ADAPTIVE INTELLIGENCE™ CONSORTIUM

Disease site: Prostate, Prostate and Nodes, Prostate Bed and Nodes

Author Names, Titles, and Institutions:

- **Icon Group, Australia:** Mikel Byrne - Senior Medical Physicist, Ben Archibald-Heeren - Medical Physicist, Amy Teh – Radiation Oncologist, and Trent Aland – National Director of Medical Physics
- **Medisch Spectrum Twente (MST), Enschede, The Netherlands:** Lisanne Zwart-Technical Physician, Erik Van Dieren-Medical Physicist, Marleen Heinemann-Segerink RTT/Advanced Adapter, and Ina te Veluwe-RTT/Advanced Adapter
- **Queen's Hospital, Romford, United Kingdom:** Dom Withers - Head of Radiotherapy Treatment Planning and Siobhan Graham - Head of Radiotherapy

Purpose: This document provides general advice on treating a conventionally fractionated prostate or prostate bed with online adaptive radiotherapy on the Ethos platform v. 1.1. It assumes that the reader has been trained in the use of the Ethos system. The advice given is not intended to cover all aspects of the treatment process but rather summarize the Ethos and prostate-specific aspects. This is general advice from a consortium of early Ethos users, and detailed supporting data has not been included here but may be published elsewhere. Clinics may use this treatment advice and local discretion, understanding, and regulations to set up a safe and high-quality prostate or prostate bed online adaptive treatment workflow.

Introduction

I. Initial Planning

a. Interactive prescriptions

Treatment sites covered include conventionally fractioned prostate, hypofractionated prostate, prostate and nodes, and prostate bed and nodes.

The patient needs to have good bladder control and be able to lay still on the couch due to potential for extended treatment times. The presence of a hip prosthesis leads to significant image artefacts that can make the adaptive process unfeasible due to the large amount of contour editing required. This document does not include SBRT or the use of foreign substances, such as hydrogel.

Patient selection, dose regime, and OAR tolerances should be based on established guidelines (e.g. eviQ guidelines).

RapidPlan models can be used in Ethos but have not been extensively tested at this stage. The DVH estimates can be seen in plan review but not during the on-couch session.

b. Segmentation

Influencer contours should be smooth, should not overlap, and match the anatomy contoured by the AI models as closely as possible. We would recommend contouring influencers based on CT (not MR) so that the planning contouring matches the on-treatment contouring as closely as possible.

Prostate CTV contours will not necessarily match the prostate influencer and should be contoured considering clinical factors. If MR is used to assist target contouring, any registration errors between the MR and planning CT should be manually accounted for during planning.

The organs contoured are the Prostate, Seminal Vesicles, Bladder, Rectum, Femoral heads, Sigmoid colon, Penile bulb, Bowel bag (if treating nodes). No AI-based contouring is available in the contouring workspace at this stage.

In some situations, breaking large target structures (e.g., pelvic nodes) into smaller sections has resulted in better contour propagation in an adaptive fraction.

All centers involved in this paper are using standard IGRT margins at this stage. Each individual clinic should understand its workflows before changing margins. While the contribution from interfraction motion may be reduced from margin calculations, intrafraction motion has the potential to increase due to issues such as longer treatment times caused by CBCT image quality, quality of influencer generation/delineation, or quality of structure propagation. The CTV contouring uncertainty may also increase depending on the staff mix available at the treatment console.

PTV margins should be added in the planning directive workspace (rather than contouring) so that they are recalculated daily based on the propagation of the CTV, which can be verified by checking margin calculation in the contouring workspace.

The sigmoid colon is poorly propagated by the adaptive session due to limitations of deformable image registration in low contrast regions. Some users have found a 5mm PRV is useful for the sigmoid colon to ensure the dose to the sigmoid is clinically acceptable without the need for daily adjustment of the structure in the adaptive workflow. However, this method can unnecessarily compromise coverage.

c. Dose Preview

The Dose Preview uses a 9 field IMRT geometry to indicate a dose distribution that can define patient-specific priorities. However, it should be noted that plan creation uses the objective priority list to reoptimize the plan from the beginning. Incorporation of MLC geometry, field arrangement, more accurate dose calculation algorithm, plan normalization, and machine limitations can result in large dosimetry changes between the Dose Preview and Plan Review.

Good results have been found by prioritizing CTV/PTV coverage and maximum doses to OARs in the priority 1 category. Other important goals that need to be evaluated on treatment are put in level 2, and less important goals are in levels 3 and 4. We recommend that the number of level 1 and 2 goals are minimized to those that will determine plan selection during adaptive treatment, as only these will be displayed to users on treatment. Presenting unnecessary goals during the plan evaluation step can lengthen the plan selection process.

Users should be mindful of too many goals that do not fulfill physician's intent. The smart optimizer in Ethos is incompatible with conflicts between high-priority planning directives, and users have found that such conflicts can result in poorer quality plans with minimal optimization of lower priority structures. This is particularly problematic in adaptive treatments where the optimization re-occurs on every fraction.

Hotspots can be controlled by adding a maximum dose goal constraint. This issue can be further improved by avoiding the use of a point maximum goal and instead using a larger volume constraint (e.g., 1cc).

d. Plan Generation and Review

Best results have been found in the current version of Ethos for IMRT plans, with plan quality equivalent to Eclipse generated plans. The typical number of treatment fields used by centers participating in this workgroup ranges from 7 to 12; however, when determining the number of

beams, the planner should consider differences in dosimetric plan quality and the additional treatment time required for plans with more beams. Additional beams can increase time for optimization, calculation, QA, and delivery.

The MU/Gy of Ethos plans tends to be higher than that of equivalent plans in Eclipse. For example, an intact prostate in Eclipse treated with IMRT on a Halcyon would require 300-400MU/Gy, compared to 400-500MU/Gy in Ethos.

Eclipse would only be used if the beam arrangement or isocenter position is unsuitable, such as for a hip prosthesis case. The beam arrangement or isocenter can be determined in Eclipse, while the plan optimization would still take place in Ethos. Using Ethos for the adaptive optimization that occurs on treatment can be fine-tuned during the planning process, and the plans generated on treatment will be consistent with the planning result.

e. Pre-treatment patient-specific QA
The QA requirements used will vary based on local institutional practices, regulations, and billing requirements. Since measurement-based QA is not feasible for an online adaptive workflow, calculation-based methods are required. Extensive verification of Mobius and how it may impact the user's quality control program is recommended. We refer the reader to AAPM TG218 and the Ethos QA whitepaper for more information on patient-specific QA.

f. Documentation
A placeholder plan can be created in Aria for scheduling, dose tracking, and activity capture purposes. Ideally, compatibility between Ethos and Eclipse would allow importing the reference plan for ARIA scheduling. The RT intent report and the plan report can also be exported into Aria.

g. Team member roles and workflow
Team member roles for standard radiation oncology treatments vary greatly between countries, particularly in treatment planning. The skillset of each staff group will influence how the clinic manages adaptive treatments. For further discussion of roles during treatment, we refer the reader to the treatment competency and roles whitepaper.

h. Recommendations for contouring and treatment planning
Contouring should conform to published guidelines or departmental protocol. When contouring the anatomy for adaptive plans, it is important to consider how the structure will be created in an adaptive session. Identical contours on the planning CT can behave differently during the treatment session depending on whether AI creates them, propagated using an elastic DIR, propagated using a structure-guided DIR, or created from derived structure operations.

II. On-couch Adaptation

a. Patient setup and iCBCT
Online adaptive potentially allows reduced bladder and bowel preparation for prostate treatments. A less full bladder, or more full rectum, can partially be compensated for by adapting the plan to the daily anatomy. A greater consideration for adaptive sessions is whether the bladder filling or rectal gas changes significantly over the adaptive timeframe and whether the patient is comfortable holding their bladder over the slightly extended treatment appointment. Both gas and bladder filling should be assessed after the acquisition of the initial CBCT. Implanted fiducials may be used; however, the user should be aware of the potential impact on image artifacts and the quality of autosegmentation of the prostate.

b. Automated segmentation

Sigmoid colon, bowel bag, and femoral heads are key OARs for this region that are not influencers. A penile bulb can also be considered.

Rectum, Bladder, Prostate ± Seminal Vesicles are used as influencers for prostate cases, Rectum and Bladder are used for prostate bed cases.

When nodes are treated, the bowel can also be added, which is contoured as bowel loops. Since the bowel is not used as an Influencer structure in the pelvis by Ethos, the structure will not impact the generated target. We have found all OARs except bowel were contoured well, with no systematic problems found. Issues with the bowel OAR are the result of a combination of poor AI contouring in the presence of gas, difficulty for users in contouring bowel on the planning image, difficulty for users in interpreting correct contours in the adaptive session, and long adjustment times for correcting incorrect AI structures. For cases with nodes, we recommend using a bowel bag (not an influencer) and removing the bowel influencer.

Users should refer to the treatment competency and roles whitepaper for team member roles and workflow.

c. Contour evaluation and modification

For the majority of fractions, no changes are required to target contours. If consistent errors in target contours are seen, this can indicate a problem with the influencer structures on the planning CT, e.g., inconsistent influencer contouring between planning and treatment. In such cases, it can be beneficial to create a plan revision to address contouring irregularities on the CT image.

We recommend that target contours be created using structure-guided DIR rather than copying geometry from influencers. Two primary justifications for this choice are:

- CTV does not necessarily match the physical prostate due to microscopic invasion
- MR prostate contours are difficult to contour on CBCT

No systematic errors in propagated targets were seen, although larger errors are often observed at the superior/inferior ends of the target volumes.

Evaluation of the targets and non-influencer OARs can typically be done in 1-2 minutes if no changes are needed. However, if editing is required, the time required can exceed 5 minutes.

It should also be noted that any adjustment of contours in the edit contour workspace results in a complete re-optimization of the adaptive plan, which increases the treatment time on the order of 5-10 minutes.

For nodal treatments, the primary contour requiring amendment is the bowel bag. On adaptive treatments, if any loops shift proximally to the nodal CTVs, the bowel contour is edited to include these loops to minimize small bowel toxicity.

The contouring tools in the adaptive workspace include the lasso and brush tools. These tools are ill-suited to adjusting thin concave structures and can result in difficulties adjusting some target volumes.

Documentation of what was done by the treatment team on an adaptive fraction and the reasons is recommended. This has the benefit of acting as a checklist for the treatment team whilst also recording steps performed.

In particular, as a minimum, we would suggest checking and recording; whether the CTVs/non-influencer OARs were edited, whether the synthetic CT is accurate, bladder/rectal doses, which plan was selected, and any comments or reasons for the target editing or plan choice. This documentation can effectively be done using Aria questionnaires or other software.

Users should refer to the treatment competency and roles whitepaper for team member roles and workflow.

Thoroughly check and adjust the influencers to the anatomy of the CBCT. Check that targets are matching planning scan contouring. Visually ensure that any non-influencer OARs are matching the CBCT anatomy. Initial experience indicates that within 3cm of the PTV(s) the user should ensure contours agree with the daily CBCT anatomy within the range of inter-user variability (e.g. 2mm). Further away from the PTV(s), a larger tolerance can be used, as minimal impact on the plan generated has been observed.

d. Plan generation

Ensure contradictory goals do not have the same priority when creating the planning directive. Consider that goals that are not contradictory on the planning CT may become contradictory due to changes in anatomy on a given day. E.g., an OAR moving into a PTV margin.

There are no site-specific QA considerations.

The total adaption time from CBCT beam-on to treatment delivery seen clinically is typically 10-20 minutes depending on plan complexity and whether nodes are included. Some changes in the bladder can be seen in this timeframe, as well as occasional changes in rectal gas.

Plan selection should be based on the clinical goal results, isodose analysis, and oncologist patient-specific preference. We have not seen significant differences in modulation between scheduled and adaptive plans and do not use this as a plan selection criterion.

The plan that passes more of the clinical goals is predominantly selected for treatment. In practice, differences between plans are often significant, with the adapted plan being chosen in almost all cases (between 90-100% depending on site).

If the scheduled plan is selected, no further QA is required, as this was done as part of the initial plan approval. We refer the reader to the QA whitepaper for further details on the QA process for adaptive plans.

The synthetic CT used for dose calculation also requires QA. This cannot easily be visualized in the adaptive workflow, although a deformed external and deformed high-density structure can be visualized. It is important that these structures are checked against the anatomy in the acquired CBCT to ensure the generated synthetic CT is accurate. If they do not agree, this indicates the density used for adaptive re-optimization is incorrect, and we would recommend selecting the scheduled plan or restarting the adaptive process. The synthetic CT can also be visualized in the Mobius session and session report.

Users should refer to the treatment competency and roles whitepaper for team member roles and workflow.

Generally, the plan that is passing more of the clinical goals should be selected for treatment. Only high priority goals (levels 1 and 2) are shown to the user on treatment to assess the preferred plan without presenting the user unnecessary information. Oncologist input should be considered when both scheduled and adapted plans do not meet high-priority clinical goals. This

does not necessarily require the Oncologist to be present at the console during treatment, but instead could be via documented methods for prioritizing goals when there are multiple failing goals.

e. Treatment delivery
We recommend the acquisition of a verification image post-adaptive planning. An automatic soft tissue match can then be performed between the initial adaptive CBCT and the second verification CBCT. This ensures the adapted plan remains valid and allows for comparing adapted contours against the current anatomy. The couch is then shifted to account for any motion over the course of the adaptive fraction. Often changes up to 1cm are seen in the superior part of the bladder; however, this rarely makes a significant change to the dose distribution in the prostate region.

The live-view monitoring is not used as it is not designed for this application.

Users should refer to the treatment competency and roles whitepaper for team member roles and workflow.

The treatment delivery time is the same as other modulated deliveries. The beam-on time is typically 2-3 minutes for 7-12 field IMRT plans.

The scheduling and dose tracking of treatment delivery is tracked within Aria using a placeholder plan with a single beam and 1MU. This placeholder plan is manually completed after treatment each day.

f. Recommendations for on-couch adaptation
Ensure workflow is optimized to ensure contour edits are minimized wherever possible. Ensure any decisions required within the workflow are pre-thought out and documented (for example, areas of contouring that require particular attention, plan priorities around conflicts, visual dose distribution criteria, Mobius criteria).

III. Treatment monitoring

a. Automated dose monitoring
Dose accumulation has not yet been validated; thus, this functionality is not used clinically. Clinical usage of dose accumulation is considered to incur considerable risk due to limitations in DIR algorithms when propagating the dose. Ethos issues alerts if any structure value that should remain constant between reconstructed and propagated doses (like dose max value and mean dose value) exceeds predefined deviation. Thus far, it has been noted that many fractions show a DIR alert indicating problems with the dose accumulation. Furthermore, using structures like PRVs for DIR guidance (if they have goals of priority 1 or 2) should be considered when validating dose accumulation. Those structures do not necessarily track anatomy and may lead to DIR errors.

Regular review of the session dose is advisable to monitor trends in the goals achieved during adaptive sessions.

b. Automated structure monitoring
Structure volume changes can be used and are free from potential errors in the dose accumulation step. They allow for the monitoring of unexpected structure volume changes. However, forecast structure alerts have not been implemented into clinical practice yet as they are based on the dose accumulation deformable registration and have not yet been validated.

c. Offline adaptation, if applicable
A revision of the plan due to anatomical changes (i.e., offline adaptation) is rarely required. No formal procedures are recommended to trigger this workflow, as the frequency is expected to be very low and required workflow highly situation-specific.

d. Frequency of treatment course review
During the implementation of Ethos, a daily review of the treatment course by the Oncologist is recommended. Thereafter, a multi-disciplinary team should agree on review frequency depending on familiarity with the site being treated and clinical factors. Oncologist feedback to the treatment team can be provided through the alerts system in the Ethos system. The alert system provides a message to treatment staff on the machine that must be accepted prior to treatment.

e. Team member roles and workflow
Users should refer to the treatment competency and roles whitepaper for team member roles and workflow.

f. Recommendations for treatment monitoring and offline adaptation
We recommend regularly reviewing the session dose, contouring, and achieved goals on individual fraction structures and CBCT. We do not recommend reviewing the dose accumulated on the planning CT (whether per fraction or accumulated over the whole course), as this is potentially subject to dose accumulation DIR errors. At current, there are both insufficient tools and literature verifying the accuracy of the Ethos DIR to use in clinical dose accumulation.

IV. Conclusion with final recommendations

a. Final group recommendations on the treatment of prostate cancer using adaptive therapy on Ethos

General recommendations for Ethos online adaptive on the prostate:

- Avoid contradictory optimization goals
- It can be beneficial to split large target structures into smaller regions to maximize the quality of target propagation
- If performing treatments without the oncologist present at the console, ensure oncologist instructions are well documented and understood, and radiographer/RTT actions and their reasons are well documented.
- Document all treatment decisions made for each fraction and conduct a review of each treatment, at least during the initial implementation of any adaptive workflows.

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