

SIF, 17 Settembre 2020

Individual automatic plan optimization in radiotherapy by Knowledge-based (KB) models: Clinical implementation and potential for multi-Institute extension

C. Fiorino

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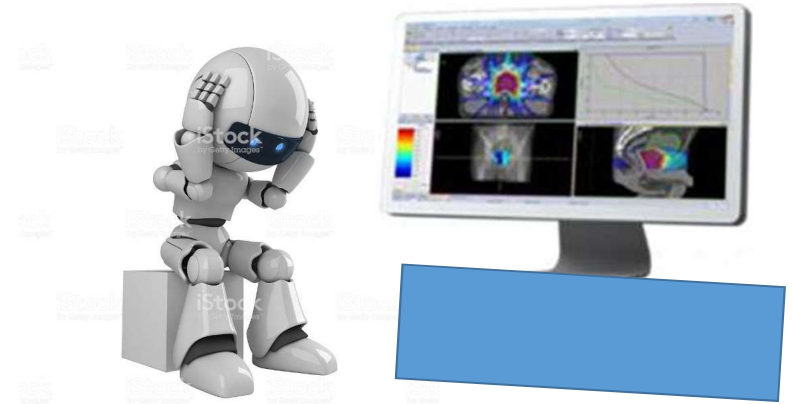
I.R.C.C.S. Ospedale
San Raffaele



Summary

- AI in RT, coming changes...
- AI for planning vs the auto-plan scenario
- KB based auto-plan: clinical implementation
- KB planning: pro's & con's
- The frontier: large-scale, multi-institutional KB planning.

The MIKAPOCo national study



AI IN RT: Coming (disruptive ?) applications....



Contents lists available at ScienceDirect

Radiotherapy and Oncology

Journal homepage: www.thegreenjournal.com



Review

Artificial intelligence in radiation oncology: A specialty-wide disruptive transformation?

Reid F. Thompson^{a,b,*}, Gilmer Valdes^c, Clifton D. Fuller^d, Colin M. Carpenter^e, Olivier Morin^c, Sanjay Aneja^f, William D. Lindsay^g, Hugo J.W.L. Aerts^{h,i}, Barbara Agrimson^a, Curtiland Deville Jr.^j, Seth A. Rosenthal^k, James B. Yu^l, Charles R. Thomas Jr^a

^aOregon Health & Science University, Portland; ^bVA Portland Health Care System, Portland; ^cUniversity of California San Francisco, San Francisco; ^dMD Anderson Cancer Center, Houston; ^eSiris Medical, Inc, Redwood City; ^fYale University, New Haven; ^gOncoxia Medical, Philadelphia; ^hBrigham and Women's Hospital, Boston; ⁱDana Farber Cancer Institute, Boston; ^jJohns Hopkins University School of Medicine, Baltimore; and ^kSutter Medical Group and Sutter Cancer Center, Sacramento, USA

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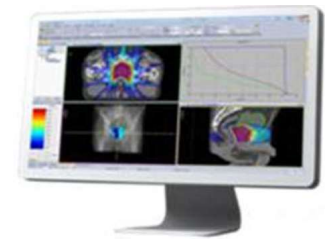
Nb: Disruptive = Dirompente
Disruptors = Perturbatore



**MP IN RT ALWAYS HAD A
DISRUPTIVE ROLE !!!**

AI IN RT: Coming applications....

Image segmentation and contouring, atlas-based, deep learning....



TPS



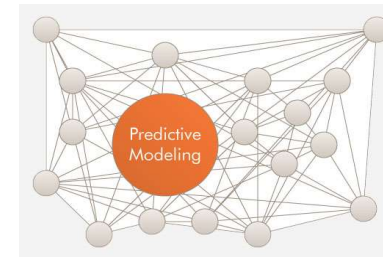
Learning Health systems, patient analytics, decision support systems, data sharing and AI-based prediction...



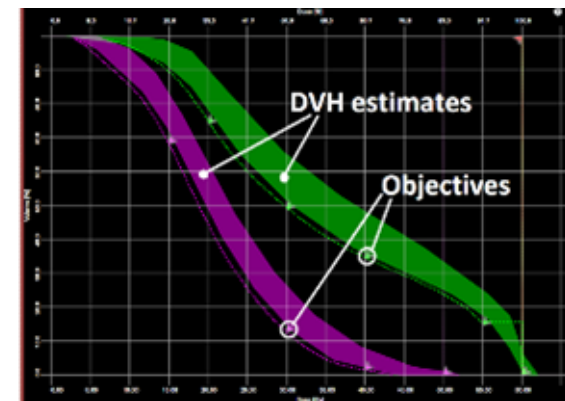
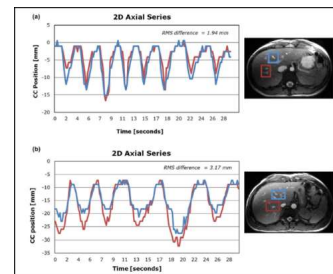
Dosimetry and QA, Linac safety and maintenance, Outliers identification for patient QA,...



Machine learning systems to develop predictions, data sharing & big data integration, distributed learning...



Fast Image recognition for patient-setup, tracking, 4D IGRT.....

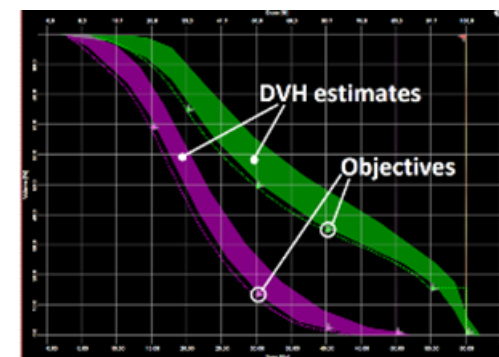


Planning Optimization,
.....plan QA, AI-based remote planning, on-line adaptive planning, QA of clinical trials....

AI IN RT: Coming applications....



Planning Optimization,
.....plan QA, AI-based remote
planning, on-line adaptive
planning, Qa of clinical trials....

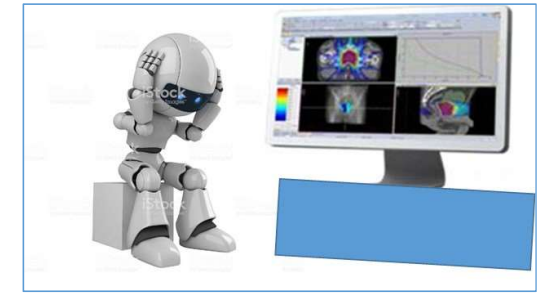


Why AI clinical implementation is more advanced in plan optimization (*and auto-contouring*) ??

- Large availability of «high quality» data (plan experience)
- Generally well-posed quantitative problem (defining constraints & cost functions during optimization)
- Potentially large cost-benefit ratio (plan quality, time, resources....)
- Interpretable (and then usable) models

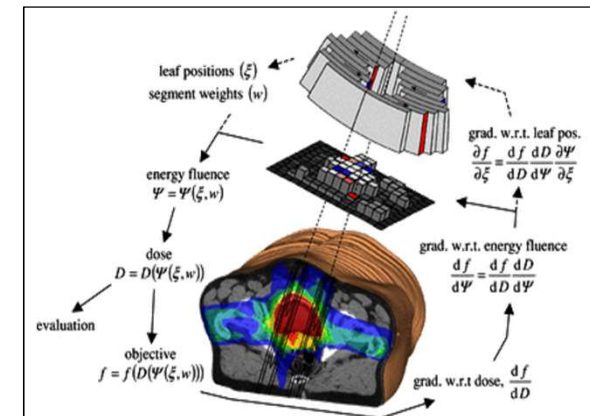
- Pivotal position of Medical Physicists...no need of external professionals
- (Commercial systems available)

AI for planning & the auto-plan scenario



→ IMRT planning is based on the inverse problem optimization:

- not physical solution which fulfils the ideal objectives
- multi-objective problem with conflicting objectives
- trial-and-error procedure

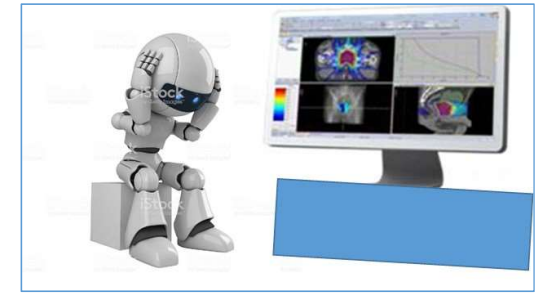


→ IMRT planning optimization result:

- time consuming
- strongly planner depending
- strongly Institution depending
- variable risk of clinically relevant sub-optimal plans



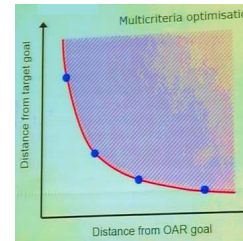
AI for planning & the auto-plan scenario



To overcome limitation of manual optimization

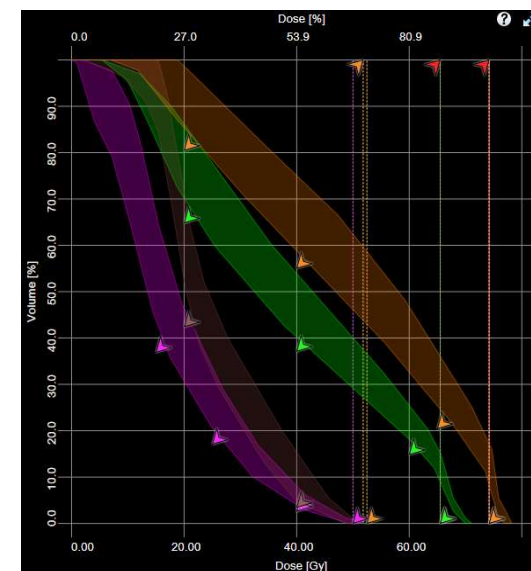
→ Automatic planning optimization

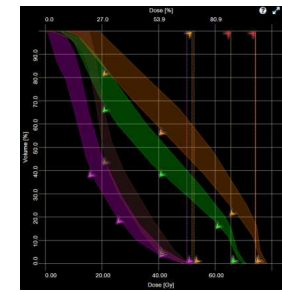
- Multicriteria optimization (MCO), Pareto-like
- Protocol-based optimization



Dose cGy (RBE)	Volume at Primary Goal Dose	Result
6316.700000	Min 95.678 %	OK
5849.100000	Min 98.405 %	Met
4231.300000	Min 97.006 %	Met
4179.500000	Max 0.000 cm ³	Met
3973.700000	Max ---	Met
2400.100000	Mean ---	Met
2446.900000	Mean ---	Met
6128.900000	Mean ---	Not Met

- AI Knowledge-based models
...CAN be used for automatic plan

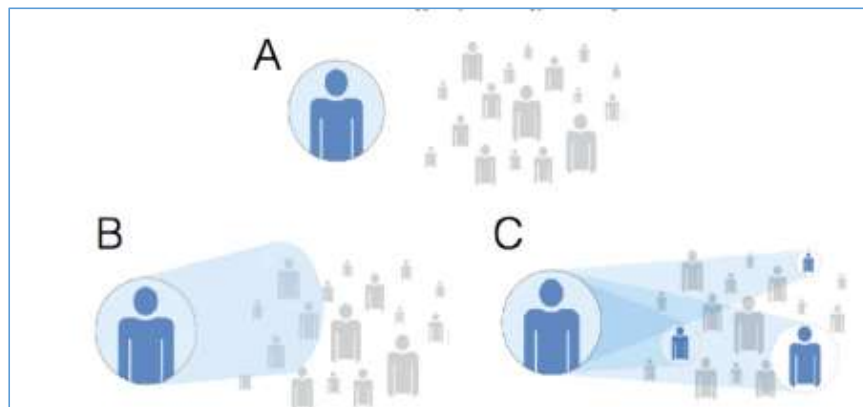




-Knowledge-based (KB) planning: the concept


- Plan prediction: can the plan on a new patient be «predicted» based on its similarity/dissimilarity against a (large enough) sample?

Example: Plan classification based on pts characteristics (anatomical, medical, intent, physics,...)



Decision support system

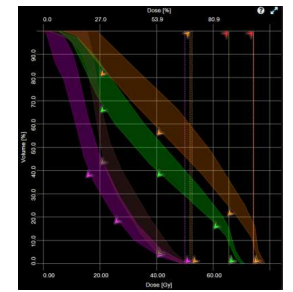
Clinical decision support of radiotherapy treatment planning: A data-driven machine learning strategy for patient-specific dosimetric decision making



Gilmer Valdes^{a,*}, Charles B. Simone II^b, Josephine Chen^a, Alexander Lin^c, Sue S. Yom^{a,d}, Adam J. Pattison^e, Colin M. Carpenter^e, Timothy D. Solberg^a

Table 1
Feature-set categories used to predict dose for a radiation treatment plan.

Feature category	Example features
Anatomical information	Distance, volume, geometric relationship, and importance of structures and surrounding structures
Medical record	ICD-9/10 code, gender, ethnicity
Treatment intent	Ractionation schedule, treatment margin, number of beams/arcs, and the clinicians who are part of the team creating the radiation treatment plan
Radiation transport	Penumbra, aperture, incident angle, beam energy, radiation type (proton vs photon), depth of structure, and existence of bolus



- KB-models of planning data

- DVH prediction

- Dose metrics prediction

- Voxel-dose prediction



Plan QA

Automatic Optimization

- Beam parameters prediction

- Patient QA prediction

- (Objective function weights)

Knowledge-based planning for intensity-modulated radiation therapy: A review of data-driven approaches

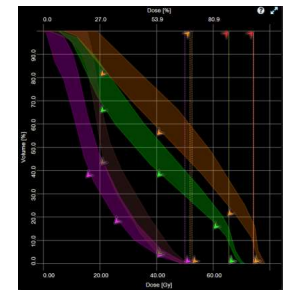
Yaorong Ge

Department of Software and Information Systems, University of North Carolina at Charlotte, Charlotte, NC 28223, USA

Q. Jackie Wu[✉]

Department of Radiation Oncology, Duke University Medical Center, Durham, NC 27710, USA

Med. Phys. 46 (6), June 2019 0094-2405/2019/46(6)/2760/16



- KB-models of planning data

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Plan QA

Automatic Optimization

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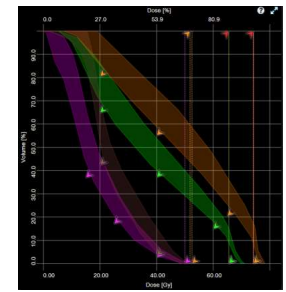
Knowledge-based planning for intensity-modulated radiation therapy: A review of data-driven approaches

Yaorong Ge
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- KB-based auto-planning: methods

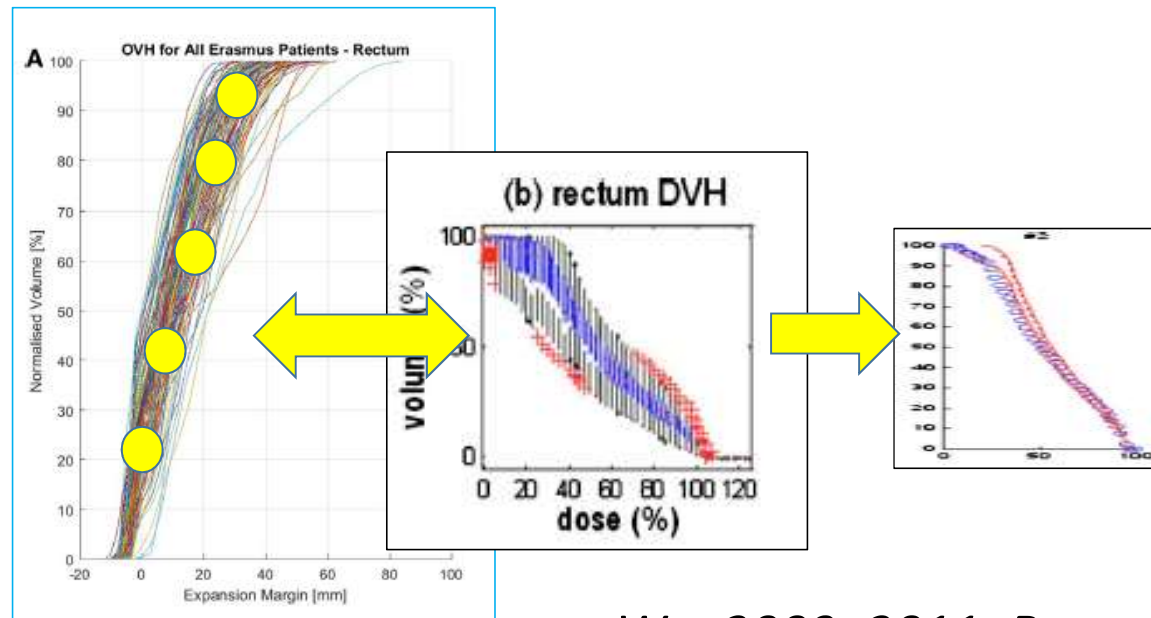
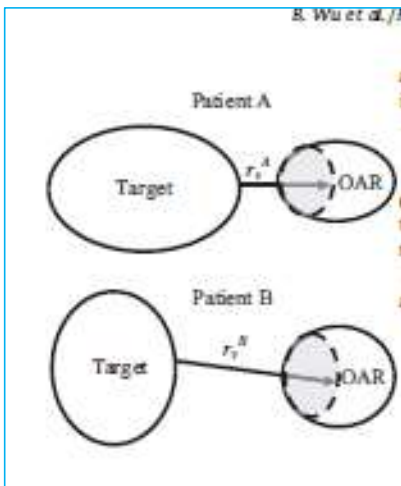


- Case and Atlas-based methods

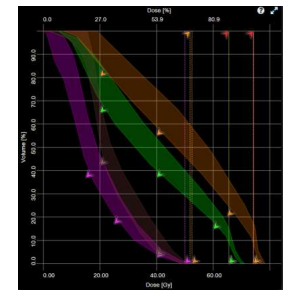
- Statistical and machine learning methods

Fitting one new case with the most similar case in a dbase: a) similarity measurement to assess the most similar plan; b) transfer the knowledge to the new patient

Ex: OVH (overlap volume histogram) approach



Wu, 2009, 2011; Burton 2018



- KB-based auto-planning: methods

- Case and Atlas-based methods

- **Statistical and machine learning methods**

Creating a predictive model using the prior plans dbase; most based on regression models (multi-linear, logistic, stepwise...) or other methods (curve fitting, artificial neural network, random forest, support vector machine,)

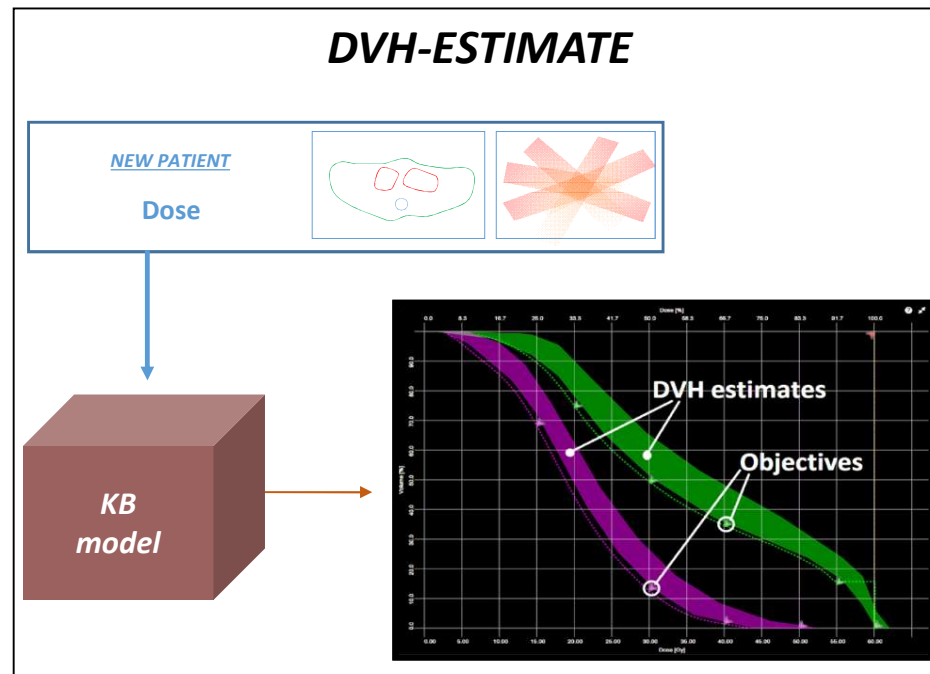
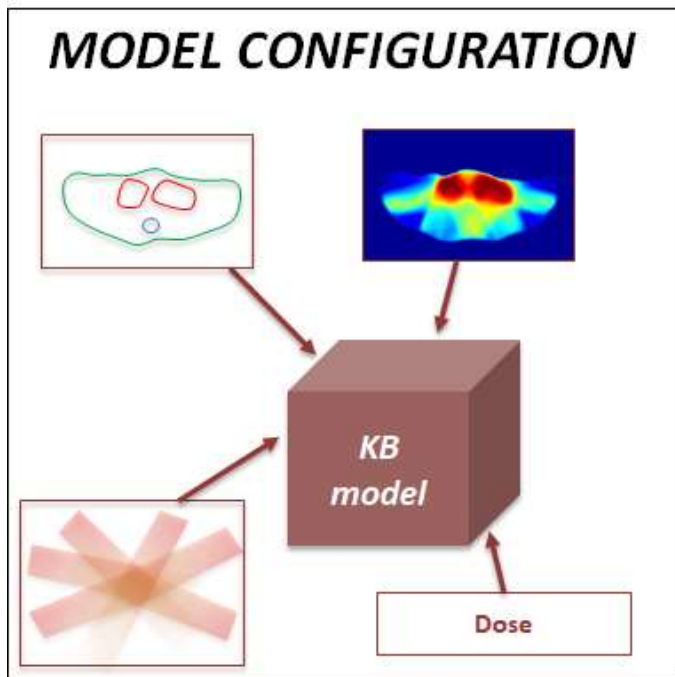
The most popular (commercially available, Rapidplan Varian©) is the multi-variable linear regression (Yuan 2012), using Principal Component Analysis (PCA)

Pioneering papers by Fogliata et al, 2014, 2015; Tol et al 2015

- KB-based planning: examples of clinical implementation

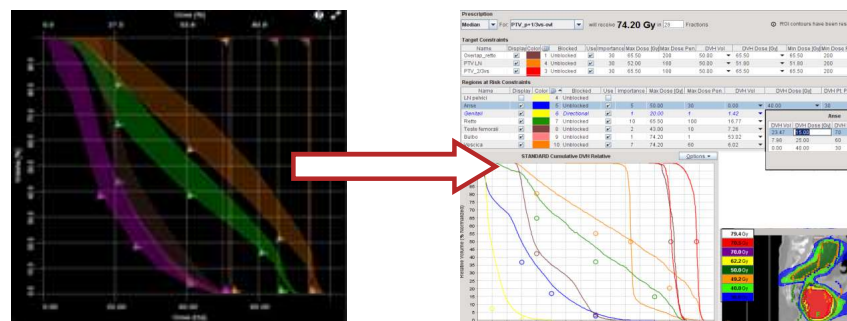
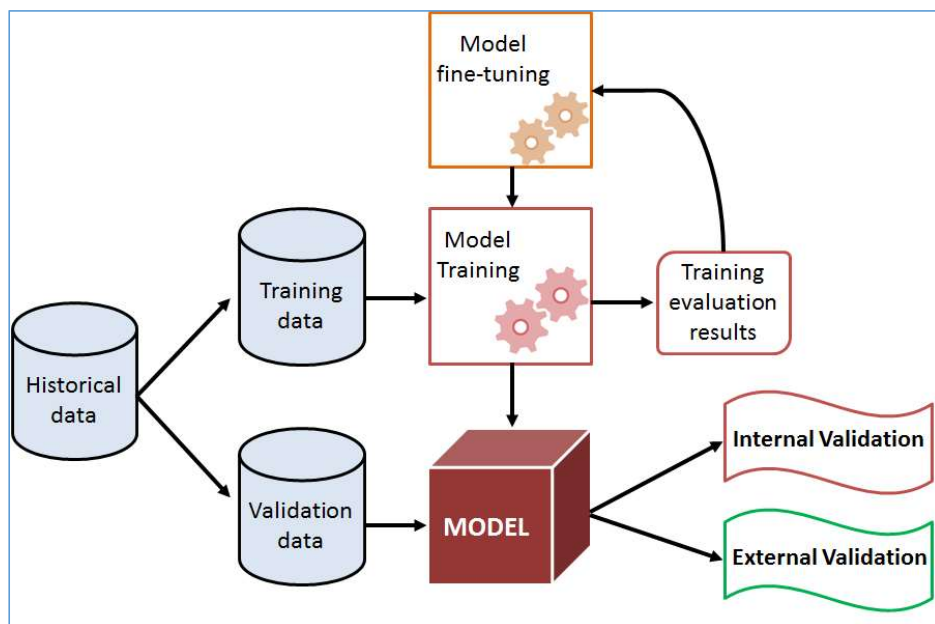
.....using RapidPlan

- **MODEL CONFIGURATION** – existing clinical treatment plans are used to estimate the most likely dosimetric features of a similar treatment plan in a new patient case.
- **DVH-ESTIMATE** – based on previously modelled patients data, the KB-model generates an estimated DVH range suggesting where the DVH of a structure will most likely land.



- KB-based planning: examples of clinical implementation

- **KB-BASED (INDIVIDUAL) TEMPLATE FOR PLAN OPTIMIZATION** – based on the DVH estimate, this information may be used to generate a template for automatic plan optimization
- **“FINE TUNING” OF THE TEMPLATE IS CRUCIAL AND NEED CAREFUL “ITERATIVE” OPTIMIZATION, TO EFFICIENTLY TRANSLATE KB-PREDICTION IN EXECUTABLE AUTOMATIC OPTIMIZATION !**
- **KB-BASED TEMPLATES FOR AUTOMATIC PLANNING NEED TO BE EXTENSIVELY VALIDATED BEFORE CLINICAL IMPLEMENTATION !**

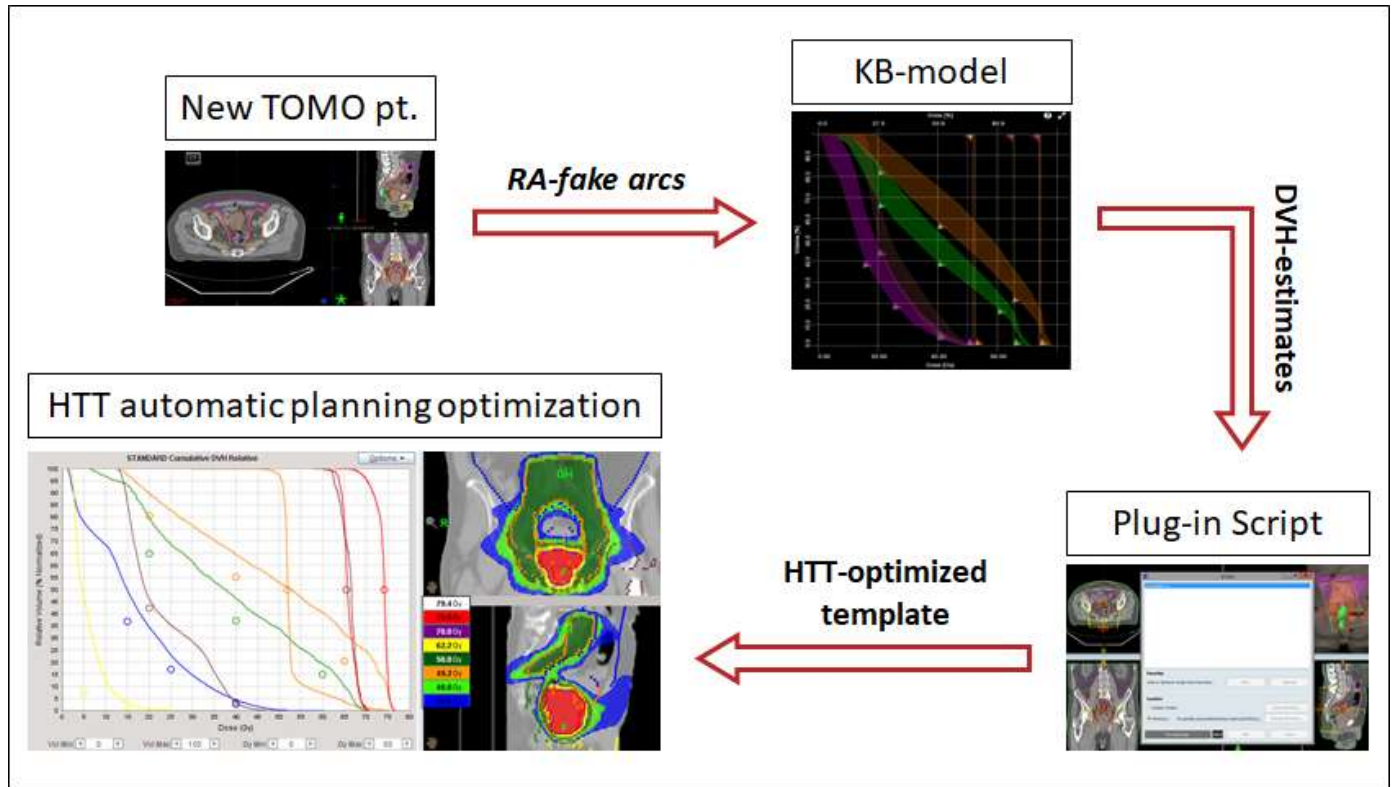


- **Internal:**
re-optimization of plans of the training cohort vs clinical plans.
- **External:**
re-optimization of plans of the validation cohort vs clinical plans

- KB-based planning: examples of clinical implementation

Models developed and validated @ San Raffaele Institute (year of clinical implementation)

- Post-operative prostate ca: pelvis + boost (2017) ➡ *Castriconi PM 2019*
- Rectal ca: including early-regression guided adaptive boost (2018) ➡ *Castriconi PM 2020*
- Prostate ca (Tomotherapy): high and intermediate risk pts (2019) ➡ *Castriconi Submitted*
- Breast ca: tangential-field like (ViTAT) right (2020) and left (ongoing...) ➡ *Esposito PM 2020*

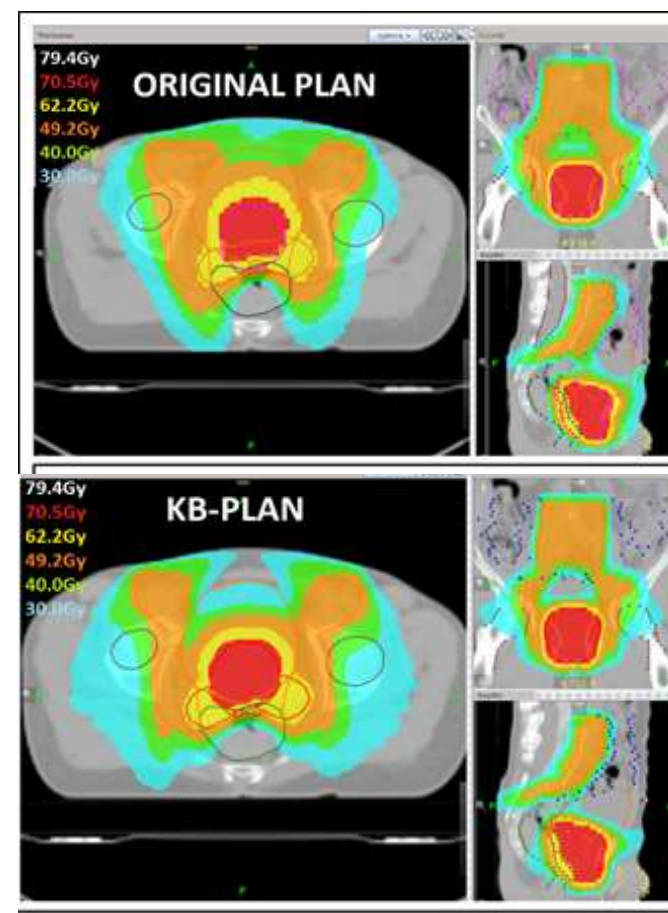
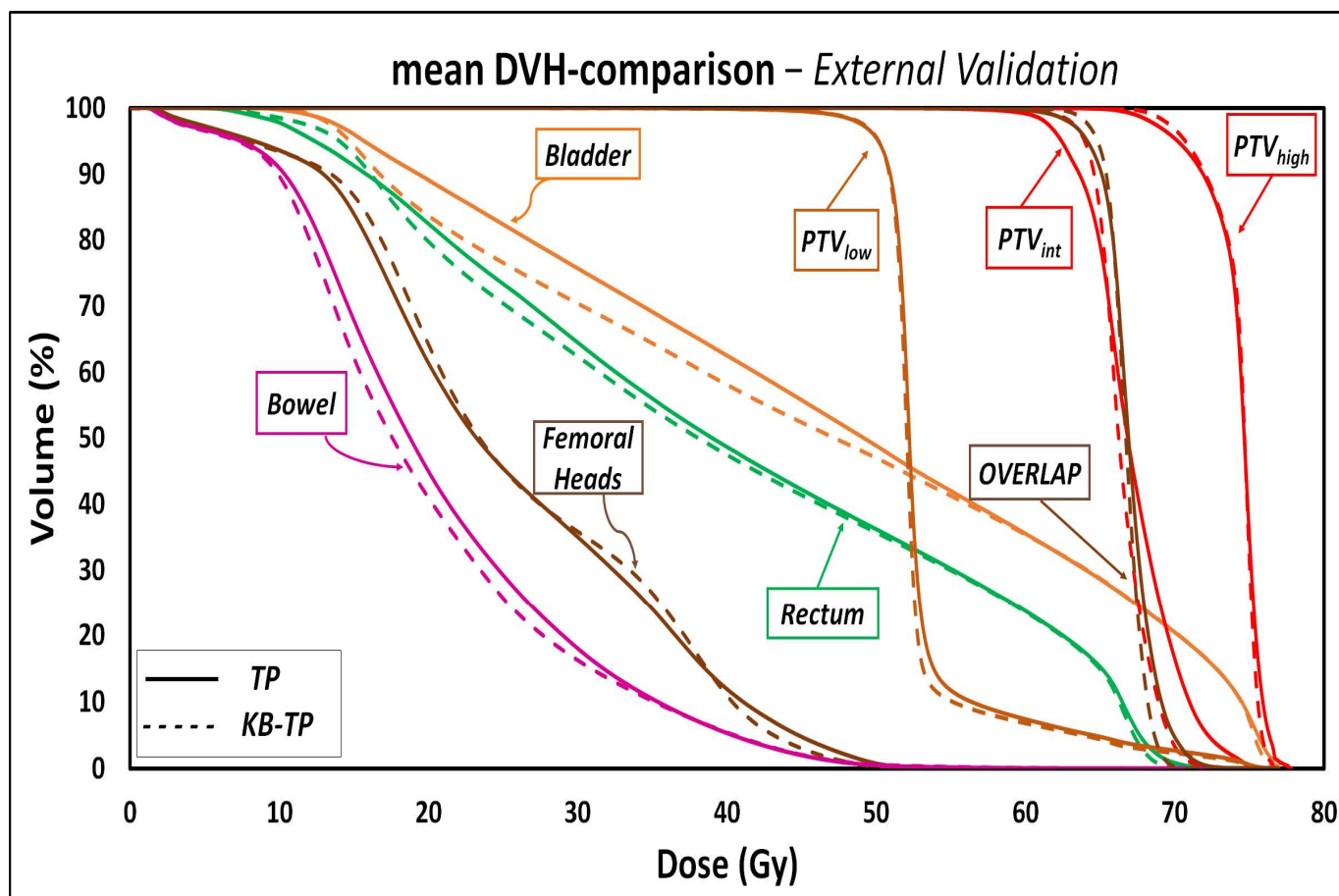


Ex: Workflow of fully automatic plan optimization in Tomo

OSR Prostatic KB-TOMO – Model validation

→ External Validation:

- re-optimization of 30 plans (treated in 2018-2019 and not included in the model) by KB-approach;

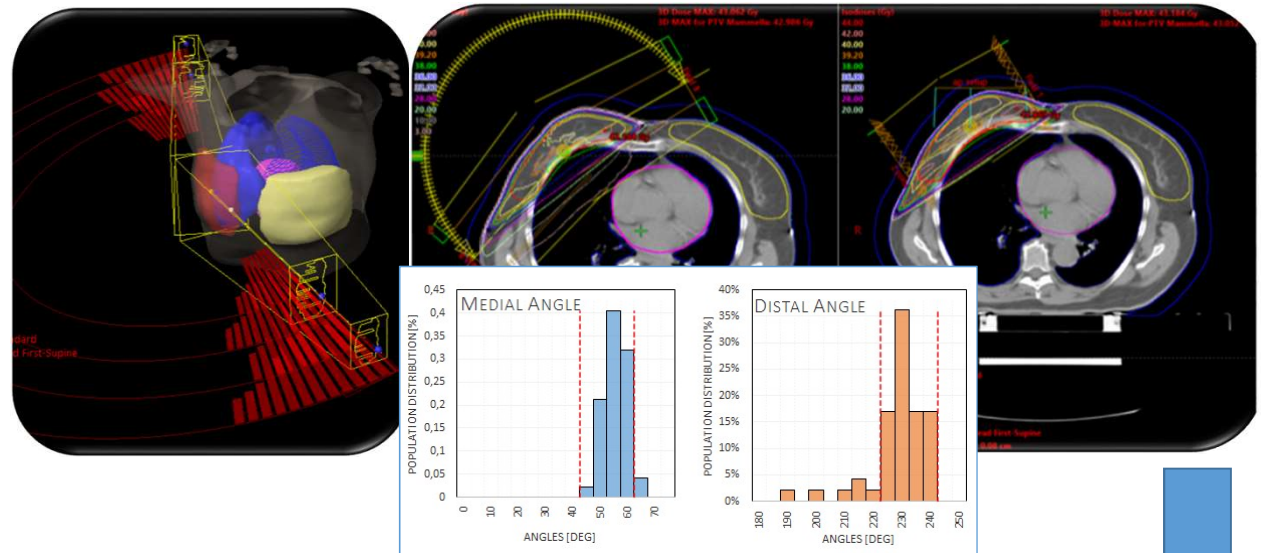


→ Up to now, 95 clinical plans delivered in 10 months wout or with minimal (<20 min) human intervention

OSR experience – ViTAT, KB breast

- Right-sided BREAST OK
 - 40 Gy to whole breast – 15 fractions
 - 4 arcs (6 MV) completely blocked - apart the first and last 20° of rotation (60-40°/220-240°).

- Left-sided BREAST (ongoing)



KB-model for tangential using ViTAT approach:

Right-sided BREAST implemented

- 6 pts treated

*ViTAT: Virtual Tangential Arc Therapy

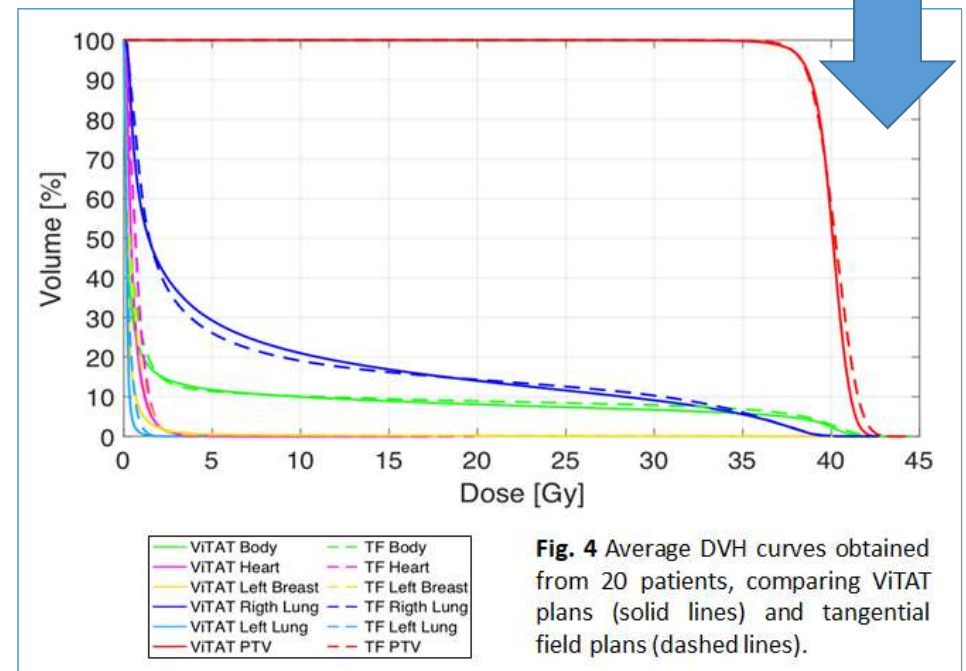
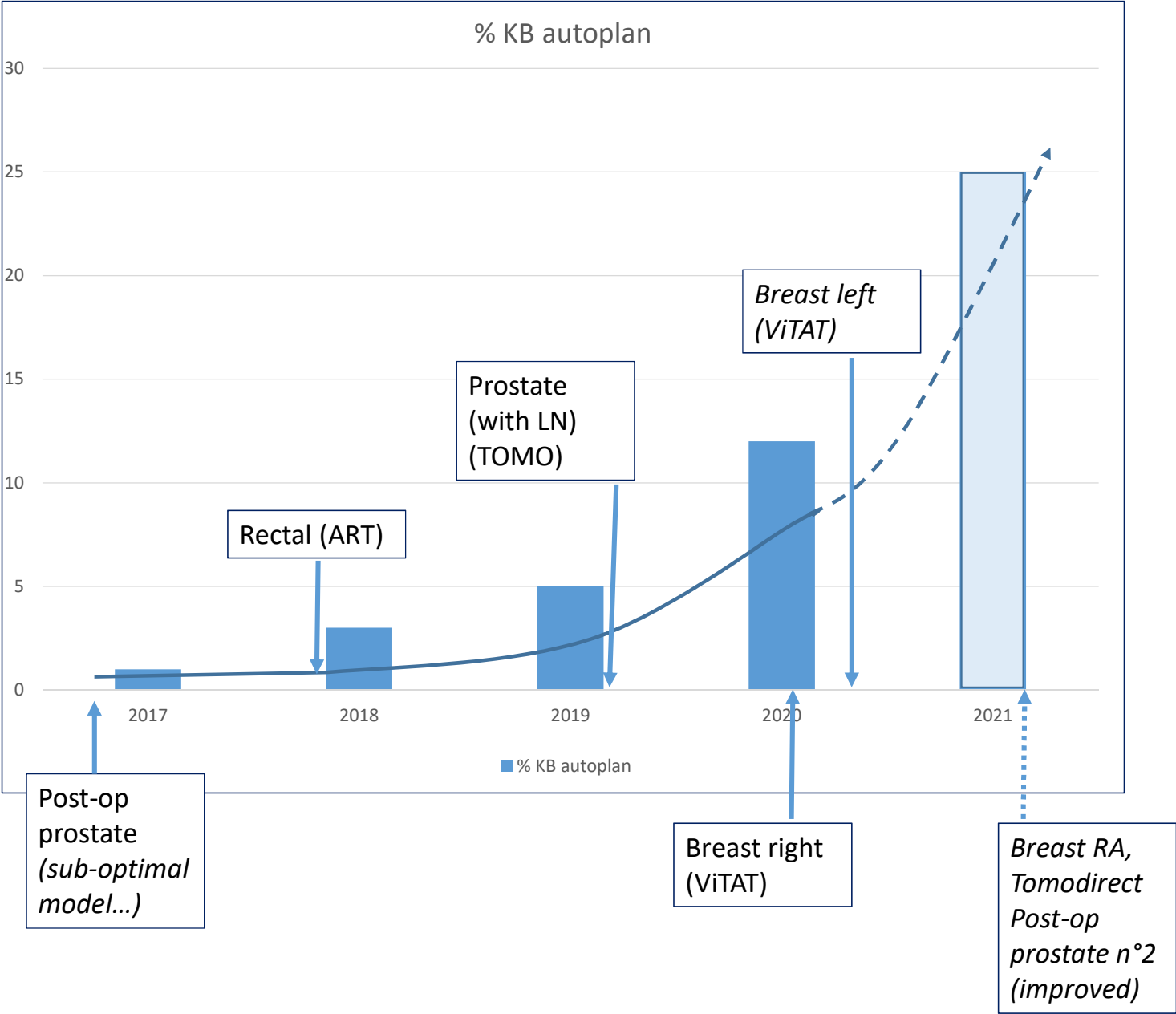


Fig. 4 Average DVH curves obtained from 20 patients, comparing ViTAT plans (solid lines) and tangential field plans (dashed lines).

OSR KB-based autoplan clinical implementation



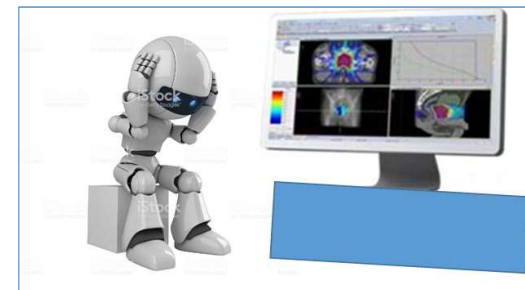
KB planning: pro's and con's

PRO'S

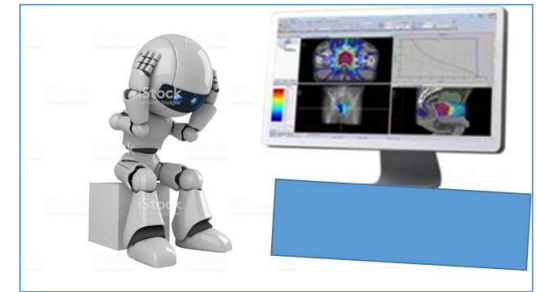
- Reduce/eliminate sub-optimal plans
- Reduce/eliminate inter-planner variability
- Moderately improve plan quality, depending on the quality of KB implementation; resulting auto-plan solutions are «individually» optimized
- Keep past experience, avoid dose distributions too far from your experience
- Strong reduction of planning time for individual optimizations
- Push to optimize and homogeneize the whole planning chain, including support structures contouring

CON'S

- Risk of «garbage in – garbage out»
- Plan quality is not expected to increase dramatically
- Needs time to generate and validate DVH estimate models
- Needs time to translate DVH prediction into effective and automatic automatic plan solutions
- Needs (continuous) update
(...last three issues maybe not a CON's....)



KB planning: pro's and con's



Additional «large-scale» PRO'S

- Potentials in QA of clinical trials and remote plan QA/plan assistance
- Rational «in-silico» plan comparison, cost-benefit analysis, HTA
- Potentials in patient selection for specific technology solutions (for instance: heavy particles vs photons)
- Educational, Tutorial
- Measuring plan quality changes with time
- Potentials for shared/multi-institutional KB models (?)

Multi-Institutional Validation of a Knowledge-Based Planning Model for Patients Enrolled in RTOG 0617: Implications for Plan Quality Controls in Cooperative Group Trials

James A. Kavanaugh MS^{a,*}, Sarah Holler BS^b, Todd A. DeWees PhD^c, Clifford G. Robinson MD^a, Jeffrey D. Bradley MD^a, Puneeth Iyengar MD, PhD^d, Kristin A. Higgins MD^e, Sasa Mutic PhD^a, Lindsey A. Olsen PhD^f

Analysis of EORTC-1219-DAHANCA-29 trial plans demonstrates the potential of knowledge-based planning to provide patient-specific treatment plan quality assurance



Jim P. Tol^a, Max Dahele^a, Vincent Gregoire^b, Jens Overgaard^c, Ben J. Slotman^a, Wilko F.A.R. Verbakel^{a,*}

Using a knowledge-based planning solution to select patients for proton therapy

Alexander R. Delaney^a, Max Dahele, Jim P. Tol, Ingrid T. Kuijper, Ben J. Slotman, Wilko F.A.R. Verbakel
Department of Radiation Oncology, VU University Medical Center, Amsterdam, The Netherlands



The frontier: large-scale, multi-institutional KB planning

Promises and pitfalls.....open issues

- Inter-Institute protocols variability (dose, fractionation, technique...)
- Inter-Institute OARs/CTV/PTV definition and contouring variability
- Inter-changeability/esportability of a model from an institute to another
- Meta-models incorporating Inter-Institute variability
- Generating/adapting benchmark models

- Measuring plan quality Inter-Institute variability

RESEARCH ARTICLE

Intercenter validation of a knowledge based model for automated planning of volumetric modulated arc therapy for prostate cancer. The experience of the German RapidPlan Consortium

Carolin Schubert¹, Oliver Waletzko², Christian Weiss³, Dirk Voelzke⁴, Sevda Toperim¹, Arnd Roeser⁵, Silvia Puccini⁴, Marc Piroth⁵, Christian Mehrens⁶, Jan-Dirk Kueter⁷, Kirsten Hierholz³, Karsten Gerull⁷, Antonella Fogliata⁸, Andreas Block⁶, Luca Cozzi^{8*}

PlosOne 2017

Evaluation of multiple institutions' models for knowledge-based planning of volumetric modulated arc therapy (VMAT) for prostate cancer



Yoshihiro Ueda¹, Jun-ichi Fukunaga², Tatsuya Kamima³, Yumiko Adachi⁴, Kiyoshi Nakamatsu⁵ and Hajime Monzen^{6*}

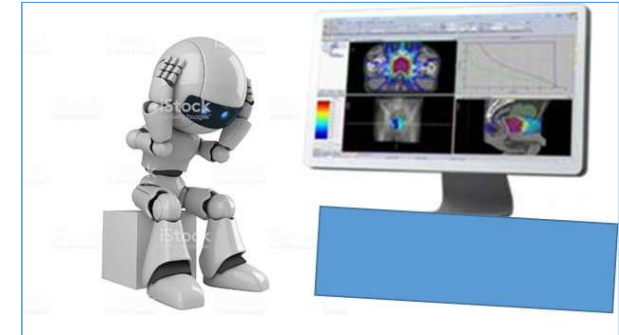
Radiat Oncol 2018

Experience of national RapidPlan consortia:
UK, Germany, Japan, Italy,...

The frontier: large-scale, multi-institutional KB planning

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- Measuring plan quality Inter-Institute variability



Opportunities.....

- Clinical trials
- Education/Tutorial
- Tools to compare your performance against the community and to improve/change practice
- To guarantee high quality plans in case of limited skill available (for instance: «cancer epidemy» in the less developed countries....)

Warnings/dangers....

- Planning as a mere technical service, sold with the machine
- Risk of malpractice, gradual elimination of planners
- Knowledge-based kills the local knowledge ?
- Risks of forced adaptation with poor interchangeability (for instance: robustness against contouring....)

MIKAPOCo: Multi-Institutional Knowledge-based Approach for Plan Optimization for the Community

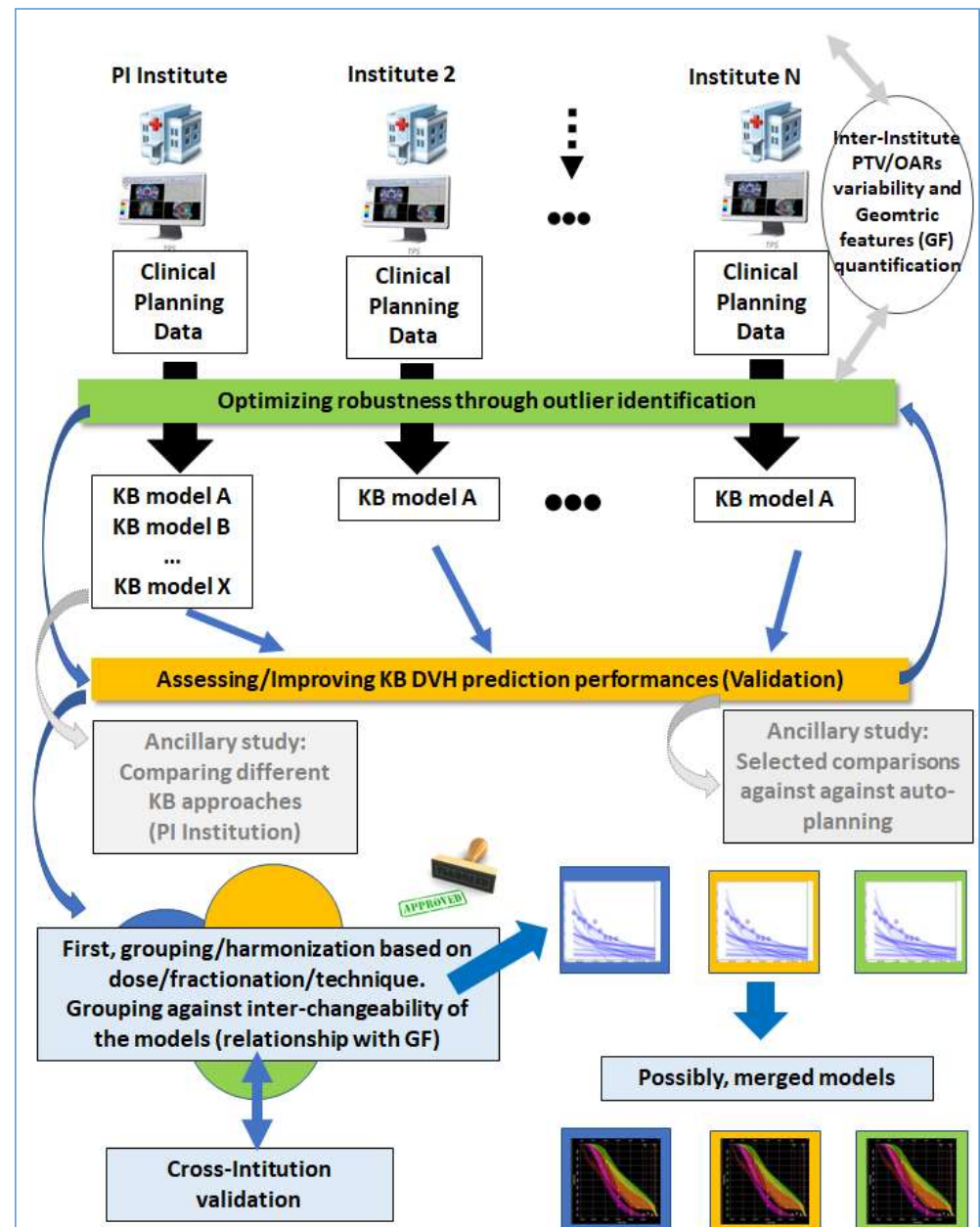
A 5-year national funded project

- 9 Institutes involved
- «Open Access» (to other Institutes*)
- AIFM official support
- Expected to generate «community tools» for plan QA, remote plan support, tutorial/education, technique selection, benchmarking (?),....



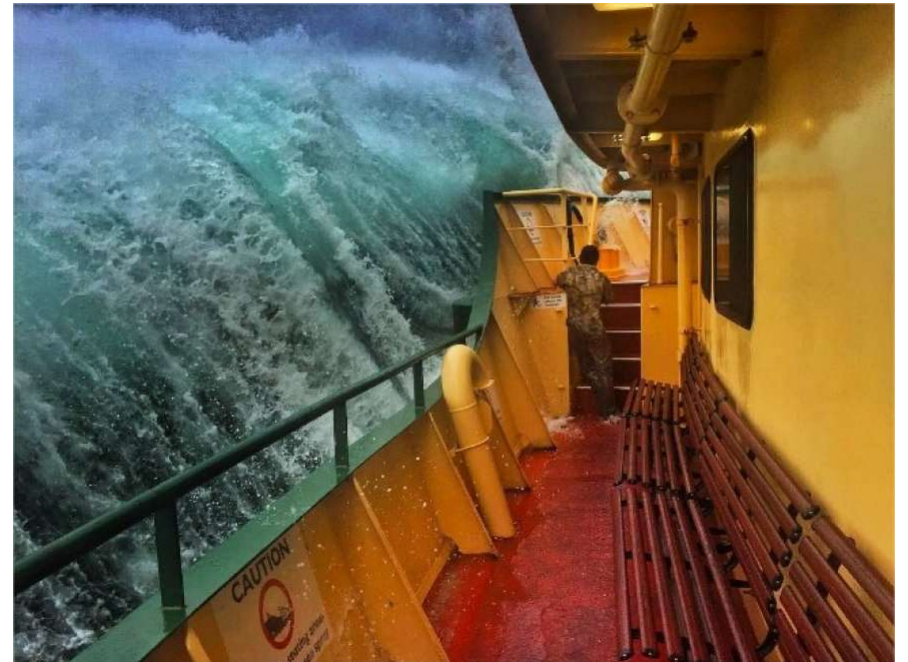
Improving the quality of Radiotherapy by multi-Institution Knowledge-Based planning optimization models
AIRC IG-23150

*contact: fiorino.claudio@hsr.it



Grazie

- R. Castriconi, P Esposito, A Tudda, S Broggi, P Mangili, L Perna, GM Cattaneo
- N Di Muzio, C Cozzarini, A Fodor (RT OSR)
- Gli amici di MIKAPOCo
- M Stasi (AIFM)
- E Lanzi & M Acerbi (Varian Italia)



*Un mare calmo non ha mai fatto un buon marinaio.
(Proverbio inglese)*

*Non esiste vento favorevole per il marinaio che non sa dove andare.
(Lucio Anneo Seneca)*