Clinical outcome after MRI guided (chemo-)radiotherapy for advanced cervical cancer; a single center experience

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ABSTRACT

Purpose:
Treatment of patients with locally advanced cervical cancer (LACC) with (chemo) radiation has been subject to several major improvements including the implementation of 3D MRI guided and adaptive radiotherapy. For these patients UMCU is using MRI guidance for external beam radiotherapy and brachytherapy treatment planning since 2006 and since then has participated in international multicenter studies. Aim of this analysis was to report clinical outcome data of two consecutive UMCU patient cohorts included in the international Retro-EMBRACE and EMBRACE I studies (https://www.embracestudy.dk/ Potter, Tanderup et al. RO 2018).

Materials & Methods:
Data of 139 patients were investigated; all of them were treated with MRI guided (chemo)radiotherapy using IMRT or VMAT for external beam treatment in combination with cisplatinum monotherapy. Brachytherapy was delivered using MRI compatible applicators for intra-cavity/interstitial utero-vaginal applications (Utrecht applicator, ELEKTA, Veenendaal) and MRI based treatment planning. Within the Retro-EMBRACE cohort 39 patients received Pulsed Dose Rate (PDR) brachytherapy and 7 patients High Dose Rate (HDR) or a mix of HDR and PDR. In EMBRACE I 38 patients were treated with PDR and 55 with HDR schedules. Total planning aim for D90% HR-CTV was increased during time from >80 to >84 Gy EQD2. Chemotherapy consisted of weekly cisplatinum monotherapy. Outcome data of 46 patients treated in the early period including our learning phase (2006-2008) were retrospectively registered in Retro-EMBRACE, whereas data of 93 patients were prospectively registered in EMBRACE I (2008-2015). Analysis included tumor related outcome and morbidity data.
Results:
Median follow-up was 41 months for patients in Retro-EMBRACE and 36 months for EMBRACE I patients, respectively. FIGO stage distribution was comparable in both cohorts with about 80% of the patients having stage I/II disease and 20% having stage III and IV. Lymph node involvement at diagnoses defined by 3D imaging was 43% in Retro-Embrace and 63% in EMBRACE I. The actuarial rates for local control, cancer specific and overall survival at 3 years were 93, 74 and 65% in Retro-EMBRACE versus 98, 85 and 85% in EMBRACE I. Prospectively scored crude CTCAE morbidity rates grade 3 and higher in EMBRACE I were 7% for bladder, 7% gastrointestinal including rectum and 7% for vagina. Proctitis and rectal bleeding grade 2 and higher was scored in 15% of the PDR patients and 7% of HDR patients, while for vaginal stenosis grade 2 this was 42 and 25%, respectively.

Conclusions:
Treatment outcome for LACC patients has improved over time. MRI in the setting of 3D image guided brachytherapy with increasing dose to the primary tumor results in excellent local control rates and improved survival. With respect to treatment related side effects we still see some room for improvement. A promising tool for this is MRI guidance in combination with adaptive approaches for fractionated HDR brachytherapy as currently explored in the ongoing EMBRACE II study.