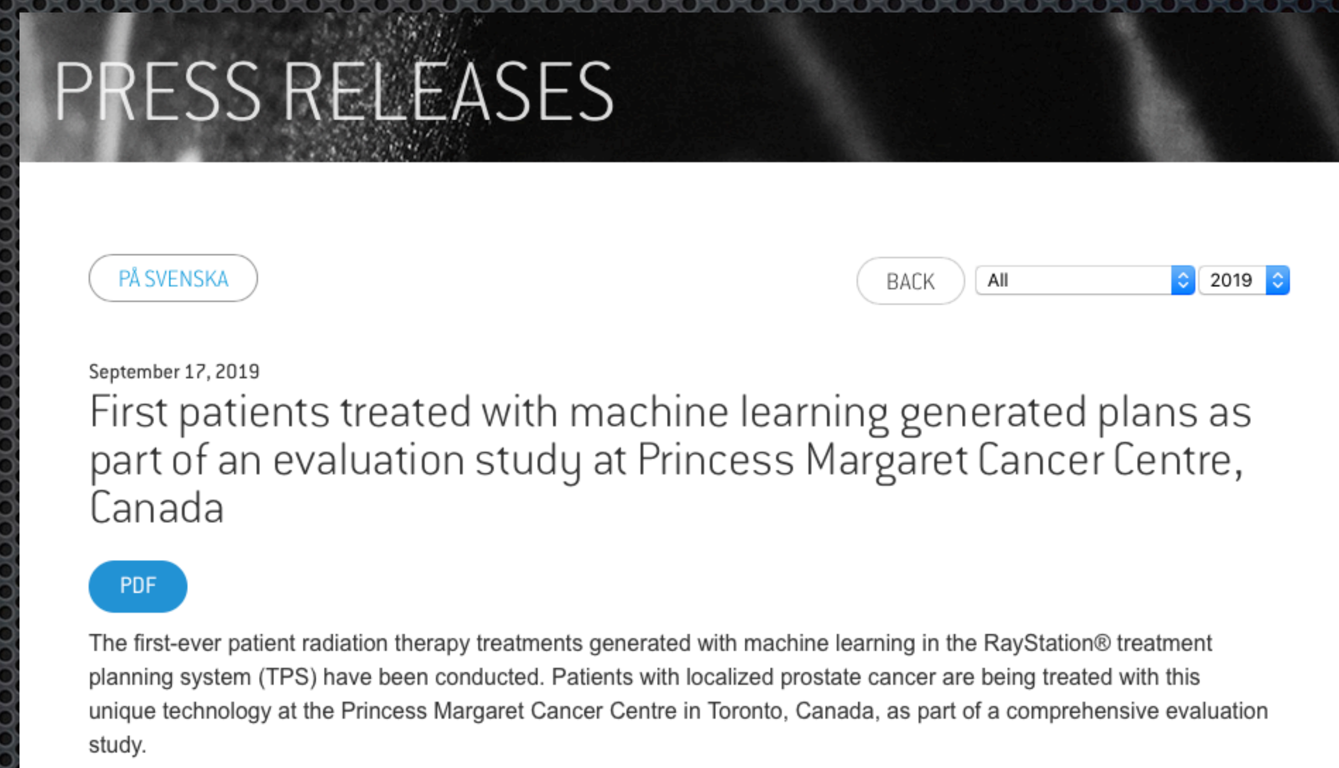
University Health Network > Corporate > Newsroom > Artificial intelligence feeds need for speed

Artificial intelligence feeds need for speed

8/9/2018

AI

The technology uses machine learning to harvest information from a massive database of approved and peer-reviewed radiation therapy plans from the Princess Margaret Cancer Centre. (Image: iStock)



PRESS RELEASES

PÅ SVENSKA

BACK All 2019

September 17, 2019

First patients treated with machine learning generated plans as part of an evaluation study at Princess Margaret Cancer Centre, Canada

PDF

The first-ever patient radiation therapy treatments generated with machine learning in the RayStation® treatment planning system (TPS) have been conducted. Patients with localized prostate cancer are being treated with this unique technology at the Princess Margaret Cancer Centre in Toronto, Canada, as part of a comprehensive evaluation study.

"The AI plan was deemed superior for that specific patient, and got the 'green light' after meeting all our protocol and quality assurance metrics"

Mapping our (ongoing) road

Day 0

Method Discovery & Performance QA

n=116

AI v1.0
H v1.0

Retrospective Validation (control)

n=50 (x2)

AI v2.0
H v1.0

Intra-observer V
H & AI Performance

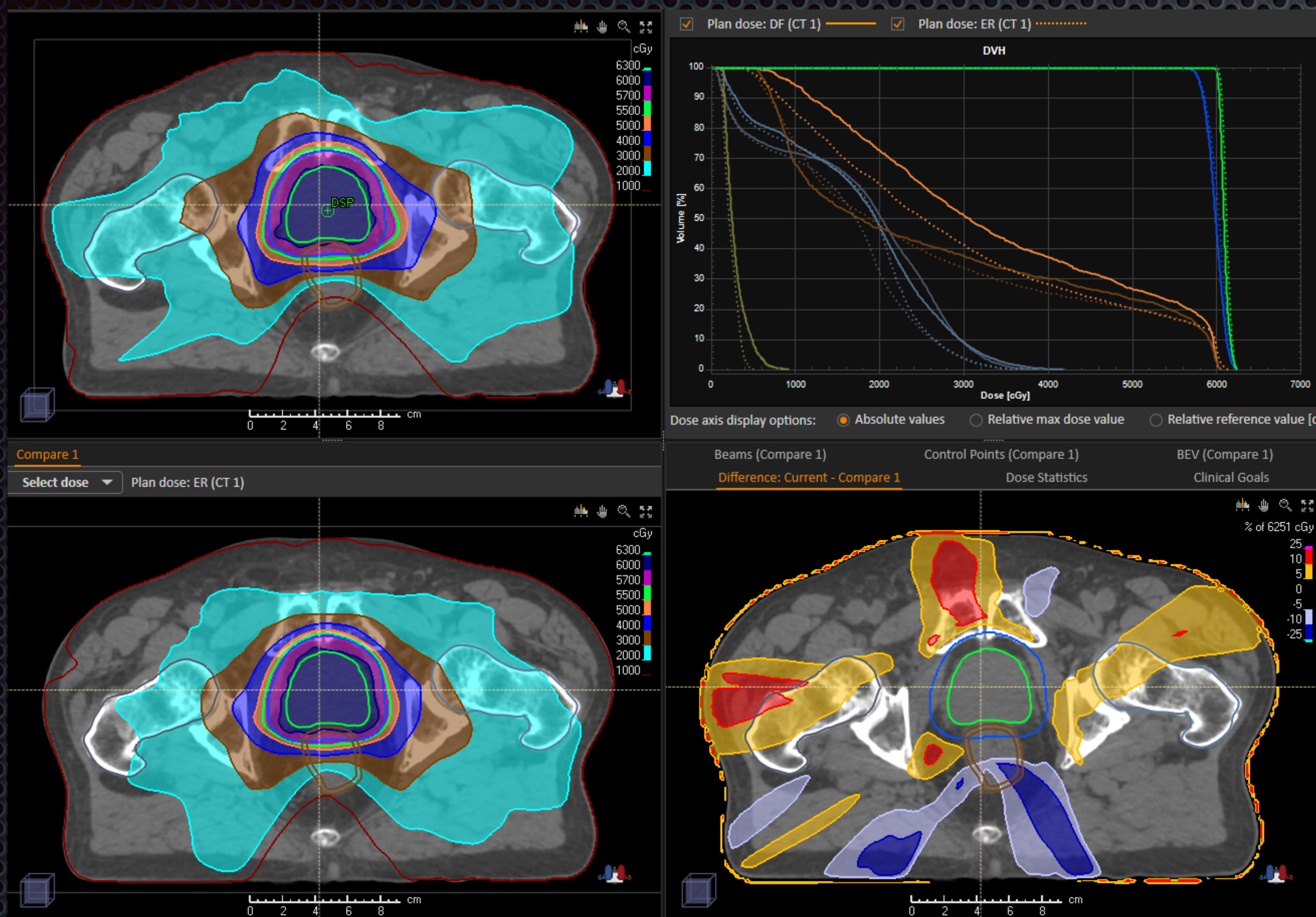
Prospective Validation

n=50

AI v2.0
H v2.0

H & AI Performance
QA, Peer-review

Every patient coming through the doors ...



Prostate AutoPlanning Evaluation

Reviewer

Patient ID (First 3 digits of MRN only) *

Plan Comparison. Which plan has better: *

	Prostate_A1	Prostate_A2	They are Equivalent
Target Coverage	○	○	○
OAR Sparing	○	○	○
High Dose Conformity	○	○	○
Rectal Dose Gradient	○	○	○
Lateral Dose Symmetry	○	○	○

Plan Acceptability *

	Acceptable	Unacceptable
Prostate_A1	○	○
Prostate_A2	○	○

Preferred Plan *

	Preferred Plan
Prostate_A1	○
Prostate_A2	○
Equivalent → go with Prostate_A1	○
Equivalent → go with Prostate_A2	○
Do not like either plan	○

Which plan do you think is the Automated Plan? *

	Automated Plan
Prostate_A1	○
Prostate_A2	○

Submit

Preliminary Results

Day 0

%	Human	AI	Equivalent
Target Coverage	4 %	22 %	74 %
OAR Sparing	16 %	66 %	18 %
High D Conformity	40 %	18 %	42 %
Rectal Gradient	20 %	66 %	14 %
Symmetry	16 %	48 %	36 %
Acceptable?	98 %	**90 %**	
Preferred	26 %	**74 %**	

n = 50

%	Human	AI	Equivalent
Target Coverage	4 %	22 %	74 %
OAR Sparing	16 %	66 %	18 %
High D Conformity	40 %	18 %	42 %
Rectal Gradient	20 %	66 %	14 %
Symmetry	16 %	48 %	36 %
Acceptable?	98 %	**90 %**	
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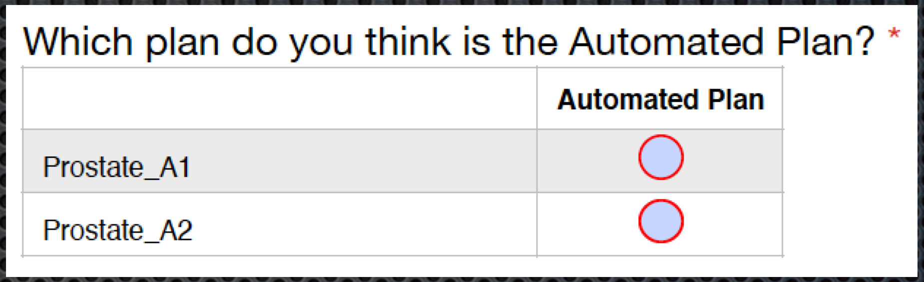
n = 38

Preliminary Results (2)

Alan Turing (1912-1954)

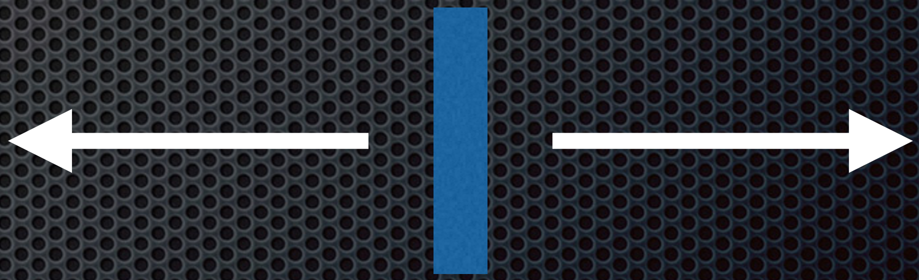
“I believe that at the end of the century the use of words and general educated opinion will have altered so much that one will be able to speak of **machines thinking** without expecting to be contradicted.”



Which plan do you think is the Automated Plan? *

	Automated Plan
Prostate_A1	○
Prostate_A2	○

Day 0



0.78
(0.25 - 1.00)

0.74
(0.00 - 1.00)

Future Roads

- **Integration** of auto-planning with MR-based **auto-segmentation**

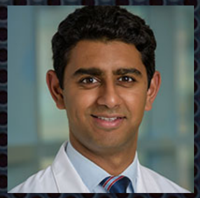
AbbVie-CARO Award
Sanofi Grant

- Expand to **other GU treatment** scenarios

- **International collaboration** to evaluate judgment/assessment/acceptability of AI plans
  - Paving road to international applications








- Collaboration to **assess performance in Phase III trial** cohort
  - Model impact of true standardized planning
  - Outcome-based AI planning?


Future Highway!



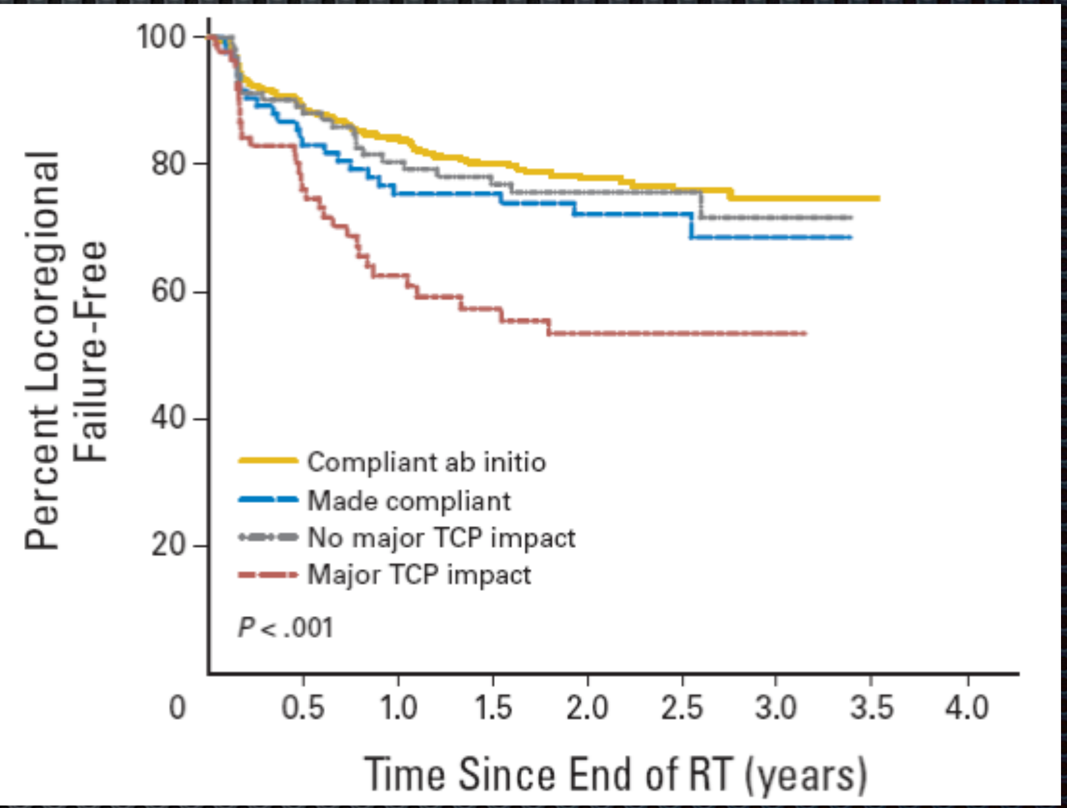


- Challenge: **Drug** + RT
  - Consistency
  - Quality
  - Education
  - ……

Evaluation phase

↓

RW **application**



AI planning/QA methods could be leveraged to develop a R-GMP framework

Summary & Thoughts

- **Automation** will be an essential component for many radiotherapy processes.
- The development and ascertainment of AI/automation methods deepens **need for team / multi-professional approaches**.
- Robust **methods are necessary but insufficient** to change, impact or even enter clinical practice.
  - **Value**: Outcomes / Cost … Performance of method <u>might</u> be a surrogate.
- Principles remain principles: **Start with the problem**, then method, its role and value proposition.
- **Prospective validation is where the value resides**: lessons, challenges and **opportunity to lead the field**.

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