PD-0186

Dosimetric evaluation of the electronic brachytherapy system Esteya

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Purpose/Objective: The Esteya® electronic brachytherapy system (Elekta Brachytherapy, The Netherlands) has been recently developed for HDR brachytherapy treatment of skin lesions, using a 69.5 kVp X-ray source. The purpose of this study was to evaluate the surface dose rate of the Esteya by using different detectors and calibration protocols. Results are compared considering the uncertainty of each method.
Materials and Methods: The surface dose rates of the 15, 20, 25 and 30 mm diameter applicators of Esteya were measured with the plane parallel ionization chamber T34013 (PTW-Freiburg, Germany) and the parallel plate ionization chamber Exradin A20 (Standard Imaging Inc., USA). The first one was calibrated in both air and water, whereas the second one was provided with calibration in air. Measurements in air were performed according to dosimetric protocol established by the Task Group 61 of the American Association of Physicists in Medicine, whereas measurements in water were performed in a CIRS Plastic Water® phantom, using the methodology proposed by the International Atomic Energy Agency in its report TRS-398. Measurements were corrected by the effective point of measurement in each case.
Results: Table 1 shows the relative differences between the experimental measurements of this study and the internal values used by Esteya to determine the treatment times. The relative uncertainty (with coverage factor k = 1) of the absorbed dose measurements are: 2.5% for the T34013 chamber calibrated in water, 2.7% for the T34013 chamber calibrated in air, and 2.6% for the A20 chamber calibrated in air. Relative differences between the output factors measured in air with the ionization chamber T34013 and the A20 are below 2%, which are lower than the uncertainties of the dose measurements, so the stem effect of the PTW chamber can be considered to be negligible for this application.

Table 1. Relative difference (%) between the surface dose rate measured with each detector and protocol, and the surface dose rate used by Esteya to plan the treatments.

Applicator diameter (mm)	Detector and calibration method		
	TM34013 in water	TM34013 in air	Exradin A20 in air
30	-3.0	0.3	2.2
25	-2.5	-0.5	2.8
20	-3.5	-0.7	2.8
15	-3.7	-2.7	0.9

Conclusions: The two ionization chambers and the two dosimetric protocols have been shown to provide consistent results with the internal values from Esteya, considering the uncertainties. Further investigation is needed to evaluate the equivalence between plastic water and liquid water. Because measurements in air require more correction factors and because the experimental setup used with solid plastic is more similar to the real patient setup, measurements with a chamber calibrated in water seem to provide a more direct methodology to characterize dosimetrically the Esteya system.

Proffered Papers: Clinical 3: IAEA

OC-0187

IAEA-HypoX. A randomized study of nimorazole with accelerated radiotherapy in HNSCC. Report of an incomplete trial

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Purpose/Objective: To test the hypothesis that radiotherapy (RT) of head and neck squamous cell carcinoma (HNSCC) can be improved by hypoxic modification using nimorazole (NIM) in association with accelerated fractionation.
Materials and Methods: The IAEA-HypoX protocol was activated March 2012 as an international multicentre randomized trial in patients with HNSCC. The tumour was treated to a dose of 66-70 Gy, 33-35 fractions, 6 fractions per week. NIM was administered as a total dose of 1.2 g per m^2 body surface area, 90 minutes before the first daily RT fraction. The primary endpoint was loco-regional failure. The analysis was perfor-med as intention to treat among evaluable patients. The trial was closed prematurely by June 2014 due to insufficient recruitment. This was caused by inability to obtain the approval for using the drug in three major centres and an insufficient recruitment rate in the active participating centres. An associated quality assurance program was performed to insure the consistency with the protocol guidelines.
Results: The trial was dimensioned to include 600 patients in 3 years, but between March 2012 and May 2014 only 104 patients were randomized. All 20 patients from two centres had to be excluded from the final analysis due to the unavailability of the follow-up data. Thus, only four of nine centres originally planned to participate did contribute to the study.
Among the 84 eligible patients, 2 patients did not start RT after randomization. The remaining 82 patients were evaluable (39 and 43 patients in the RT+NIM and the RT-alone arms, respectively). The treatment compliance was good with only six patients not completing the full planned radiotherapy course, and with 32 patients (82%) out of 39 allocated for nimorazole, achieved at least 75% of the prescribed drug dose. The cause of failure to fulfil the treatment was mainly due to the acute side effects.
At the time of evaluation, 36 patients had failed to achieve persistent loco-regional control, and a total of 40 patients

had died. The use of nimorazole improved the loco-regional tumour control with an 18 months post-randomisation cumulative failure rate of 31% versus 54% in the control group, yielding a risk difference of 23% (CI 2%-45%; *P*= 0.03). The corresponding values for overall death was 39% versus 68%; risk difference 28% (CI 4%-52%; *P*= 0.02).

Conclusions: Although the trial was incomplete and suffered from small and incomplete number of patients, did the analysis indicate a loco-regional control and survival benefit in patients given the hypoxic modifier nimorazole in addition to accelerated fractionation for advanced HNSCC.

However, the trial also revealed that conducting multicenter and multinational clinical studies combining drug and radiotherapy in developing countries, may suffer from uncontrolled and unsolvable problems.

OC-0188

IAEA randomised study on optimization of treatment of locally advanced NSCLC using radiotherapy and chemotherapy

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Purpose/Objective: Patients with incurable locally advanced non-small cell lung cancer (NSCLC) (mainly Stage IIIB) usually receive palliative treatment with either radiotherapy (RT) alone (39 Gy in 13 fractions or 10-17 Gy in 1-2 fractions) or several cycles of doublet chemotherapy (CHT) regimens. In order to optimize treatment approach in this disease and improve access to RT in limited resource setting, International Atomic Energy Agency conducted a prospective randomised study (NCT00864331) comparing protracted RT course with CHT followed by one or two fractions of RT.

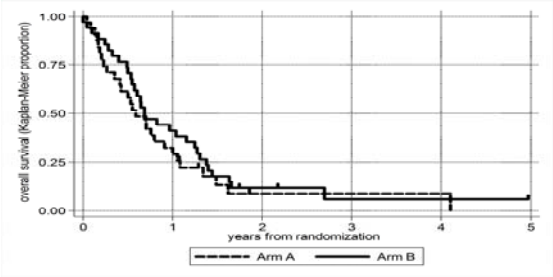
Materials and Methods: Total of 65 patients from 7 institutions aged ≥ 18 years, with histologically confirmed NSCLC, stage IIIA/IIIB, Karnofsky performance status (KPS) 60-90, previously not treated for NCSLC were randomised, 31 to arm A and 34 to arm B. Exclusion criteria were RT field > 200 cm^2 and pregnancy. In arm A, RT consisted of 39 Gy in 13 fractions. In arm B, 2 to 3 platinum-based CHT cycles were prescribed, and were followed by 10 Gy given in a single fraction or 16 Gy given in 2 fractions separated by one week. Further treatments depended on disease progression and patient condition and were left to the discretion of involved radiation oncologist. Primary outcome was overall survival.

Results: Treatment groups were balanced with respect to various variables (Table 1). Treatment compliance was also given in Table 1.

CHARACTERISTICS	ARM A (n=31)	ARM B (n=34)	p
Gender (M:F)	26:5	29:5	1.0
Mean Age (yr)	59.6	60.2	0.8
KPS 60:70:80:90	2:14:12:3	2:18:14:0	0.4
Mean BMI	23.7	24.0	0.9
SQC:ADC:LC:Other	15:13:0:3	14:15:3:2	0.4
no-effusion:effusion	20:11	16:18	0.2
Staging bone scan	14	17	0.8
Staging CT brain	9	9	1.0
N pts with 39 Gy	31	0	
N pts with cycle 1	0	32	
N pts with cycle 2	0	32	
N pts with cycle 3	0	26	
N pts with 16 Gy	0	25	
N pts with 10 Gy	0	2	
Mean RT field size (cm)	12.8 x 13.4	13.4 x 14.2	0.4 ; 0.1

M = Male; F = female; KPS= Karnofsky Pefrormance Status score; BMI = Body mass index; SQC = squamous cell carcinoma; ADC = adenocarcinoma; LC = large cell carcinoma; CT = computed tomography; RT = radiotherapy

With follow-up through Feb 2014, 6/65 remained alive, 3 in each arm (all 6 being lost to follow-up at > 1 yr of observation). Median survival for all 65 patients was 0.66 yr (maximum 5.0 yr), while median survival was 0.59 and 0.68 yr for the two arms, respectively (log-rank p=0.4 by study arm, and p=0.6 by Cox regression, stratified by country and sub-stage). One- to three-year survival rates for the two arms were 29%, 9% and 9% vs 41%, 12% and 6%, respectively) (Figure 1).



There was no difference in any of the following endpoints (all values, p>0.5): any failure, occurring in 26 cases each in A and B; local failure, occurring in 18 cases each; regional failure, occurring in 6 and 8 cases in the two arms, respectively; contra-lateral thoracic disease, occurring in 3 cases each; and distant failure, occurring in 13 and 14 cases in the two arms, respectively. Post-initial treatment, in arm A more courses of palliative RT were administered (17 courses in 11 cases, vs. 4 in 4 cases in arm B), along with slightly more palliative CHT cycles (19 cycles in 7 cases, vs. 11 in 2 cases in arm B).

Conclusions: There were no differences in survival, relapse patterns and symptoms between the two arms. When compared to high-dose palliative RT, CHT followed by one or two fractions of RT produced similar results. It can be recommended as treatment approach, especially in limited resource setting, where access to RT remains inadequate.

OC-0189

Irradiation of the supraclavicular nodal region in post-mastectomy radiotherapy; an IAEA randomized trial

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