RECENT ADVANCES IN LINEAR ACCELERATORS

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MR LINEAR ACCELERATOR

- Magnetic Resonance Simulation (MR-Sim) is a diagnostic magnetic resonance imaging (MRI) platform that has been adapted to optimize radiotherapy treatment planning by making a hybrid of CT scan and MRI
- It allow for online real time MR imaging for high-precision adaptive radiotherapy.[2,3]
- The term used for it is MR guided radiotherapy [MRgRT]
- MR-linac systems offer real-time tumour tracking and beam gating.[4]
- The first MR-Sim was approved by Health Canada in 2010,[42] and the first MR-linac system was approved by Health Canada in 2017.[43]

- MR linac is a hybrid device with a linear accelerator to deliver radiotherapy and a MRI scanner[21] [somewhat like the CBCT acquisition in other linacs [22]]
- Combined use of MR Sim and MR Linac holds promise for better delineation and accturate delivery

- **MR-Sim is a diagnostic MRI like the CT sim that helps in contouring targets and OARs for radiotherapy planning.[1]**
- **MR Sim may or may not be used for planning purpose with a MR Linac**
- **MR CT coregistration for contouring can cause errors of 1-2mm[17] which can be minimized by using MR Sim instead of diagnostic MRI coregistration**
- **MR Sim has a MR only workflow for contouring and planning, the electron density for planning is less reliable in MRI though**
- **MR Sim has features like**
    - coil bridges to prevent deformation of the patient's body contour[6]
    - MRI compatible mobilization devices to minimize patient movement[13]
    - rigid flat table top[13]
    - laser positioning system[7]
    - wider bore[7]
    - patient imaged in treatment (as opposed to imaging) position[7]
    - dedicated scan protocols.[35,7]

- **Radiation with linear accelerator involves generating a radiation plan for a volume to account for target and OAR motion. There is no real time confirmation of the movement.20**
- **Its essential to have immobilization devices that permits placement of MRI coils close to the area to be scanned**
- **MR-linac uses fast dynamic MR sequences for tumour tracking and real-time motion monitoring.[11] MR guided Real-time adaptive radiotherapy, accounts for natural body movement to improve coverage and reduce OAR dose[20]**

Benefits from MR Linac

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- While MRI is superior in imaging of soft tissue [target and OAR]
- Has no burden of escalating radiation dose by multiple imaging
- **It will enable dose escalation**
- **It will enable margin reduction**
- **That will translate to higher cure rates and less toxicity for patients.[1]**
- **It may enable the assessment of response [by imaging] before or during the early phases of treatment which may be clinically useful,[41] for plan adaptation or changing treatment objective[35]**
- **A study examined and found no significant differences in mean lung density changes for patients who had lung stereotactic ablative radiotherapy using a MR-linac versus a linear accelerator delivery system. [25]**
- **Evidence from a study found that patients of pancreatic cancer treated with dose-escalated MR-linac demonstrated improved overall survival and freedom from local failure.[51] Stereotactic MRI-guided On-table Adaptive Radiation Therapy (SMART) study has been launched in 2019 for pancreatic cancer.**
- **Similar study for prostatic cancer, concluded that MR-linac was feasible and well-tolerated.[52]**
- **Multiple studies are ongoing for technical feasibility and assessment of outcomes for different sites using MRgRT**

COST CONCERNS WITH MR Linacs

- **Its anticipated that by the nextdecade it will be standard practice to use MR Linac [21,39]**
- **Concerns are** it comes along with longer time of image acquisition and higher cost of installation
- The equipement and installation cost ranges from 8.5-10 million dollars for the Elekta MR Linac Unity, 8-10 million dollars for ViewRay MRIdian
- It's a challenge to the value based system
- Other cost factors would be
  - Vault construction – lesser for MRIdian system due to 'split magnet' design
  - Additional staff – radiation oncologist, medical physicist, radiotherapy technician, medical radiotherapy technologist

SAFETY CONCERNS

- **There are safety issues related to the projectile capabilities of metallic objects in the strong magnetic field**
- **Its needed to screen patients for contraindications such as aneurysm clips, cardiac bypass surgery, some heart valves, embedded wires, stimulators, batteries, implanted electrodes, shunts, pumps, pacemakers, and some penile implants.[17]**
- **Even non magnetic metallic implants may cause artefacts in the MR images, such as signal loss, intense areas of signal accumulation, and distortion in areas near the implant.[35]**
- **The loud knocking noise can be a deterrant and need ear protection and can cause peripheral nerve stimulation**
- **The thermal effects of radiofrequency used can cause heating of the body**

TECHNICAL CHALLENGES IN IMPLEMENTATION

- **Assessment and resolution of technical factors regarding electron density assessment, contour generation, planning, verification and adaptation**
- **Newer quality assurance needing training of physicist**
- **Training for RTT as MR is new for them**
- **Selection of people for the work and conducting training will be a pre-requisite**
- **Areas of MRgRT-related focused training include:**[40,63]
    - New treatment planning systems
    - MR safety, patient screening
    - MR-based anatomy — image assessment on MRI versus cone beam CT versus CT
    - MR image quality, formation, scan optimization and interpretation
    - Multimodality image registration
    - Contour/modify organs at risk for adaptive radiotherapy
    - Adaptive radiotherapy strategies and methodologies
    - Novel radiotherapy delivery techniques
    - Daily/weekly quality assurance and quality control requirements.

MR Linac configurations

- MR Linacs can have either fixed perpendicular or parallel beam field or both

Table 1: Different Types of MR-linac Configurations[3,27,40]

MR-linac System	Radiation	Magnetic Field Configuration	Magnetic Field Orientation	Tesla Strength	Bore Size (cm)	Rotating Couch/Gantry
ViewRay MRIdian	Cobalt-60	split superconducting	Perpendicular	0.35 T	70 Closed	Rotating gantry
ViewRay MRIdian Linac	6 MV	split superconducting Perpendicular 0.35 T	Perpendicular	0.35 T	70 Closed	Rotating gantry
MagnetTx Aurora RT	6 MV	superconducting rotating	Parallel	0.5 T	110 Open	Rotating gantry
Australian MRI Linac	6 MV	superconducting open bore	Parallel/ Perpendicular	1.0 T	82 Open	Rotating couch
Elekta Unity	7 MV	superconducting close bore	Perpendicular	1.5 T	70 Closed	Rotating gantry
MRgRT Suite	6 MV, Ir-92	MR on rails	NA	1.5 T	70	Rotating

MR = magnetic resonance; MRgRT = magnetic resonance guided radiotherapy; MV = megaelectronvolt; NA = not applicable; RT = radiotherapy; T= tesla.

There are several MR-linac systems available:

- Elekta Unity that incorporates a Philips 1.5 Tesla MRI and a 7.5 megavolt (MV) (acceleration rate) linear accelerator,[73]
- MRIdian by ViewRay that integrates a 0.35 Tesla magnet with a 6 MV Linac,[74]
- The rail-mounted MRgRT Suite.[40]
- Aurora RT radiotherapy system from MagnetTx, combines a 6 MV linear accelerator and a 0.5 Tesla MRI magnet, and has a non-clinical working prototype.[75]

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- the international MR-linac Consortium established in 2012
- It published its study MOMENTUM (Multiple Outcome Evaluation of Radiotherapy Using the MR-linac) in 2019 [54]
- has selected tumour sites for which MRgRT will initially be used, though later it might be expanded to all sites.[31]
  - Brain
  - Breast
  - Cervix
  - Esophagus
  - Lung
  - Oropharynx
  - Pancreas
  - Prostate
  - rectum

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Review Article

Technical design and concept of a 0.35 T MR-Linac

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ABSTRACT

The integration of magnetic resonance (MR) imaging and linear accelerators into hybrid treatment systems has made MR-guided radiation therapy a clinical reality. This work summarizes the technical design of a 0.35 T MR-Linac and corresponding clinical concepts. The system facilitates 3D-conformal as well as IMRT treatments with 6MV photons. Daily MR imaging provides superior soft-tissue contrast for patient setup and also enables on-table adaption of treatment plans, which is fully integrated into the treatment workflow of the system. Automated beam gating during delivery is facilitated by cine MR imaging and structure tracking. Combining different novel features compared to conventional image-guided radiotherapy, this technology offers the potential for margin reduction as well as dose escalation.

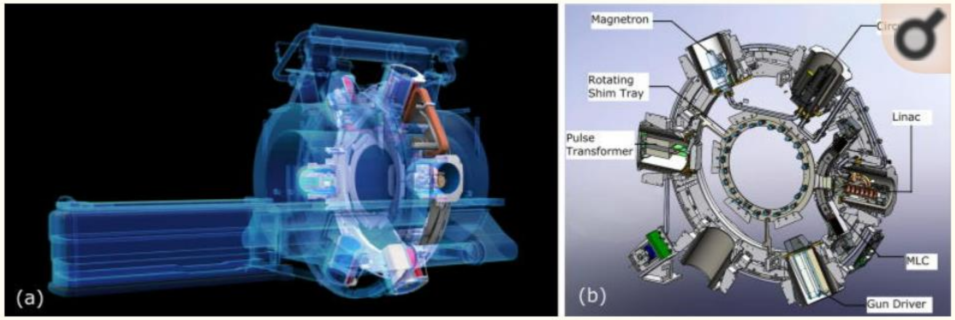

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Fig. 2

(a) Schematic drawing of the system depicting the main hardware components: superconducting double-donut magnet, circular radiation gantry and patient couch; (b) schematic drawing of the radiation gantry with linac components and MLC. Images courtesy of ViewRay Inc.

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Original Article

ESTRO-ACROP recommendations on the clinical implementation (hybrid MR-linac systems in radiation oncology

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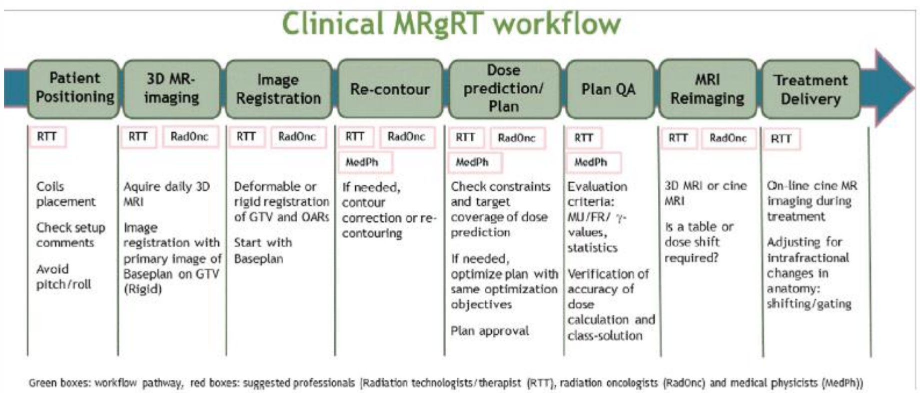

Fig. 2. Exemplar oMRgRT workflow.

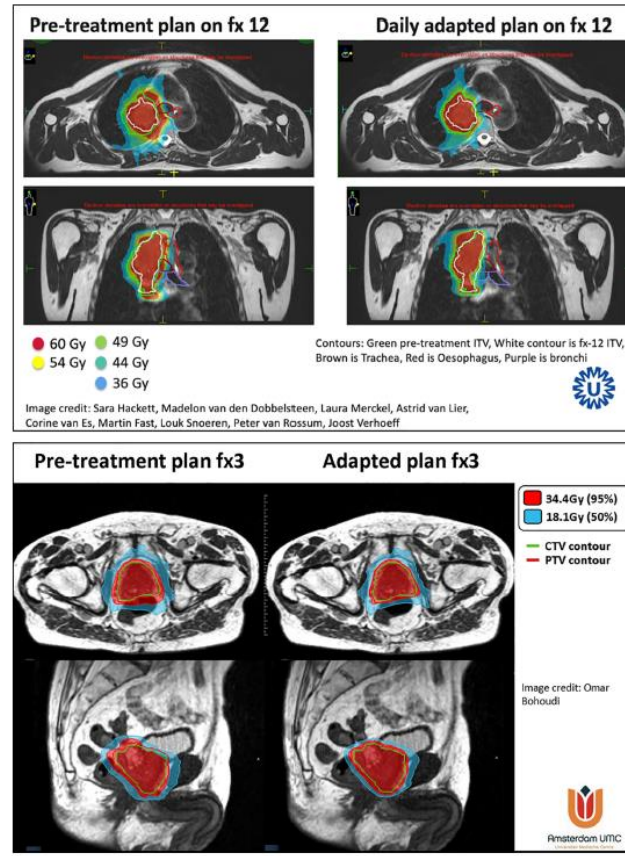

Fig. 3. Exemplar daily plan adaptation. (A): full re-optimization for a lung cancer patient on treatment fraction 12 to fulfill constraints of organs at risk. (B) full re-optimization for a prostate patient on treatment fraction 3 to fulfill constraints of organs at risk.

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The Patient Experience of the MR-Linac

Amber Robinson • Mikki Campbell • Darby Erler

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ONGOING TRIALS

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- UMBRELLA-II

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The MR-Linac Technical Feasibility Protocol (UMBRELLA-II)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Know the risks and potential benefits of clinical studies and talk to your health care provider before participating. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT04351204

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See **Contacts and Locations**

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MR-Linac Radiotherapy in Year One: Experience's in Imaging, Patient Treatment and Data Collection

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Purpose/Objective(s): To present our institutions initial clinical experience with a high field MR-Linac with regards to patients treated, data collected, functional imaging performed and general performance of the machine.

Materials/Methods: From Aug 15, 2019 to Feb 7, 2020, thirty-three patients were treated on our 1.5 T MR-Linac with all patients enrolled in the MOMENTUM study (ClinicalTrials.gov, identifier: NCT04075305). Two types of workflows were used: one accounting for daily patient shifts only (adapt to position or ATP) and the other involving online plan adaptation through re-contouring and re-optimization based on daily MRI images (adapt to shape or ATS). Of the thirty-three patients, thirty were CNS brain patients (15 GBM and 15 other) treated using ATP and three were prostate cancer patients treated using ATS and SBRT to a dose of 40 Gy in 5 fractions. Imaging involved T_1 (brain ATP) or T_2 (prostate ATS) weighted scans captured online for registration/planning. Functional imaging sequences for brain ATP (DWI, MT, BOLD, CEST) were taken before, during and post irradiation in addition to T_2-FLAIR. DWI was done for the prostate cases before, during and post irradiation. Timing was recorded for the various stages of the workflows. Machine performance was characterized in terms of unscheduled downtime events.

Results: A total of 540 fractions were delivered on the MR-Linac over its initial 25 weeks of use. The average session time (n = 200 fractions) for the brain ATP workflow (excluding post imaging) was 26.9 minutes (3.7 min setup, 5.5 min pre-tx imaging, 5.1 min image registration, 4.5 min plan optimization, 2.0 min physics QA, and 6.1 min beam on). The minimum session time was 24 minutes for the brain ATP. The average session time for the prostate ATS workflow (n = 10 fractions) was 47.7 minutes (6.6 min setup, 3.2 min pre-tx imaging, 3.5 min image registration, 15.1 min contouring, 5.6 min plan optimization, 1.5 min physics QA, 2.9 min verification imaging and 9.3 min beam on). Additional post beam research scans took, on average, 12.5 minutes for the prostate cases. The following multi-parametric imaging maps were generated for

the brain patients: T_1 and T_2, ADC, T_2-FLAIR, CEST asymmetry and Amide MTR. The brain T_2-FLAIR signal, in some cases, reduced over the treatment course. Changes in ADC maps were observed for both brain and prostate over the treatment. In some instances, brain re-planning was done offline based on daily online T_2-FLAIR imaging. In terms of downtime, patients were transferred to a standard Linac for 7.1 % of fractions due to either a magnetron change, modulator tank replacement, or a cooling issue.

Conclusion: An MR-Linac program has been implemented at our institution involving a multi-disciplinary group with both machine data and patient data being captured. The current status, clinical and technical considerations, and most recent image-based findings will be presented.

Author Disclosure: **B.M. Keller**: None. **M. Campbell**: None. **M.E. Ruschin**: None. **A. Kim**: None. **C. McCann**: None. **A. Lau**: None. **H. Soliman**: None. **D. Vesprini**: None. **J. Detsky**: None. **C. Tseng**: None. **A. Sahgal**: International Society of Stereotactic Radiosurgery, AO Spine.

correlated with decreased FCDs in pain perception and modulation in TN patients.

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Impact of Pelvic Intensity-modulated Radiotherapy (IMRT) on Lymph Node Coverage and Dose to Critical Organs, Compare to Three-Dimensional Conformal Radiation Therapy (3D-CRT), in Localized High-Risk Prostate Cancer

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- *IJROBP, poster Q&A session, 2020*

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Online Adaptive Radiation Therapy: Implementation of a New Process of Care

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Original Article

Validation of an MR-guided online adaptive radiotherapy (MRgoAR program: Deformation accuracy in a heterogeneous, deformable, anthropomorphic phantom

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ABSTRACT

Background and purpose: To investigate deformable image registration (D
accumulation accuracy of a clinical MR-guided online adaptive radiotherap
ing clinically-based magnitudes of abdominal deformation vector fields (D
Materials and methods: A heterogeneous anthropomorphic multi-modality
tom was comprised of MR and CT anatomically-relevant materials. Th
(TLDs) were affixed within regions of interest (ROIs). CT and MR simulat
was deformed to MR for dose calculations. MRgoART was executed on a M
fractions. Before each fraction, a deformation was applied. Ground truth
TLD position, and TLD dose measured by an accredited dosimetry calibr
the range of applied deformations, phantom DVFs were compared to
MRgoART fractions. MR-MR deformation accuracy was quantified throu
(DSC), Hausdorff distance (HD), mean distance-to-agreement (MDA),
(MAE) for CT-MR-MR deformation. Arithmetic-summation of calculated do
and deform-accumulated dose (MIM) was compared to TLD measured dose
mation statistics were quantified for MRIdian and MIM.
Results: Mean phantom DVFs were 5.0 ± 2.9 mm compared to mean DVF of
5.2 ± 3.0 mm. Respective mean DSC, HD, MDA was 0.93 ± 0.03, 0.74 ± 0.80 c
and 0.93 ± 0.03, 0.54 ± 0.27 cm, 0.08 ± 0.03 cm for MIM (N = 80 ROIs). Mean
mean and median dose differences were 0.3%, −0.3% for arithmetic-su
deformed-accumulation. Maximum differences were 0.21 Gy (arith
(deformed-accumulation).
Conclusions: MRgoART deformation and dosimetric accuracy has been ben
DVFs of 5 mm in a multiple-rigid-body deformable phantom. Deformatio
criteria and clinically acceptable end-to-end MRgoART dosimetric agreeme
tom. Further efforts are needed in validation of deform-accumulated dose.
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Clinical implementation of artificial intelligence-driven cone-beam computed tomography-guided online adaptive radiotherapy in the pelvic region

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ABSTRACT

Background and purpose: Studies have demonstrated the potential of online adaptive radiotherapy (oART). However, routine use has been limited due to resource demanding solutions. This study reports on experiences with oART in the pelvic region using a novel cone-beam computed tomography (CBCT)-based, artificial intelligence (AI)-driven solution.

Material and methods: Automated pre-treatment planning for thirty-nine pelvic cases (bladder, rectum, anal, and prostate), and one hundred oART simulations were conducted in a pre-clinical release of Ethos (Varian Medical Systems, Palo Alto, CA). Plan quality, AI-segmentation accuracy, oART feasibility and an integrated calculation-based quality assurance solution were evaluated. Experiences from the first five clinical oART patients (three bladder, one rectum and one sarcoma) are reported.

Results: Auto-generated pre-treatment plans demonstrated similar planning target volume (PTV) coverage and organs at risk doses, compared to institution reference. More than 75% of AI-segmentations during simulated oART required none or minor editing and the adapted plan was superior in 88% of cases. Limitations in AI-segmentation correlated to cases where AI model training was lacking. The five first treated patients complied well with the median adaptive procedure duration of 17.6 min (from CBCT acceptance to treatment delivery start). The treated bladder patients demonstrated a 42% median primary PTV reduction, indicating a 24%-30% reduction in V_{45Gy} to the bowel cavity, compared to non-ART.

ONLINE ADAPTIVE RADIOTHERAPY

MEDICAL PHYSICS INTERNATIONAL Journal, vol.8, No.2, 2020

MAKING ON-LINE ADAPTIVE RADIOTHERAPY POSSIBLE USING ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING FOR EFFICIENT DAILY RE-PLANNING

Yves Archambault, Christopher Boylan, Drew Bullock, Tomasz Morgas, Jarkko Peltola, Emmi Ruokokoski, Angelo Genghi, Benjamin Haas, Pauli Suhonen, and Stephen Thompson

Varian Medical Systems, Inc. Palo Alto, California USA; Baden, Switzerland; and Helsinki, Finland

Abstract— **Adaptive therapy involves the ability to alter a radiotherapy treatment plan based on tumor and anatomical changes over a course of therapy. The goal is to better target the tumor, reduce dose to healthy tissue and potentially improve overall outcomes. To date, achieving this has typically required time-consuming re-planning between treatment sessions or monopolizing a linac for an extended period while a patient waits on the treatment couch for new plans to be generated. Neither of these alternatives has been deemed practical or affordable at scale, as very often clinics don't have the resources even if they have the tools.**

Consequently, Varian Medical Systems developed Ethos™ therapy, a radiotherapy treatment system that uses artificial intelligence (AI) and machine learning to accomplish adaptive radiotherapy. In this paper, we describe the technology that underlies the adaptive capabilities of the system.

Keywords— **Adaptive radiotherapy, artificial intelligence, machine learning, Ethos, RapidPlan, treatment planning, neural networks, .**

Additionally, plan generation in existing commercialized systems typically requires moderately complex user interactions which distract the focus during the on-couch session.

The Ethos system was designed to address these challenges. In this paper, we take a deeper look at the technologies within the Ethos system that address these challenges.

VIII. ON-COUCH ADAPTIVE THERAPY WORKFLOW

The challenges involved in delivering on-couch adaptive therapy are addressed, in the Ethos system, through a re-planning workflow that has been reduced to well-defined and predictable clinical decision points in order to lower the cognitive load of the clinician.

Figure 1 (p. 3) illustrates the on-couch adaptive work-

The challenges involved in delivering on-couch adaptive therapy are addressed, in the Ethos system,through a replanning workflow that has been reduced to well-defined and predictable clinical decision points in order to lower the cognitive load of the clinician.

FOUR Decision points

- Accepting the image
- Assessing and modifying the ‘influencer’ structures or OARs
- Assessing and modifying the target organs – creating the session model
- Selecting the plan – scheduled or adapted

FOUR Decision points

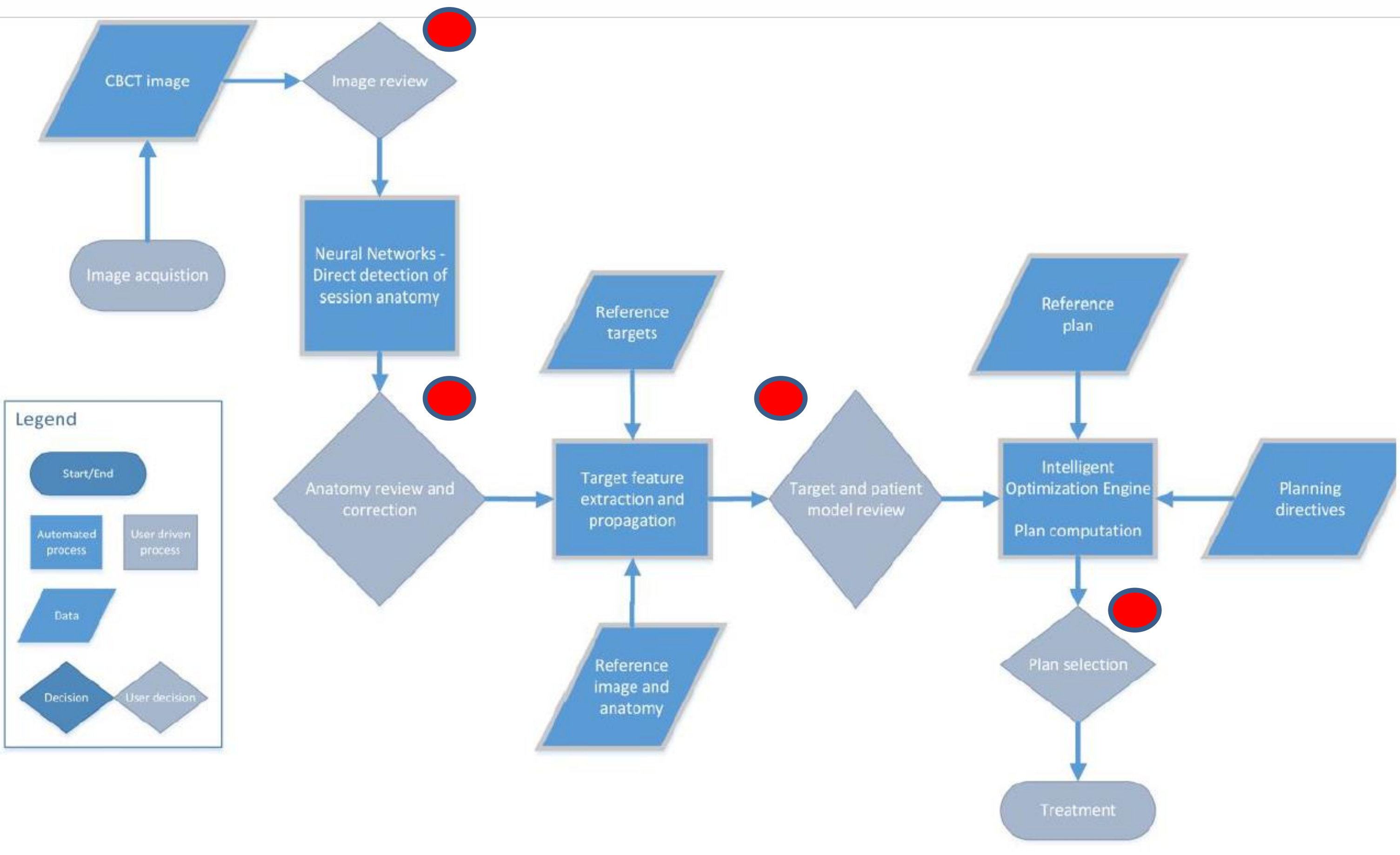

Fig. 1: Ethos therapy on-couch adaptive workflow

- Deep learning convolutional neural network [CNN] and hyperparameters in these models are used
- Uses the acquired 3D iCBCT as input to the neural network and gives a similar output that the clinician can assess and accept

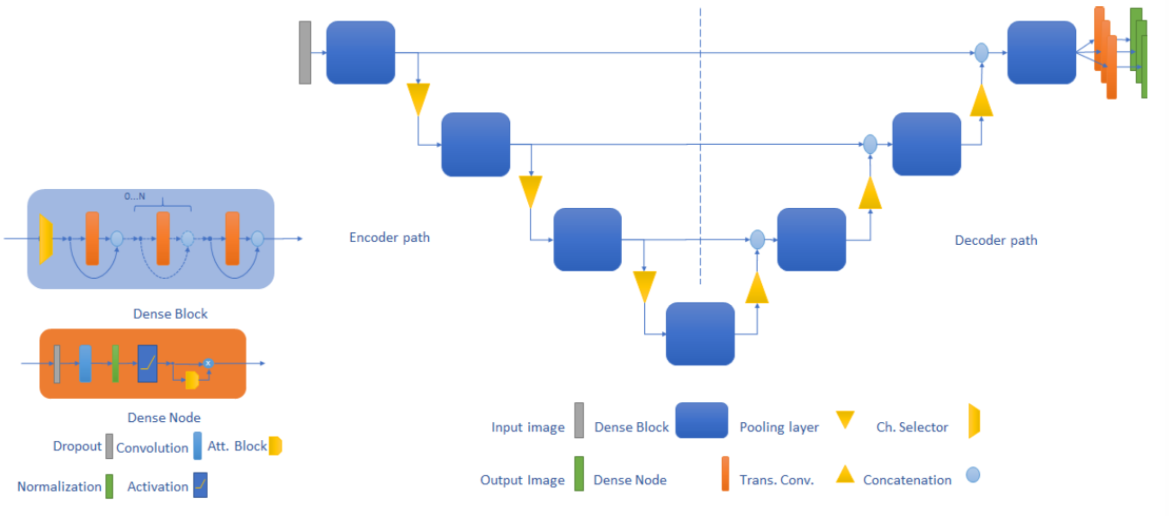

Fig. 2: An example of Varian's deep convolution neural network architecture.

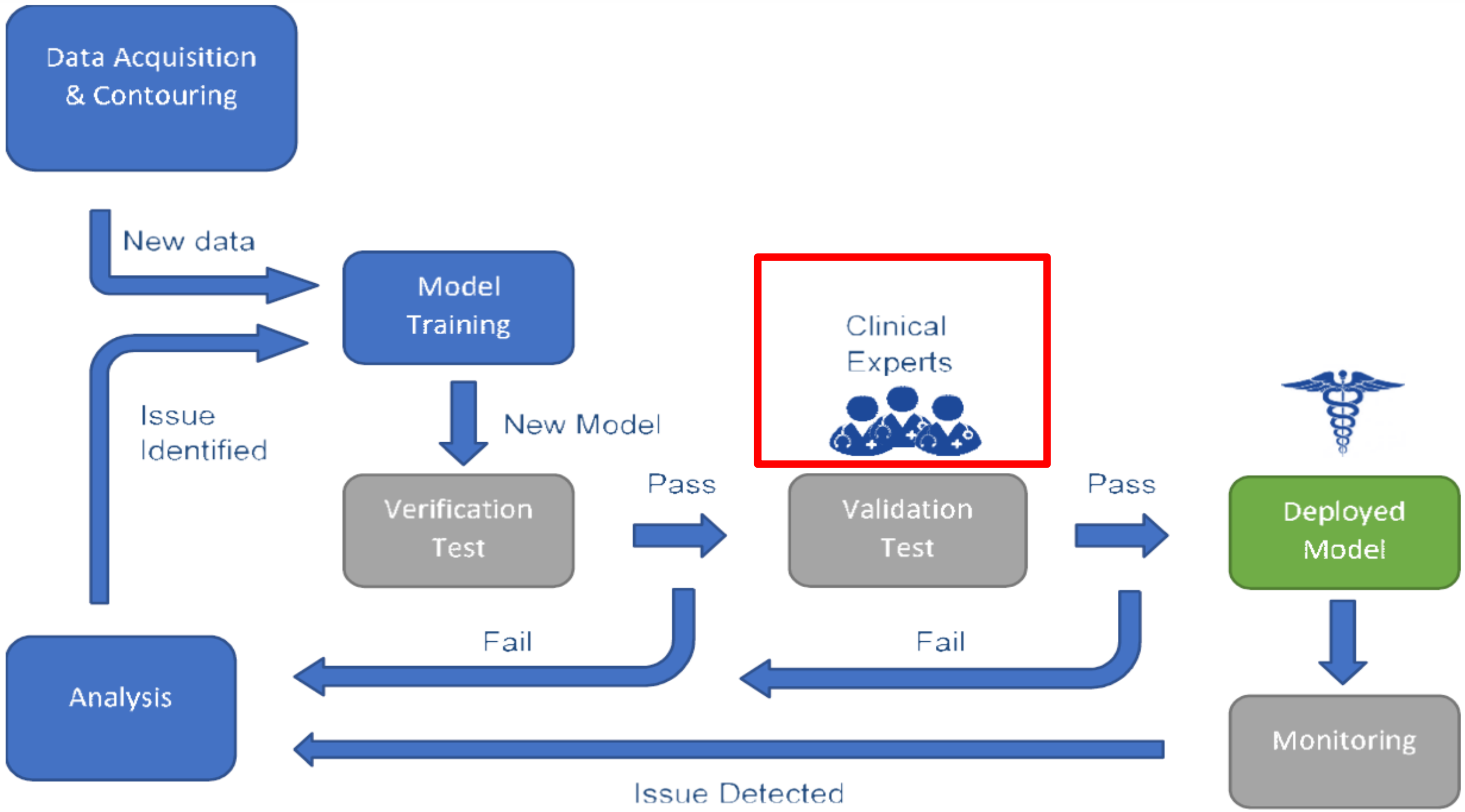

Fig. 3: Machine learning model production process

- Once image is approved, deformable registration is used by the system to make an image sCBCT that conforms with the CBCT
- Then the IOE (Intelligent optimization engine) generated IMRT/VMAT plans with high degree of dose conformity and OAR doses, and an intelligent trade off clinically
- The IOE works by having Q-functions [quality functions] laid down before hand for the planning purpose
  - Target upper dose [TUD] goal
  - Target lower dose [TUD] goal
  - Organ upper dose [OUD] goal

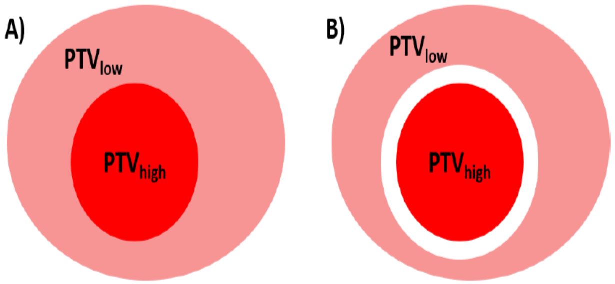

Fig 4. Conflict from multiple overlapping targets. **A)** High dose target (PTV_{high}) overlapping with lower dose target (PTV_{low}). **B)** User specifies a goal for maximum dose in PTV_{low} which is in direct conflict with the minimum dose goal for PTV_{high}. The system crops the PTV_{low} from PTV_{high} (with some margin for dosimetric fall-off) and then applies a maximum dose objective which follows the needed form for the PO algorithm (created from the input maximum dose goal) to the remainder of PTV_{low}.

- It works by making physics volumes, reiterations, more control functions

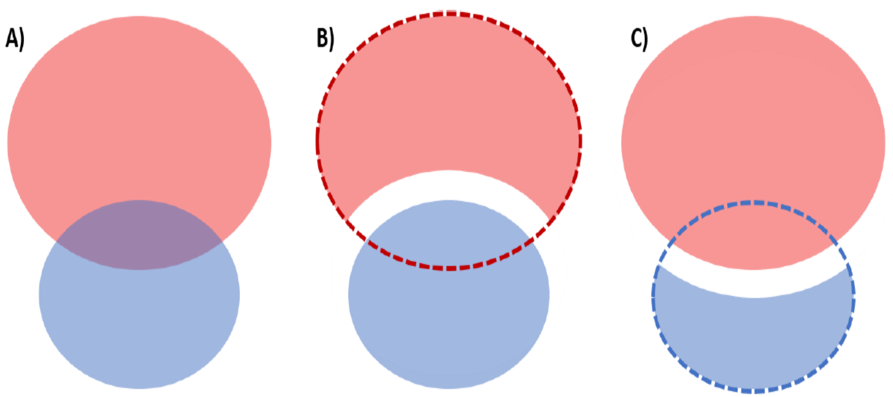

Fig 5. Conflict from organ (blue) overlapping with target (red). **A)** Target in shaded red with overlapping organ in shaded blue. **B)** Organ goal has higher priority than target goal: the target is cropped with the organ including a margin for dosimetric falloff. **C)** Target goal exists with higher priority than organ goal: the oar is cropped with the target, again with a margin for dosimetric falloff. The dashed lines show the unmodified structure outline.

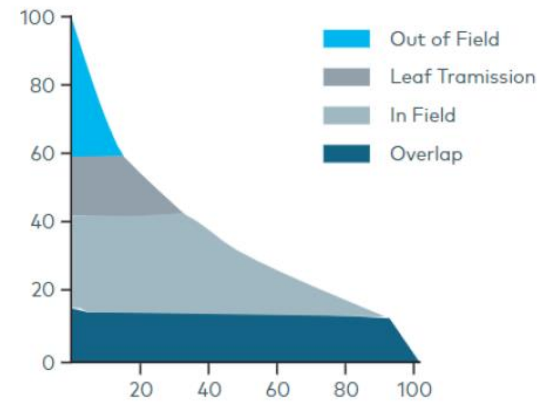

Fig 8. Organ volume partitions used in the machine learning DVH models. Each partition contributes to the sum total DVH as shown.

Decision-making guided by AI

The goal of Ethos therapy was to design a simple adaptive therapy workflow for both the initial planning and daily re-planning sessions.

During initial planning, Ethos therapy automatically produces several plan candidates with various beam geometries and techniques using prioritized target and organ at risk goals from the physician's intent. The clinician chooses the most suitable plan and authorizes it for delivery. This step provides confidence that the goals and patient geometry are compatible, and that plan automation can be performed each day. Each treatment day, once the daily anatomy is reviewed and accepted, Ethos therapy will prepare a new adapted plan using the beam geometry of the initial plan, the initial set of target and organ and risk goals, and give the clinician the choice of either the original or adapted plan for delivery.

The process is guided by the technology, as follows:

- A decision tree guides the entire adaptive therapy process
- Treatment management and treatment planning applications are tightly coupled and context-aware
- Clinician approvals move the process from one step to the next
- Every step of the workflow is optimized for speed and engineered for safety

Automated dose accumulation

Each day, the Ethos therapy system automatically reconstructs delivered dose in relation to today's anatomy. This capability:

- Demonstrates that the patient is receiving the intended dose
- Improves understanding of the treatment progress
- Helps identify when re-simulation may be required
- Simplifies off-line adaption

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Online adaptive radiotherapy compared to plan selection for rectal cancer: quantifying the benefit

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Abstract

Background: To compare online adaptive radiation therapy (ART) to a clinically implemented plan selection strategy (PS) with respect to dose to the organs at risk (OAR) for rectal cancer.

Methods: The first 20 patients treated with PS between May–September 2016 were included. This resulted in 10 short (SCRT) and 10 long (LCRT) course radiotherapy treatment schedules with a total of 300 Conebeam CT scans (CBCT). New dual arc VMAT plans were generated using auto-planning for both the online ART and PS strategy. For each fraction bowel bag, bladder and mesorectum were delineated on daily Conebeam CTs. The dose distribution planned was used to calculate daily DVHs. Coverage of the CTV was calculated, as defined by the dose received by 99% of the CTV volume (D99%). The volume of normal tissue irradiated with 95% of the prescribed fraction dose was calculated by calculating the volume receiving 95% of the prescribed fraction or more dose minus the volume of the CTV. For each fraction the difference between the plan selection and online adaptive strategy of each DVH parameter was calculated, as well as the average difference per patient.

Results: Target coverage remained the same for online ART. The median volume of the normal tissue irradiated with 95% of the prescribed dose dropped from 642 cm3 (PS) to 237 cm3 (online-ART)($p < 0.001$). Online ART reduced dose to the OARs for all tested dose levels for SCRT and LCRT ($p < 0.001$). For V15Gy of the bowel bag the median difference over all fractions of all patients was – 126 cm^3 in LCRT, while the average difference per patient ranged from – 206 cm^3 to – 40 cm^3. For SCRT the median difference was – 62 cm^3, while the range of the average difference per patient was – 105 cm3 to – 51 cm^3.
For V15Gy of the bladder the median difference over all fractions of all patients was 26% in LCRT, while the average difference per patient ranged from – 34 to 12%. For SCRT the median difference of V95% was – 8%, while the range of the average difference per patient was – 29 to 0%.

Conclusions: Online ART for rectal cancer reduces dose the OARs significantly compared to a clinically implemented plan selection strategy, without compromising target coverage.

Trial registration: Medical Research Involving Human Subjects Act (WMO) does not apply to this study and was retrospectively approved by the Medical Ethics review Committee of the Academic Medical Center (W19_357 # 19.420; Amsterdam University Medical Centers, Location Academic Medical Center, Amsterdam, The Netherlands).