Simultaneous integrated boost in external radiotherapy for breast cancer. Skin toxicity

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Purpose/Objective: External radiotherapy after surgery is considered standard for breast conserving treatment. In some patients, boost over the breast region at risk for local recurrences can be administered sequentially or concomitantly (simultaneous integrated boost: SIB) with whole breast irradiation. This SIB technique reduces the total time of treatment and sometimes determines best dose homogeneity. Acute cutaneous toxicity is due to the cumulative dose and dose per fraction administered, so it can be thought that SIB increases this side-effect. Our objective was to evaluate acute skin toxicity in radiotherapy breast cancer and differences between concomitant and sequential boost.

Materials and Methods: We analyzed 160 patients with breast conserving treatment, aged from 33 to 80 years. Radiation treatment was delivered with Linear Accelerator (SIB) with whole breast irradiation (WBRT)). Tracking the tumor bed after breast-conserving therapy (lumpectomy followed by whole breast irradiation (WBRT)). The addition of chin fixation doesn’t improve the stability of the supraclavicular lymph node area, nor does it prevent great deviations in individual patient set-up. Limitations of the current study could be the small sample size, the learning curve in the fabrication of the chin fixation and its use.

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Conclusions: In our Institution, acute skin toxicity in external radiotherapy with boost for breast cancer is mild, with less than 1% of grade III complications. There are a greater number of patients with grade I and grade II/III in sequential boost vs SIB, but these differences were not statistically significant so we can conclude that Simultaneous Integrated Boost does not increase acute cutaneous toxicity, and reduces the overall duration of treatment. One more in-depth analysis of the data and other parameters (irradiated volume, dosimetry,...) could confirm this results or establish differences in toxicity between these two techniques.

Accuracy of boost volume tracking in whole breast irradiation using conebeam CT imaging of surgical clips

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Purpose/Objective: Most local recurrences occur in or near the tumor bed after breast-conserving therapy (lumpectomy followed by whole breast irradiation (WBRT)). Tracking the boost volume instead of the thoracic wall using implanted surgical clips might reduce RT planning margins. In this study, the accuracy of surgical clip matching on conebeam CT (CBCT) and the relative motion of the clip area relative to the thoracic wall was investigated.

Materials and Methods: The accuracy of the clip matching was studied by determination of the interobserver variation using the standard deviation of the X, Y and Z-direction in all matches. In a group of 20 breast cancer patients, 5 to 8 CBCT’s were acquired (128 scans in total). During surgery 2 to 5 clips were implanted with a median of 4 clips per patient. Each CBCT was registered by 3 or 4 Radiation Therapy Technicians (RTTs) to the planning CT in XVI software (Elekta AB) resulting in 484 independent registrations (on average 3.8 per scan). For registration, a clipbox encompassing the clips area was defined. Next, the automatic seed match option

Results: Radiation boost: SIB was applied in 65 patients (40.3%); Sequential boost in 95 patients (59.75%)

Results are presented in table 1. This study shows no significant differences between the setup accuracy of both groups. The systematic translation error in the cranial-caudal direction is the largest for both patient groups. The systematic error of the left-right, cranial-caudal and anterior-posterior rotations didn’t show a significantly smaller rotational error in the supraclavicular area for the group with the chin fixation. Conclusions: The addition of chin fixation doesn’t improve the stability of the supraclavicular lymph node area, nor does it prevent great deviations in individual patient set-up. Limitations of the current study could be the small sample size, the learning curve in the fabrication of the chin fixation and its use.

Skin Toxicity : Global Grade I radiodermitis was evaluated in 86 patients (54.1%); Grade II in 72 patients (45.3%); Grade III only in 1 patient (0.61%)

According to the boost technique: (fig.1)

-SIB: Gr I, 38 pts (58.4% of this group); Gr II, 27 pts (41.5%). No grade III toxicity was assessed.

-Sequential boost: Gr I, 48pts (50.5% of this group); Gr II/III, 47 pts (49.4%) Differences in grade I toxicity SIB vs sequential were not statistically significant: p=0.41; and differences in grade II/III, neither were statistically significant: p=0.27

Table 1 results and translations with and without chin fixation

<table>
<thead>
<tr>
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<th>With chin fixation</th>
<th>Without chin fixation</th>
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<tbody>
<tr>
<td>Translations (mm)</td>
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<tr>
<td>Left-Right</td>
<td>Cranial-Caudal</td>
<td>Anterior-Poster</td>
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<tr>
<td>Mean (range)</td>
<td>0.9 (0.3-3.8)</td>
<td>1.9 (0.8-3.2)</td>
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<tr>
<td>Random error</td>
<td>0.9</td>
<td>1.2</td>
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Conclusions: In our Institution, acute skin toxicity in external radiotherapy with boost for breast cancer is mild, with less than 1% of grade III complications. There are a greater number of patients with grade I and grade II/III in sequential boost vs SIB, but these differences were not statistically significant so we can conclude that Simultaneous Integrated Boost does not increase acute cutaneous toxicity, and reduces the overall duration of treatment. One more in-depth analysis of the data and other parameters (irradiated volume, dosimetry,...) could confirm this results or establish differences in toxicity between these two techniques.
was used for an initial registration, and then manually adapted if this was judged necessary. Each CBCT was also registered using a clipbox encompassing a relevant portion of the thoracic wall, according to our clinical protocol for registration of the whole breast CTV.

**Results:** In more than 50% of the cases, the automatic seed match was unsatisfactory and manual correction was necessary. The interobserver variation had a standard deviation of 1.0 mm in the X (lateral) direction, 1.1 mm in the Y (longitudinal) direction and 1.4 mm in the Z (ventrodorsal) direction. These numbers apply to the entire study population. This interobserver variation showed low interpatient variation for the X and Y directions (0.4 mm), but was somewhat larger for Z (0.9 mm). The relative motion of the center of mass of the clips (representative for the boost volume) with respect to the thoracic wall was 0.5 ± 2.7 mm (mean ± overall standard deviation) for X, 1.0 ± 2.8 mm for Y and 1.0 ± 3.4 mm for Z. A significant trend (p=0.0006) was observed in the magnitude of the relative motion of the center of mass of the clips with breast size, as shown in Fig. 1.

**Conclusions:** For position verification, surgical clips in CBCT matches can be registered within an average accuracy of about 1 mm using routine clinical image registration procedures. However, the relative motion of the clips with respect to the surrounding anatomy must be taken into account for appropriate margin calculation. We will study the implementation of dual registration (simultaneous clip and global anatomy matching) to detect outliers with large relative motions in clinical practice.

**Proffered Papers:** Radiobiology 2: Novel treatments, models, and survivorship

**OC-0264**

Determination of RBE in the rat spinal cord after carbon ion irradiations with different LET and fractional doses

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**Purpose/Objective:** Carbon ions (12C-ions) allow highly conformal dose distributions due to the inverted depth-dose profile (Bragg peak). In addition, 12C-ions exhibit an enhanced relative biological effectiveness (RBE) with increasing depth. The RBE is a complex quantity and depends amongst others on the linear energy transfer (LET) and dose. These complex RBE-dependencies have to be considered in treatment planning by mathematical models (RBE-models) and substantial uncertainties are introduced by the necessity to optimize the dose distribution in terms of biologically effective rather than absorbed dose. This is of special importance for the late-responding tissues of the central nervous system, which is the dose-limiting tissue in the treatment of head and neck tumors. To improve safety of patients in 12C-ion therapy, RBE-models have to be benchmarked. We therefore performed systematic experimental studies to quantify the RBE-dependence on LET and dose.

**Materials and Methods:** The cervical spinal cord of female Sprague-Dawley rats was positioned at six different depths corresponding to different LET-values (16-99 keV/µm) along a 6 cm spread-out Bragg peak and was irradiated with either 1 or 2 fractions of 12C-ions. The field size was 10 x 15 mm² including the segments C1-C6. At each position, complete dose-response curves for single and split doses were established and TD50 values (dose at 50% complication probability) were determined for the development of forelimb paresis grade II within 300 days. RBEs were calculated using TD50 for photons of our previous study. Rats reaching this endpoint were sacrificed and the spinal cord was taken out and processed for histological examinations.

**Results:** The minimum latency time was found to be significantly LET-dependent after split dose irradiation but not after single dose irradiation. For the single dose experiment the TD50 values were 19.5±0.4 Gy (16 keV/µm), 18.4±0.4 Gy (21 keV/µm), 17.7±0.3 Gy (36 keV/µm), 16.1±1.2 Gy (45 keV/µm), 14.6±0.5 Gy (66 keV/µm), and 14.8±1.2 Gy (99 keV/µm). The corresponding RBEs increased from 1.26±0.05 (16 keV/µm) up to 1.68±0.08 at 66 keV/µm. At 99 keV/µm, the RBE was comparable to that at 66 keV/µm. The preliminary analysis of the split dose experiments show a clear decrease of TD50 values and a more prominent increase in RBE compared to the single dose experiments.

**Conclusions:** Our data suggest a linear relation between RBE and LET in the measured dose range. The results after single dose irradiation show a clear linear increase of RBE with LET at least up to 66 keV/µm, whereas the preliminary analysis of the split dose experiments reveal a linear increase up to 99 keV/µm. After finalizing the data analysis and extending the experiments to 6 fractions, a comprehensive data base will be available to benchmark and improve RBE-models applied for carbon ion treatment planning.

**OC-0265**

Whole body response to radiation in head and neck and prostate cancer patient; the serum proteome comparative analysis

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Conclusions: For position verification, surgical clips in CBCT matches can be registered within an average accuracy of about 1 mm using routine clinical image registration procedures. However, the relative motion of the clips with respect to the surrounding anatomy must be taken into account for appropriate margin calculation. We will study the implementation of dual registration (simultaneous clip and global anatomy matching) to detect outliers with large relative motions in clinical practice.