Listing of PORTEC-4a Protocol Amendments (version 2.4, 12 June 2018)

1. **Administrative changes on front page:**
    - added extra Trial Registry number for PORTEC-4a (Clinicaltrials.gov: NCT03469674)

2. Administrative changes in the protocol

- Table of Contents: Quality of Life questionnaire and Patient Information and Consent sheet deleted from the body of the protocol and added as separate documents
- Study Synopsis (p 4): Planned duration extended from 4 years to 4-5 years (because of the initiation phase with ongoing site activations from June 2016 to March 2017 with reduced recruitment)
- Brachytherapy technique and dose (7.3.2, page 13-14): some minor further specifications for clarity
- Follow-up (page 17) and Quality of life assessment (page 21): inconsistency resolved by deleting the mention of a QOL questionnaire at 10 years on page 17, and keeping the correct text (7 years) on page 21 and in Appendix G and H.
- Appendices: deleted full text of Quality of Life questionnaire and Patient Information and Consent sheet (now added as separate documents). Former Appendix I and J now renamed to Appendix G and H. Quality of life questionnaire now added as separate document (unchanged)

3. Amendments

- Tissue specimen collection and molecular profile (8.2, page 16-17): some further specification of profile outcome assignment in case of double classifiers.
- Data handling, monitoring and quality control (10.3, pages 19-20): Some more detailed specification of principles of data handling, validation and data management and of central and on-site monitoring.
- Paragraph 15 (page 25): Specification in the publication policy that PIs of the participating groups will be included as authors in the publications, and when PIs of single participating sites in a country will be author.
- Paragraph 16, page 26: specification of planned international participation and sites/groups in preparation and/or set-up
- Appendix E: some minor further details on brachytherapy planning.
- Patient information and consent sheet: added specific information according to privacy laws and transparency requirements in the sections on the Quality of Life Questionnaire, Address Permission Sheet, and confidentiality statements. Added text to specify coding of medical information, who will know the code, and which persons or organisations have the right of inspection of the medical data (such as study monitors and Inspectors of the Ministry of Health Inspection team). Some further specification of the legal storage period of trial related information.
- ABR form: Registry numbers ISRTCN and NCT added to section B4a; Projected end date extended to april 2021in section C23; Inclusion of more countries in section C6a (Belgium, Germany, France, Ireland) as sites and/or groups in these countries are in the preparatory phase of participation.