Radiotherapy Appendix

Patient pre-treatment preparation

All preparation with fixation should be done at one of the university hospitals participating in the Skandion network. A custom lower limb immobilization device for supine patients is required to minimize setup uncertainty. The use of a belly board is allowed.

To minimize bladder volume variability, the patients should be subjected to following procedure: after voiding, the patients should be asked to drink 300 ml liquid. Pre-treatment imaging should be performed 30-45 minutes afterwards. The same routine should be repeated before each treatment fraction.

Pre-treatment imaging

Dose-planning CT and MR (optional) should be done at one of the university hospitals participating in the Skandion network. Maximum acceptable rectum diameter on planning imaging is 5 cm. For proton treatment planning, dose calculations must be performed on a CT study without contrast, with a CT scanning protocol validated for protons.

Target Volumes

Target definition and dose-planning should be done at one of the university hospitals participating in the Skandion network. Structure delineation should be performed on a registered CT/MR image.

The definition of volumes should be done in accordance with the ICRU Report #83 (1), and ICRU #78 (2).

The Gross Tumor Volume (GTV) is defined as all known gross disease as determined from a combination of physical exam, colonoscopy, CT, MRI and PET-CT if performed.

The Clinical Target Volume (CTV) is defined as the GTV plus areas considered at significant risk of harboring microscopic disease.

The Planning Target Volume (PTV) should provide a margin around the CTV to compensate for the inter- and intra-fraction uncertainty consequent to daily setup uncertainty and to potential internal organ motion. By definition, the PTV should consist of a symmetrical 6 mm expansion around the CTV. For protons, additional range margin needs to be considered, and instead of using a PTV, robust optimization of the CTV may be performed instead of a PTV.

The following are guidelines for generating CTV and a unified PTV.
Rectal GTV (+15 mm radially and 20 mm cranio-caudally) = CTV

Nodal GTV + 10 mm symmetrical expansion = CTV
Uninvolved iliac vessels + 7-8 mm= CTV

For details regarding target volume definition see "Target volumes Appendix"

Organs at risk (OARs)

Bladder, bowel bag, femoral heads, sacral nerves, pelvic bones should be defined [RTOG]. Pelvic bone should be contoured including all bone structures for at least the full extent of the PTV.

Planning Constraints

Standard structure name (SSM 2021:27)	Structure description	Priority	Dose constraint	Description
BowelBag	Bowel bag (5, 6)	2	$V_{18Gy(RBE)} \leq 450cc$	The volume receiving 18 Gy (RBE) should be equal or less than 450 cc
FemoralHead_L FemoralHead_R	Femoral heads	2	$D_{mean} < 25$ Gy	The mean dose should be less than 25 Gy (RBE)
Sacrum	Sacrum (spinal canal at the level of S1-S2). Definition of lumbosacral plexus (7) is optional	2	$V_{25Gy(RBE)} < 60\%$	The volume receiving 25Gy (RBE) should be less than 60%
PelvicBones	Pelvic Bones	3	As low as reasonably achievable. Aviod hotspots	Total bone for the full extent of the PTV
Bladder	Bladder	3	As low as reasonably achievable. Avoid hotspots	

Table 1. *Dose-volume constraints. RBE value/model 1.10 is used.*

Absorbed dose prescription

All patients should receive 5 fractions of 5 Gy (RBE) 1 fraction per day, five days per week up to a total dose of 25 Gy (RBE). Treatment starts preferably on Monday. Overall treatment time should be maximum eight days.

The prescribed absorbed dose should be specified to a dose reference point/volume.

Standard treatment with photons. Arm A:

Preoperative radiotherapy should be delivered on a linear accelerator. Volumetric modulated arc therapy (VMAT) is mandatory for all patients for the initial pelvic field encompassing the gross tumor and at-risk lymph nodes in the pelvis.

The dose distribution should be calculated based on CT scans or synthetic CTs based on MRI scans.

Target dose-volume constraints	Target type	Priority	Description
$D_{95\%} \geq 100\%$	GTV	1	At least 100% of the prescribed dose to 95% of the GTV volume
$D_{98\%} \geq 93\%$	PTV	2	At least 93% of the prescribed dose to ≥ 98% of the PTV volume
$D_{10\%} \leq 105\%$	PTV	2	At most 105% of the prescribed dose to ≤ 10% of the PTV volume
$D_{5\%} \leq 110\%$	PTV	2	At most 110% of the prescribed dose to ≤ 5% of the PTV volume
$D_{max} < 115\%$	PTV	2	Maximum dose in the PTV should be < 115% of the prescribed dose.

Table 2. *Target dose-volume constraints.*

Experimental treatment with protons. Arm B:

A PTV should be defined by the same principles as for photons and used for prescribing and reporting dose according to the recommendations of ICRU 78 (8). During treatment optimization help structures with customized margins to the CTV can be created in order to include range uncertainties and to ensure homogeneous and robust dose delivery to the CTV.

For proton therapy, the dose prescriptions should be in both physical dose and RBE-weighted absorbed doses. The RBE value of 1.1 should be used for protons and the prescribed dose is the corresponding dose for photons (Gy(RBE)).

Treatment planning and delivery

RT plans should generally consist of either (1) a single PA (posterior-anterior) field to encompass the primary tumor, mesorectum, and internal iliac lymph nodes, with a single AP (anterior-posterior) field to treat the external iliac lymph nodes or (2) posterior oblique RT fields. Single-field optimization should be used with intensity modulated gradients for regions of overlap, or a (3) 3-field (posterior/anterior, right lateral, and left lateral) approach with a 2-to-1 field weighting by dose contributed to the target volume.

Dose computation and optimization

To account for air within the rectum when designing the proton plan, the Hounsfield units (HU) need to be overridden for the air-filled portion of the rectum. For protons, artifacts in the tissue

as well as clips, markers, etc. must also be contoured. HU overriding should be performed whenever a, for the purposes of dose calculation, more accurate HU is available.

Dose calculation

o Reference dosimetry is carried out according to the IAEA report TRS 398 (2000) (9)

or TRS-398 Rev-1 (2024) (10).

o The calculation grid shall be at a maximum of 3 mm.

In order to facilitate the optimization procedure, help structures and volumes may be defined.

For proton treatments, see treatment planning and optimization guidelines in the Skandion Clinic treatment planning instruction manual.

Treatment plan evaluation

A robustness test should be performed for each proton treatment in 14 test cases, with +/- 6 mm perturbations along the cardinal axes and 3.5% uncertainty on the HU-values; two scenarios in which only the HU-uncertainy are included and with 12 with both perturbations and HU-uncertainty. Tolerance levels that should be fulfilled in the robustness test for treatments described in table 3.

	Tolerance levels
CTV: all test cases	D90% ≥ 95%
CTV: for at least 12 of 14 robustness test cases	D98% ≥ 95%
GTV: all test cases	D95% ≥ 100%
GTV: for at least 12 of 14 robustness test cases	D98% ≥ 100%
DVH parameters of OARs used for definition of objectives and constraints (table 1)	According to clinical judgement

Table 3. *Tolerance levels that should be fulfilled in the robustness test. RBE value/model 1.10 is used.*

Image-guided treatment delivery

The usage of IGRT is essential since the total number of fractions is limited to five. For both protons and photons, the position of the patient shall be verified daily based on CBCT.

Additionally, an optical surface scanning system can be used as a complement for positioning and monitoring the patient intrafractionally.

CBCT is used for daily positioning and corrections are made in 4DoF daily, accordingly. For improved definition, localization and monitoring of target and OAR position, CBCT images of each fraction are evaluated daily, offline and online (optional) by a physician and/or a physicist. Anatomy including surface/skin, bone, gas, urinary bladder as well as the CTV is evaluated.

If large anatomical changes can be seen on the CBCT and replanning is deemed necessary, it may be performed either on a new CT or on the current planning CT.

Quality assurance

The aim of the RT-QA program is to ensure the consistency of radiotherapy treatment delivery across all participating centers as well as the verification of adherence to the protocol guidelines described above. Pre-treatment patient specific quality assurance (QA) must be performed according to local clinical routine.

Radiotherapy-related data should be collected, transferred and reported to QA-centre by each participating site. The data transfer is handled through the Sharefile service provided by the Skandionkliniken https://skandionbasa.sharefile.eu/

Each participating center has the access to Sharefile folder "PRORECT NNN", where NNN is the name of the centere. For each patient a subdirectory to "PRORECT NNN" should be created and named "XX-YYY", where XX-YYY is the patient identification number (XX defines participating centre and YYY is a running patient number).

The following data should be exported:

1. Exported in DICOM-format and saved under the directory "XX-YYY"

- CT-images
- Structures
- Treatment plan
- Total dose distribution (in Gy) in DICOM-format
- Co-registered MR or PET-images
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2. Treatment record, saved as a document (Word, Excel, Text of .pdf) stating the date of the first and last treatment fractions. The file should be named "XX-YYYY" and saved in the directory "XX-YYY"

The RT QA program is divided in two parts:

1. **Pre-study RT-QA (before inclusion of patients)**

Benchmark cases
All participating centers are required to delineate the target volumes and the organs at risk on CT images from two test cases. The delineation should be done according to the above instructions.

Additionally, all centers are required to submit a radiotherapy plan for each technique on two further test cases with predefined targets and organs at risk. The radiotherapy plans should respect the dose constraints described above.

All the benchmark cases should be evaluated by the RT-QA coordinating center before the participating centers can proceed with the patient inclusion.

Dosimetry audit
In order to check the reference dosimetry of the accelerators that should be used to deliver the treatment, it is recommended that all participating centers should take part in an external dosimetry audit alternatively to provide a reasonable recent documentation about it.

2. During study RT-QA

In order to maintain the compliance to the RT protocol throughout the duration of the study, the RT-QA coordinating centre should keep performing the evaluation according to the following steps:

Pre-treatment review:

This stage is composed of two levels:

- Level 1:
  Within this level, evaluation of the delineation (target and organs at risk) and of the treatment plan should be performed.
  The first radiotherapy plan from each treating centre, for photon respectively proton treatment, should be reviewed. All centres are required to send RT data at least one week, counted as five working days, before the start of the treatment. Feed-back to the treating centre should be provided within three working days from reception.
  If major violations are identified a re-planning should be requested before the start of the treatment. The modified plan must be submitted for review, but approval should not be required prior to the start of the treatment unless otherwise specified by the RT-QA committee. For these centres, one more patient should be reviewed according to the above-described procedure.
  Once an acceptable quality level is achieved, centres may progress to level 2.

- Level 2:
  Within this level evaluation of the treatment plans should be performed and RT data is to be sent the first day of the treatment at the latest.
  All centres should keep being audited with one in every five patients randomly selected by the RT-QA committee for review. However, preapproval from the RT-QA coordinating centre should not be required to begin the treatment.
  If a continued level of acceptable quality is maintained, the rate of sampling may be decreased at the discretion of the RT-QA committee.

Continuous monitoring of RT treatments:
For the rest of the patients included in the study, a continuous monitoring of RT data should be performed and therefore it is required that all RT data should be sent the first day of the treatment at the latest. If major deviations are found under the period of the study the RT-QA coordinating center should provide feedback. This should, however, not affect ongoing treatments.

All centers are required to submit the final RT data of all involved patients within two weeks after completion of the RT treatment.

Documentation

Detailed information on how to prepare, process and send the RT data for all involved patients should be provided separately. Likewise, instructions on feedback communication from the RT-QA coordinating system should be given separately.

References:

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