Supplementary material for Hassan Metwally MA et al., Radiotherapy quality assurance of the IAEA-HypoX trial of the accelerated radiotherapy in the treatment of head and neck squamous cell carcinoma with or without the hypoxic radiosensitizer nimorazole, Acta Oncologica, 2015; doi: 10.3109/0284186X.2015.1074721.

SUPPLEMENTARY MATERIAL

IAEA-HypoX Trial

Radiotherapy Quality Assurance Program

Ver 1.2

6/20/2012

Quality assurance program allows a reliable inter-comparison of results among different radiotherapy centers, and ensuring uniform treatment delivery compliant with the trial protocol. This is necessary for the clinical trial and also for sharing clinical experience and transferring it between centers.

At the start of patients' accrual:

Contact with the participating centers will be established to make sure that all items in the trial protocol are clear especially those concerning treatment guidelines of radiotherapy treatment.

For centers using 3D-CRT or IMRT, a dummy run procedure will be performed with a representative sample of the dataset. The participants will be asked to perform treatment planning according to the protocol guidelines and to send it to the trial secretariat. Upon receiving the datasets, the QA procedures will be applied to ensure consistency and validity of the data. If the treatment planning data do not conform to the protocol, the participant will be asked to modify procedures and redo treatment planning, and then the data will be checked again for validity.

The centers will be asked to send scan copy of the treatment planning files for the first 5 patients (of each kind of treatment technique, i.e. 2D planning or 3D-CRT/IMRT): e.g. planning images (simulator films, beams arrangement and dose distribution images), together with the dose prescription's report and DVH (for 3DCRT & IMRT plans).

The plans will be evaluated by the quality coordinator, for compliance with the protocol guidelines. A feedback report will be sent back to each center, with either acceptance of the plans or reporting early deviation from the protocol.

During the trial life time:

Monitoring for the participating departments will be done by site visits at reasonable intervals. Review of radiotherapy plans, radiotherapy treatment documentations for the treated patients, and comparing them against protocol-specified criteria for protocol deviations, will be done. Treatment interruptions must be clearly documented in the treatment record along with the reason(s) for this interruption(s).

Protocol specified compliance/deviation criteria:

Patient is considered protocol compliant if fulfilled all the protocol specified treatment guidelines including:

- Target volumes definitions and critical structures volumes definitions
- Radiotherapy dose specifications (allowing only 1-2% deviation) and dose distribution.
- Radiotherapy treatment fractionation and correction of treatment interruptions.

Protocol specified deviation criteria:

- Minor deviation= deviations that not expected to be of significance to the treatment outcome, or 3% or more but less than 5% deviation from the protocol specified values.
- Major deviation= deviations that expected to be of significance to the treatment outcome, or 5% or more deviation from the protocol specified values.

	Per protocol	Minor deviation	Major deviation
RT target dose *2D planning Total dose in ICRU point -small field: 66Gy	66Gy	64Gy ≥ to >62Gy or 68Gy ≤ to <70Gy	62Gy or less 70Gy or more
68Gy	68Gy	66Gy ≥ to >64Gy or 70Gy ≤ to <72Gy	64Gy or less 72Gy or more
70Gy	70Gy	68Gy ≥ to >66Gy or 72Gy ≤ to <74Gy	66Gy or less 74Gy or more
-large field (at least 46Gy) *3DCRT	46Gy≤	44Gy ≥ to > 42Gy	42Gy or less
Mean dose PTV-T: 66Gy	66Gy	64Gy ≥ to >62Gy or 68Gy ≤ to <70Gy	62Gy or less 70Gy or more
68Gy	68Gy	66Gy ≥ to >64Gy or 70Gy ≤ to <72Gy	64Gy or less 72Gy or more
70Gy	70Gy	68Gy ≥ to >66Gy or 72Gy ≤ to <74Gy	66Gy or less 74Gy or more
Mean dose PTV-E(at least 46Gy)	46Gy≤	44Gy ≥ to > 42Gy	42Gy or less

*IMRT Mean dose PTV1: 66Gy 68Gy 70Gy Mean dose PTV2: (at least 60Gy) Mean dose PTV3: (at least 50Gy) **RT normal tissue dose** (provided proper definition of critical target volumes) *total dose to spinal cord(0.01cc) *total dose to brain stem(0.03cc)	66Gy 68Gy 70Gy 60Gy≤ 50Gy≤ 50Gy or less 52Gy or less	64Gy ≥ to >62Gy or 68Gy ≤ to <70Gy 66Gy ≥ to >64Gy or 70Gy ≤ to <72Gy 68Gy ≥ to >66Gy or 72Gy ≤ to <74Gy 58Gy ≥ to >56Gy 48Gy ≥ to >46Gy 50Gy< to ≤52Gy 52Gy< to ≤54Gy	62Gy or less 70Gy or more 64Gy or less 72Gy or more 66Gy or less 74Gy or more 56Gy or less 46Gy or less More than 52Gy More than 54Gy
*In case of improper definition of critical target volume, each case will be evaluated if that has an impact on either target volume coverage or dose received by the critical structure, after correction of volume definition and recalculation of the dose distribution.			
-Overall RT treatment time 38day 39day 40day	 38-39day 39-40day 40-41day	 40-44day 41-45day 42-46day	 ≥45day ≥46day ≥47day
-GTV definition and RT beam arrangement.	All known gross disease determined from CT, clinical information, endoscopic findings and MRI.	Missing part or all of the gross disease in target definition or in RT beam arrangement /or treating the patient on the opposite side of the disease.	
-Homogeneity in dose distribution.§ HI= ($D_{2\,\%}$ - $D_{98\,\%}$) / $D_{50\,\%}$	 0 – 0.12	 0.12< - <0.25	 ≥0.25
§ HI =homogeneity index $D_{2\,\%}$ = $D_{near\text{-}max}$ (dose covering 2% volume of the PTV) – obtained from the cumulative DVH $D_{98\,\%}$ = $D_{near\text{-}min}$ (dose covering 98% volume of the PTV) $D_{50\,\%}$ = D_{median} (dose covering 50% volume of the PTV)			

A final review of all noncompliant patients will be done by the quality coordinator. The objective of this review was to separate the noncompliant patients into those in which the deviations were predicted to have a major adverse impact on tumor control, toxicity, or both, from those that might be considered to be compatible with a reasonable standard of care if the patient had been treated off-protocol.

At the time of trial closure:

- After completion of treatment, investigators will be asked to submit full documentation of radiotherapy given to patients.

- The trial coordinator will carry on a closure visit to participating sites and will review the radiotherapy plans and the radiotherapy treatment documentations for the last treated patients and comparing them against protocol-specified criteria for protocol deviations.