ADAPTIVE INTELLIGENCE™ CONSORTIUM
Individual Disease Site White Paper

Disease site: Rectum

Ethos version: Ethos Treatment Management 2.0 (Version 02.00.10) & Ethos Treatment Planning 1.0 (Version 01.00.10)

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Introduction

Colorectal cancer is currently the third most common cancer worldwide and second most common cause of cancer death. Approximately one-third of colorectal cancer occurs in the rectum. Rectal cancer occurs in the region of bowel below the peritoneal reflection, including approximately 12 cm of intestine above the anal verge [1].

Although surgery remains the cornerstone of treatment in rectal cancer, there is a high incidence of local recurrence and metastases in patients with locally advanced stages of rectal cancer. The risk of local recurrence is related to the extent of radial surgical clearance, which is determined by the Tumor and Nodal stages and surgical technique. It has been documented that tumor which has extended into peri-rectal fat (T3) carries a high risk of local recurrence [2-4].

Local control is essential as symptoms arising from local recurrence are severely debilitating, with symptoms including pelvic pain, rectal bleeding, rectal discharge, bowel obstruction, sciatica and neurogenic bladder. Local recurrence is usually in the presacral space outside the rectal wall. Salvage treatment with surgery, radiotherapy or chemotherapy is seldom successful.

Short course pre-operative radiotherapy, long course pre-operative chemo-radiotherapy and more recently Total Neoadjuvant Therapy (TNT) are accepted management pathways for patients with locally advanced rectal adenocarcinoma to improve disease control [5].

Technology advancement in radiotherapy has seen an evolution from 3D conformal radiation therapy (3DCRT) to intensity modulated radiation therapy (IMRT). The use of IMRT has enabled differential dose prescriptions to be delivered in a single phase of treatment and dose distributions which conform to delineated target volumes. Interfraction anatomical changes e.g. bladder volume, have an impact on the anterior border of the mesorectum, which is used to define the clinical target volume (CTV) [6]. A margin-based internal target volume (ITV) is often employed to compensate for such interfraction changes, which may not encompass all anatomical changes, exposing the potential for under-dosing of target volumes, or expose surrounding organs at risk (OAR) to higher than planned doses [7].
The Ethos online adaptive radiotherapy (ART) system leverages use of auto-segmentation, deformable registration, automatic optimization and planning, unlocking the potential to correct and account for interfraction anatomical changes that impact tumor targeting and normal tissue sparing. The purpose of this document is to aid implementation of online ART for rectum patients.

Initial Planning

Patient cohort demographics and description

Inclusion/exclusion criteria

All rectal cancer cases are discussed at a multidisciplinary tumor board and the decision to recommend pre-operative radiation is based on consensus at the meeting. As a general principle, the inclusion/exclusion criteria are recommended to follow international consensus guidelines [5, 6] and/or Australian eviQ guidelines [7].

a. Inclusion
    i. Tumor types: Rectal Adenocarcinoma
    ii. Tumor & clinical staging:
        i. Pre-operative: lower edge of tumor <12 cm of anal verge or below peritoneal reflection, stage T3-4 with threated mesorectal fascial (MRF) margin, node positivity close to MRF or pelvic side wall nodal involvement not in standard mesorectal excision
        ii. Post-operative: patients who have undergone total or partial mesorectal excision for stage T3-4, N1-3, close circumferential surgical margin in lower tumors, disrupted or incomplete mesorectal excision (rarely recommended)
        iii. Pre-operative therapy in an attempt to obtain organ preservation (i.e. avoid an abdomino-perineal resection especially). If complete response, can be entered onto a watch and wait protocol [8].
    iii. Performance status: ECOG 0-2
    iv. Medically fit to undergo both radiotherapy and chemotherapy
b. Cautions
    i. Non-rheumatoid collagen vascular disease/scleroderma
    ii. Inflammatory bowel disease and/or history of adhesions/bowel obstruction
c. Exclusions
    i. Prior high dose radiation therapy to the lower pelvis
    ii. Pregnancy

Treatment management and intent

Treatment management informed through patient work up, including diagnostic imaging, tumor staging and multi-disciplinary decisions to determine if surgery will occur prior or post chemo-radiotherapy. The overall treatment intent is radical. Post-operative patients are managed with long course chemo-radiotherapy, while pre-operative patients are managed with short course radiotherapy or long course chemo-radiotherapy with or without neoadjuvant chemotherapy.

a. Long course radiotherapy prescription: 50-45 Gy/25 fractions
    i. An elective boost to un-resectable gross nodal disease is considered: 54 Gy/25 fractions
b. Short course radiotherapy prescription: 25 Gy/5 fractions

Characteristics of patients more likely to benefit from ART

In principle, it is expected that all patients may benefit from application of ART to the treatment design. There may be selected patients who receive greater benefit, and this group of patients may be prioritized. The individual institution should evaluate their cohort of patients to consider those who may receive greater benefit from application of ART. Considerations for rectal adenocarcinoma patients include;

a. Patients with bladder preparation and/or compliance issues
b. Patients with a partial mesorectal excision, resulting in a key target area which is subject to differences in position and shape with changes in bladder volume on the inter-fraction timescale
c. Patients prescribed with an integrated boost to gross nodal disease, where application of an IGRT workflow may result in a compromised online image match due to interfraction target geometry variation

Supporting imaging

Multi-modality imaging can be used to aid delineation of target volumes for initial planning. The utility of supporting imaging is limited by the image registration accuracy. The pertinent supporting imaging for this patient cohort includes;

a. MRI: mandatory for rectal cancer patients. The superior soft tissue contrast can be used to help define regions not so clearly identified on CT imaging as a result of lower contrast resolution.
b. PET/CT (optional): where known or potential regional or distant disease is present, PET avidity is assessed and compared to features on planning CT images for consideration and inclusion in target volumes.

Recommended template used to capture physician's intent with target dose and OAR constraints

The development of treatment planning templates is an important component to successful implementation of online adaptive radiotherapy within the Ethos platform. The template design should conform to the physician's intent (i.e. radiotherapy prescription to target volumes) and at a minimum include target coverage and organ at risk (OAR) metrics as per local protocol, radiation oncologist preference, relevant published guidelines and/or clinical trials.
The Intelligent Optimization Engine (IOE) used for plan optimization requires clinical objectives to be ordered in clinical priority and importance. This ordered approach is driven by the sequential nature of plan optimization and associated structure cropping logic in management of overlapping structures. This plan optimization approach requires clinicians to expand their clinical objectives to effectively increase the instruction given to the auto-planning algorithm across a greater number of dose and volume points in the dose volume histogram (DVH) space in an effort to maximize plan quality. Furthermore, it is important to consider and evaluate the robustness of any developed treatment planning template across the typical inter- and intra-patient variations. While adjustments can be made to the planning template from patient to patient, any authorized RT intent for a given patient sets the planning instruction for each adaptive treatment session. An additional consideration is how a template interacts with the adaptive plan generation process on treatment i.e. any contour that may require editing and/or review require both a planning objective and also must be included in priority 1 or 2 in the planning template.
The template development process for rectum Ethos adaptive planning followed the above mentioned logic, comparing plan quality and dose distributions produced from each Ethos template to our local comparator/gold standard, which for the purposes for developing an Ethos planning template was Eclipse based planning, driven through use of RapidPlan DVH estimates. The template development is an iterative and time consuming process, however is key and fundamental to the success of Ethos planning for the online adaptive workflow.
The key learning outcomes from the abovementioned template development include;

a. Multiple templates may be required for patient subgroups e.g. elective nodal boost

b. Additional low dose clinical goals may need to supplement existing rectum treatment planning guidelines for OARs e.g. bladder & small bowel
c. Additional hot spot control clinical goals may need to be defined to improve dose conformity and reduce the volume outside each target/prescription volume

An example planning template and dose preview order is outlined in Table 1 below.

Table 1: Example rectum planning template used for Ethos planning, including plan preview ordering of priorities.

Priority 1 – Most Important	
Structure	*Planning Goal*
GTV	$V100\% \geq 100\%$
GTV LN	$V100\% \geq 100\%$
Small Bowel	$D0.1\ cm^3 \leq 51.0\ Gy$
CTV HD	$V100\% \geq 98\%$
CTV LD	$V100\% \geq 98\%$
Small Bowel	$D100.0\ cm^3 \leq 40.0\ Gy$
PTV VHD	$V100\% \geq 95\%$
PTV HD	$V100\% \geq 95\%$
PTV HD	$D0.5\ cm^3 \leq 105\%$
PTV LD	$V100\% \geq 95\%$
PTV LD	$D0.5\ cm^3 \leq 105\%$
Priority 2 – Very Important	
Structure	*Planning Goal*
PTV VHD	$D0.5\ cm^3 \leq 105\%$
Bladder	$V50.0\ Gy \leq 10\%$
Bladder	$V40.0\ Gy \leq 25\%$
External Genitalia	$V20.0\ Gy \leq 10\%$
Priority 3 - Important	
Structure	*Planning Goal*
Femoral head and necks	$V30.0\ Gy \leq 15\%$
Small Bowel – PTV	$V15.0\ Gy \leq 65\%$
Small Bowel – PTV	$V21.0\ Gy \leq 30\%$
Bladder	$V15.0\ Gy \leq 66\%$

GTV = Gross Target Volume, CTV = Clinical Target Volume, PTV = Planning Target Volume
LN = Lymph Node, VHD = Very High Dose, HD = High Dose, LD = Low Dose
Individual institution priorities may result in changes to goals and order of priorities

RapidPlan DVH estimation in Ethos planning

RapidPlan was evaluated using the existing implementation used at NSCC within the Eclipse treatment planning environment. The RapidPlan models used at NSCC are based on the use of cropped target volume structures e.g. PTV subtracts out any inner CTV and GTV. This was a noted difference between the design of IOE and the inherent cropping logic applied.
It was expected that inclusion of RapidPlan may not impact target coverage, but may benefit OAR dose using the basis that RapidPlan operates on a line objective across all dose and volume points.

Initial observation from application of DVH estimates showed no improvement to target coverage or OAR sparing.

RapidPlan was considered a template development aid/tool, although the full potential of RapidPlan hasn't been evaluated in this work. Clinical consensus guidelines and protocols commonly include higher-dose OAR objectives and therefore are more reliant on normal tissue objective (NTO) approaches, such as that employed within the IOE. The template development process has highlighted that additional clinical objectives along the DVH may assist optimization of plan quality. Review of existing RapidPlan models or current planning methods enable the user to understand these additional metrics.

Planning CT simulation

Patient preparation

It is important to review the patient preparation from CT simulation to minimize downstream uncertainties in patient treatment. Considerations should be afforded to bladder and rectal filling, with the aim to minimize uncertainties in sCT generation, target and OAR structure propagation and maximize organ stability throughout treatment i.e. intra-fraction motion. Margins should be evaluated and may be tailored to account for these uncertainties.
An empty rectum is recommended for simulation and treatment. Bladder preparation is recommended to incorporate a neutral filling state, which is typically achieved with the patient emptying their bladder 1-2 hours prior to simulation and treatment. Each institution should evaluate this approach, the impact on inter-fraction and intra-fraction bladder changes, in order to define their patient preparation protocol and margins. A temporal CT or CBCT study evaluating bladder size and shape changes over defined time periods may provide a quantitative basis for revised intra-fraction motion margins.

Immobilization and set up

Patient setup and immobilization should follow standard radiotherapy.

Site specific setup accuracy and precision should be assessed, including an evaluation of intrafraction motion uncertainties, informing appropriate margins to be applied to target volume. Additional immobilization measures may be considered and adopted following this evaluation.

Common setup and immobilization measures include supine patient positioning and use of patient comfort aids such as head rest/neck support, knee and ankle supports. A vacuum bag may also be used as an alternative and may improve setup reproducibility.

Image acquisition

Patient CT simulation should conform to departmental practices and respect the applicable mass density to HU calibration. Image acquisition protocols should be evaluated with the goal to optimize low contrast resolution whilst maintaining adequate spatial resolution, with a typical slice thickness less than or equal to 3 mm. The imaging field of view (FoV) and scan length should be large enough to encompass the full length of target volumes and relevant OARs. The simulation imaging is used for both initial planning, dose calculation and is the source image in the generation of the sCT used in the online adaptation workflow.

Segmentation

Patient anatomy should be segmented, outlining organs and pelvic normal tissues as per international consensus guidelines [9]. The radiotherapy target volumes should be defined in accordance with best practice guidelines [6] and conform to the concepts of prescribing, recording and reporting outlined in ICRU 50, 62 and 83 [10-12].

Targets

a. GTV
b. GTV LN / PTV VHD
c. CTV HD / PTV HD
d. CTV LD / PTV LD

Influencers

a. Bladder
b. Rectum
c. Bowel
    a. Note here the AI defined bowel contour represents bowel loops. The current version of Ethos doesn't use the bowel to influence or guide the deformation for the purposes of target propagation.

OARs

a. Bladder
b. Femoral Heads
c. Bowel
    i. It is pertinent to note that there are different types and therefore definitions of bowel structures within the Ethos system. The user should evaluate their use of these structures for planning and on couch adaptation to maximize efficiency of the complete workflow. Bowel bag is defined as per RTOG contouring guidelines which by definition crops out abutting and mobile OARs such as the bladder and uterus [9]. Consequently, the bowel bag structure is pre- and post-processed for its propagation through a deformation vector field (DVF) to respect the RTOG bowel bag definition. An alternate is the bowel (see *segmentation - influencer* above) structure, which is AI-driven contouring of the bowel loops. The user may select to include a bowel PRV using structure derivation as a surrogate of the bowel bag cavity.
d. External genitalia
e. Peripheral tissue

Margins

Derived structures should be used to minimize the amount of contour modification required throughout the adaptive process. The downstream effects of initial planning contours and template setup on the reference CT and plan should always be considered. Structure margins and derivations facilitate increased efficiency in the on couch adaptive process and increase the consistency of resultant contours. Any contour that is created as a result of an expansion or Boolean operation should be generated through use of structure derivation.
Margins should be evaluated for any changes that may result from the use of online adaptive treatment. Considerations when evaluating margins may include accuracy of patient setup and treatment, intra-fraction motion and stability, contour accuracy on CBCT imaging, treatment time, machine tolerances and plan deliverability. The inter-fraction component of uncertainty in margin calculations are minimized in the online adaptive setting. Intra-fraction motion and stability can be assessed using pre- and post-treatment imaging, surface guidance, bladder ultrasound etc. A safe and initial implementation may use standard published margins for IMRT-based treatment of rectal cancers, which typically is 7 mm, albeit based on a bone match IGRT workflow. Subsequent evaluations can be performed to scope for any changes.

Dose preview

Dose preview implements the template for treatment plan optimization, capturing the physicians RT intent i.e. radiotherapy prescription. The template outlined in Table 1 is ordered for application in dose preview and interpretation by the Ethos Intelligent Optimization Engine (IOE) [13]. The dose preview workspace provides an estimate of plan dosimetry, metrics and structure DVHs. Further, plan optimization trade-offs may be explored through adjustment of the template order. The optimization objectives applied in the photon optimizer (PO) algorithm are set from the clinical goals and ordering, and the order of clinical goals defines cropping logic of any overlapping structures. Within dose preview, the estimated DVH can be interactively dragged which acts to adjust PO objectives, with the constraint that clinical goals are prioritized and met.
Dose preview calculations are applied for a geometry closely represented as a 9 field IMRT beam arrangement, albeit generated using fluence-based optimization only i.e. physical leaf motion constraints not included. The algorithms used in dose preview include PO, IOE and Fourier Transform Dose Calculation (FTDC). The FTDC algorithm class and accuracy differs from the final dose calculation algorithm, Acuros XB, contributing to differences observed between dose preview estimates and final plan dose calculation [13, 14].
The differences observed in DVH estimation and plan quality metric calculation between dose preview and final plan calculation can be significant, highlighting a need to evaluate final plan calculations for full evaluation of the impact of changes made within the dose preview workspace. Experience across a representative cohort of rectum patients has shown that commissioned clinical goal templates may require changes, albeit small, to account for individual patient anatomy. Template adjustments have shown improvements in plan quality whilst maintaining stability and robustness in plan quality and deliverability, justifying a template adjustment per patient concept.

Plan Generation and Review

Plan generation automatically occurs in Ethos following refinement of dose preview and authorization of the RT Intent. Ethos has the potential to generate pre-defined plan types which include 2 or 3 arc VMAT, or 7, 9 and 12 field IMRT. These beam arrangements are fixed by Ethos treatment planning and cannot be optimized to individual patient anatomy, however an Eclipse beam arrangement can be imported in to Ethos for use in subsequent plan generation. As outlined in the *initial planning – template development* section, which ultimately outlines the process followed to commission and evaluate the rectum Ethos planning template, it was identified that the Ethos 12-field IMRT beam arrangement produced the optimum plan quality across a representative patient cohort. The user may wish to evaluate other beam arrangements

on a per patient basis, and consider other practical considerations such as treatment delivery time and intrafraction motion or anatomical changes.

Review of Ethos optimized and generated plans includes evaluation of key plan quality metrics of targets and OARs (included in Ethos planning template); dose distribution regarding coverage, hot spots (e.g. 105% of prescription), cold spots, low dose wash size and anatomical location; and relative beam weighting, delivery efficiency and complexity as indicated with per field and total Monitor Units (MU).

Eclipse plans can provide improved plan quality for patients with elective nodal targets, which can be related to size and location of these target volumes relative to OARs. Eclipse planning enables tailored beam arrangements, offering more degrees of freedom for leaf fitting and optimization with variable collimator angles per field. Very seldom was it identified that there was a clinical benefit or need, in regards to plan quality, to utilize Eclipse planning or beam arrangements, but was useful in the development of Ethos treatment planning and plan quality benchmarking on a per patient basis.

Pre-treatment patient specific QA

The design of pre-treatment patient specific QA for Ethos adaptive plans should consider existing guidelines and recommendations for treatment planning QA [15-17], implementation of automated treatment planning in the clinic [18] and development of robust safety checklists [19]. Additional considerations specific to the Ethos adaptive process in the pre-treatment setting includes;

- Patient factors which may conflict with inclusion/exclusion criteria e.g. large metallic implants.
- Configuration/setup of technical structures (automatic/manual density corrections), simulation isocenter and couch plane.
- Review suitability of multi-modality image registration to aid contouring on subsequent treatment sessions.
- Review RT Intent configuration, noting that this applies to all treatment sessions;
    - Suitability of selected anatomical site and laterality, if applicable, to ensure appropriate influencers and/or AI models are applied.
    - Ensure plan enabled for adaptive treatment, or as appropriate.
    - Treatment frequency set as per prescription.
    - Plan normalization, DVH estimation model and bolus set correctly.
- Contouring; activation and definition of derived structures set as per protocol (includes margin and Boolean operations).
- Review target volume length is within machine limits for single isocenter treatment, with a suggested margin to account for initial positioning uncertainties that may lead to target volume positioning outside the treatment portal e.g. 26 cm maximum length.
- Correct clinical template and associated dose preview order (used in IOE) applied i.e. RO clinical priorities reflected in plan optimization and generation.
- Assess beam arrangements and their suitability for the patient of interest.
- Evaluate MU for each field and total against normal clinical range.
- Review plan quality using isodose distribution/homogeneity, hot spot locations/magnitude and DVH limits are within site protocol.
- Dose calculation (Mobius [20]) and/or phantom measurement (suitable detector array) to independently validate the TPS dose prediction and deliverability of RT Plan.

Implementation of a rigorous pre-treatment QA process is expected to optimize the quality of subsequent adaptive treatment sessions through ensuring all aspects that may have downstream impacts have been reviewed and adjusted where required.

Documentation

All documentation should follow standard treatment plan reporting requirements (ICRU50/62/83) and pre-treatment QA requirements [15, 17, 19]. Additional attention relevant to the Ethos adaptive process may include;

- CT checklist (inclusion/exclusion criteria, patient preparation instructions)
- RT intent report, clinical plan report and technical plan report
- Independent dose calculation and plan delivery reports (Mobius)
- Patient specific QA results (e.g. phantom for plan verification or deliverability measurements)
- Physics/RT plan checklists

Team member roles and workflow

The roles and workflows may differ according to departmental practices and credentialing/assessment programs in place. An example workflow and typical tasks performed by each staff group is provided, capturing the major steps in the initial planning process and typical tasks performed by the range of clinical staff. The individual institution should tailor the roles and workflow to their jurisdictional requirements and typical departmental processes.

a. Dosimetrist/RTT/RT
    i. Add RT intent based on RT prescription and assign approved planning directive template
    ii. Review CT simulation document and document setup instructions
    iii. Import planning and diagnostic imaging, including image registration and accuracy assignment
    iv. Contour OARs and/or import targets or OARs as required from 3rd party system e.g. Eclipse
    v. Review and refine Dose Preview order and document deviations from defined template
    vi. Assess calculated treatment plan geometries against clinical protocol
    vii. Prepare plan reporting documentation & QA checklists
b. Physician/Radiation Oncologist
    i. Prescribe treatment for RT intent
    ii. Contour targets
    iii. Review and edit directive in Dose Preview and authorize RT Intent
    iv. Review calculated plan options and select clinical treatment plan
    v. Perform clinical approval
c. Physicist/Radiation Oncology Medical Physics (ROMP)
    i. Review clinical treatment plan
    ii. Sign off Technical Plan Report
    iii. Perform independent dose calculation (e.g. Mobius)
    iv. Perform phantom-based patient-specific QA (PSQA)
    v. Complete QA documentation

Table 2: Initial Ethos planning workflow

Initial planning			
Workflow	*Physicist* *ROMP*	*Radiation Therapist* *RTT* *Dosimetrist*	*Radiation Oncologist* *Physician*
Add RT intent as per RO prescription		X	X
Add clinical protocol templates and any relevant CT simulation documentation		X	
Contour normal tissues		X	X
Register planning image with any diagnostic supporting images	X	X	X
Contour target volumes			X
Import OAR and target volumes (if not contoured in Eclipse)		X	
Review and edit planning directive and Dose Preview		X	
Approve RT intent		X	X
Review calculated treatment plan options and select plan		X	X
Complete clinical approval of plan			X
Create treatment plan documentation		X	
Send plan to Mobius and plan QA phantom	X		
Review Mobius results	X		
Perform phantom measurement	X		
Complete technical approval of plan	X	X	
Complete QA documentation	X	X	

The initial planning workflow is outlined, and provides an indication of the tasks that can be performed by various staff groups. This can aid implementation of Ethos planning and treatment, and the allocation of staffing profiles and handover points required for resourcing the Ethos platform. Changes to align with local practices may be required.

Recommendations for contouring and treatment planning

The key recommendations for contouring and initial planning of rectum patients are outlined below. The detail pertaining to each recommendation is detailed in the above sections.

- The protocol should follow standard radiotherapy practice
- Evaluate the margins with scope for reduction
- Patient preparation for CT simulation and treatment is important
- Derived structures should be used carefully for optimizing efficiency and accuracy
- Commissioned and standardized Ethos templates are recommended
- Multiple templates are required for single and multi-dose level plans
- Additional clinical objectives to the protocol may be required for plan optimization
- The 12-field IMRT beam arrangement is beneficial for plan quality

On couch Adaptation

Patient setup and initial CBCT

Immobilization used for patient setup

See *Planning CT simulation section - Immobilization and set up*.

Description of image acquisition

Daily CBCT is performed as per the online adaptive workflow. Use of the Pelvis or Pelvis Large CBCT modes are recommended to optimize image contrast and resolution, which should improve the accuracy of sCT generation, AI segmentation, target/OAR propagation and volume delineation. The CBCT imaging length should capture the full length of target volumes, which may require use of extended-length CBCT imaging. This should avoid discontinuities present in the sCT at the bounding limits of the acquired CBCT i.e. stitching artefacts, which have an impact plan optimization and dose calculation.
The initial CBCT should be evaluated for image quality, bladder/rectal filling, the presence of rectal/bowel gas or artefacts that may adversely affect contour propagation or represent a significant dosimetric uncertainty in sCT generation. During implementation, impact of imaging artefacts, size and location of bowel gas should be evaluated to define tolerances to enable decision making to occur based on initial CBCT imaging.

Contouring and evaluation

The on couch contouring is driven by the automated workflows within the Ethos platform, which includes AI segmentation, deformable registration and structure propagation. The utility and considerations are outlined below.

AI segmentation

The on couch adaptation workflow utilizes AI segmentation of influencer structures, which as previously described for rectum is the bladder, rectum and bowel. The AI segmentation of these influencers is typically completed in less than a minute. The bladder and rectum AI segmentation often requires no adjustment, although the AI contoured bowel (see *initial planning – segmentation – influencers section*) was found to require major edits and increases overall treatment session time to correct.

Target and OAR propagation

The targets and OARs listed in the segmentation – targets and OARs section are typically propagated in 2 – 3 minutes. The accuracy of structure propagation is variable, resulting in the editing of these structures to vary from minor to major edits across a representative patient cohort.
The bowel structure utilized for initial planning and on couch adaptation is based on the accuracy of propagation, time required to edit at treatment and post-processing applied. The bowel bag structure type is recommended for use, and while the edits required can still be significant, this was found to be the most effective and efficient OAR approach for the bowel. The bowel influencer is therefore not used and removed as a structure from the RT intent.

Pattern of segmentation errors

The key issues affecting AI segmentation and structure propagation include poor CBCT image quality, imaging artefacts and large anatomical changes between the planning CT and the CBCT session image. CBCT image quality can be affected by large patient habitus/separation or poor choice of imaging mode. Imaging artefacts may be system-based e.g. ring artefact, or driven by patient anatomy e.g. gas in bowel/rectum, surgical clips etc. Typical anatomical changes that can impact AI segmentation and structure propagation include pelvic tilt, bladder volume differences, bowel position and proximity to target volumes and rectal filling.

Plan generation and selection

The on couch plan generation and selection requires consideration of a number of clinical and technical factors which have been structured to describe concepts to consider and processes that may be employed to aid the review and decision making in plan generation and selection.

a. The plan calculation time typically takes 1-3 minutes but is dependent on the complexity of planning technique and template design.
b. Considerations for plan selection and proceeding with treatment include;
    i. The planning CBCT quality for use in plan generation should consider the concepts outlined in *patient setup and initial CBCT – description of image acquisition*.
    ii. The accuracy of the generated sCT geometry, as indicated by review of the agreement of body/bones contours with CBCT imaging, and also by review within the MobiusAdapt slice viewer, should be reviewed. Inaccuracies may impact the plan generation and dosimetric accuracy as represented for the session anatomy.
    iii. Patient movement or large intra-fraction anatomical changes since plan adaptation may be identified on a pre-treatment CBCT, evaluated relative to the planning CBCT. Repeat adaptation or scope to utilize a scheduled plan or IGRT workflow may be required. The logistics of this pathway should be considered and defined.
    iv. The review of generated plans should follow the plan assessment recommendations outlined in the *initial planning – plan generation and review* section, with a focus on identifying sub-optimal adapted dose distribution or plan metrics.
c. Adaptive plan QA processes that can support the considerations for plan generation and selection include;
    i. Mobius can perform an independent dose verification for on couch generated plans.
    ii. Mobius can display the sCT used for plan optimization and dose calculation.
    iii. The Ethos technical plan report can show plan MU per field and composite for adapted and reference plans. This should be considered in relation to defined acceptable ranges as identified during the implementation process.
    iv. During the implementation phase, adapted plans should be validated with phantom measurements e.g. array dosimeter, for a representative cohort of patients and degree of plan adaptation for the developed planning technique and/or template.

Treatment delivery

Setup verification post planning

A (second) pre-treatment CBCT should be taken after adaptive plan selection to review the patient anatomy and geometry against that used for adaptive plan generation. The pre-treatment CBCT is compared to the initial CBCT, and rigid couch shifts may be applied to account for patient movement and anatomical changes.
The couch shifts should be reviewed to understand the magnitude or significance of intrafraction movement.
An additional post-treatment CBCT may be acquired to assess the intrafraction changes that have occurred, albeit provides a relatively close time point to the pre-treatment CBCT.
The verification CBCT images may be used for subsequent dosimetric evaluation or to evaluate site specific margins when assessed across a suitable and representative patient cohort.

Patient monitoring during treatment

The current Ethos treatment delivery system doesn't incorporate intrafraction monitoring or intervention support systems such as surface guidance or beam level kV or MV imaging. Visual assessment of patient movement can be observed as shown on the room CTV to monitor the patient during treatment.

Treatment delivery time

The treatment delivery time is typically 4 – 5 minutes, which is inclusive of the linac beam delivery and sequencing between treatment fields. The overall delivery time depends on the plan complexity and total MU.

Team member roles and workflow

The roles and workflows may differ according to departmental practices and credentialing/assessment programs in place. An example workflow and typical tasks performed by each staff group is provided, capturing the major steps in the on couch adaptive plan process and typical tasks performed by the range of clinical staff. The individual institution should tailor the roles and workflow to their jurisdictional requirements and typical departmental processes.

a. Dosimetrist/RTT/RT
    i. Review patient setup instructions
    ii. Operates Ethos interface at treatment console
    iii. Acquire and review CBCTs (image match where appropriate to workflow)
    iv. Review and edit influencers and OARs
    v. Review generated treatment plans
    vi. Complete QA documentation
    vii. Deliver treatment
    viii. Monitor patient for movement
b. Physician/Radiation Oncologist
    i. Review imaging
    ii. Review and edit target volumes
    iii. Review OAR contouring accuracy
    iv. Review and select treatment plan
    v. Perform clinical approval
c. Physicist/Radiation Oncology Medical Physicist (ROMP)

i. Provide technical support throughout workflow
ii. Review imaging and provide advice on dosimetric impact of anatomical changes
iii. Review clinical treatment plan
iv. Sign off Technical Plan Report
v. Review MobiusAdapt QA results
    i. Independent dose calculation of selected treatment plan
    ii. sCT accuracy and agreement to CBCT contours

Table 3: On couch adaptation workflow

On couch adaptation			
Workflow	*Physicist* *ROMP*	*Radiation Therapist* *RTT* *Dosimetrist*	*Radiation Oncologist* *Physician*
Set up patient		X	
Acquire CBCT		X	
Review and accept CBCT	X	X	
Review, edit and accept influencers		X	X
Review, edit and accept target volume			X
Review, edit and accept OARs		X	X
Review clinical aspects of scheduled and adaptive treatment plans		X	X
Select treatment plan		X	X
Sign off clinical plan report			X
Review technical aspects of plan	X	X	
Review MobiusAdapt results	X		
Review sCT in Mobius	X		
Sign off technical plan report	X	X	X
Acquire second CBCT, review and apply shift		X	
Deliver treatment		X	

The on couch adaptation workflow is outlined, and provides an indication of the tasks that can be performed by various staff groups. This can aid implementation of Ethos on couch treatment processes, and the allocation of staffing profiles and handover points required for resourcing the Ethos platform. Changes to align with local practices may be required.

Documentation

The documentation pertinent to the on couch adaptation process includes that outlined in the *initial planning – documentation* section. In addition to this, it is recommended to develop an on couch session checklist. The on couch session checklist may include; description of the reference plan name for comparison and review in Eclipse/Ethos during on couch treatment planning; comment section to describe CBCT image quality/artefacts; influencer, OAR and target agreement with CBCT; description e.g. location and magnitude of contouring edits; comment of body and bone contour agreement with CBCT; clinically relevant isodose levels for plan quality assessment in fractional dose; MU variation between reference and adapted plan; documentation of scheduled couch shifts; recording of select time points throughout the on couch workflow.

Treatment delivery recommendations

The key recommendations and considerations when performing on couch adaptation for rectum patients are outlined below. The detail pertaining to each recommendation is detailed in the above sections.

- Use high quality CBCT modes e.g. Pelvis Large.
- Imaging FoV should cover all target volumes. Consider extended CBCT for long target volumes.
- Ensure target and OAR contouring is consistent between the reference plan and on couch sessions.
- Consider structure definitions e.g. bowel vs bowel bag, and how this links to the required contouring and handling during structure propagation, plan optimization and generation.
- Ensure compliance with patient preparation applied at CT simulation to improve target propagation accuracy and to minimize intra-fraction anatomical changes.
- Adopt a console arrangement to allow an additional viewing terminal to review and assess CT scan, reference contours and plan in a system such as Ethos, Eclipse, Velocity etc.
- Develop a treatment QA checklist for use during each adaptive session, see on-couch adaptation – documentation section. This highlights higher priority items to check, and supports handover and observations longitudinally throughout the course of treatment.
- Implementation of a formalized handover process, to facilitate continuity of care with different staff members in the course of daily adaptive treatment.
- Recommend use of a pre-treatment CBCT to validate the patient position and review anatomical changes that have occurred since adaptive plan generation.

Treatment monitoring

Monitoring is a workspace that enables the user to evaluate technical and dosimetric aspects of the adaptive treatment course. The key workspaces include; sessions, accumulation, cine and trends. Treatment monitoring allows the user to evaluate session activity, the accumulated dose distribution for delivered treatments, longitudinal imaging comparisons, and evaluation of dose/volume trends for structures with assigned clinical goals.

a. Sessions
   The sessions workspace can be used to review the timeline for any on couch session, including plan selection (scheduled or adapted), imaging performed (e.g. initial and pre-treatment CBCT), and plan information (technical and session reports).

b. Accumulation
   The dose accumulation workspace is useful for evaluation of the spatial distribution of dose remains consistent with the clinical intent and goals.

c. Cine
   The cine workspace provides the user an ability to visualize longitudinal anatomical changes between the CBCT from each session and the planning CT. This may provide a visual complement to observations made in trends or at treatment.

d. Trends
   The trends workspace provides a summary of the current accumulated clinical goals and volumes per structure. This may be used to assess the likelihood of the prescribed clinical objectives and constraints being achieved based on the accumulated delivered dose distribution. A revised RT intent may be prompted from trend observations, which would revise the clinical objective and/or position within the dose preview order to better match the overall clinical goal.

It is important to note that there is insufficient clinical information on full treatment course adaptation and subsequent dose accumulation to make informed recommendations regarding clinical implementation and interpretation of these results. The primary issues to consider include;

- Validation of deformable registration of images and dose deformation
- Use of monitoring when using two RT intents; one for IGRT treatment and one for adaptive treatment
- Decision making processes or thresholds that may be developed for revising clinical goals based on the information provided in treatment monitoring.

The various tools within treatment monitoring lend themselves for review across different workspaces. These tools can support review of treated fractions, which can be incorporated in to a staff handover process between adaptive treatments. Additionally, treatment monitoring can support identification and rationale for noted differences in clinical objectives or volume changes in a given session, or significant adaptive changes e.g. tumor response, bladder volume changes.

Conclusion

The Ethos platform is a novel radiotherapy planning and treatment system supporting online, daily adaptive treatment. This white paper outlines the key considerations and recommendations to support implementation of adaptive rectum radiotherapy.

Acknowledgements

As members of the Adaptive Intelligence™ Consortium, the authors receive financial compensation from Varian, a Siemens Healthineers Company, for their original research.

Medical Advice Disclaimer

Varian as a medical device manufacturer cannot and does not recommend specific treatment approaches. Individual treatment results may vary.

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