Early DWI in Assessing Tumor Response in Locally Advanced Cervical Cancer: Is There a Role in 3D MRI Guided Brachytherapy?

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Target Audience: Radiologists and radiology oncologists with expertise in gynecological malignancy.

Introduction: MRI is used for treatment planning and assessment for patients with cervical cancer undergoing fractionated high dose-rate brachytherapy (HDR-BT) following placement of an intracavitary applicator [1]. Diffusion-weighted imaging (DWI) coupled with conventional MRI has shown promise for residual tumor evaluation after external beam radiation therapy (EBRT) [2]. The purpose of our study was to assess the feasibility and impact of DWI in patients undergoing serial MRI-guided HDR-BT with ring and tandem applicator *in situ*.

Methods: 21 patients (mean age 47 years, range, 30-64) with locally advanced cervical cancer (squamous ca. 18/21; adenocarcinoma 3/21) treated between March 2011 to Sept 2012 underwent MRI-guided HDR-BT following standard chemoradiation with EBRT on a 1.5T GE HDXt platform. 3D isotropic (CUBE) and 2D FRFSE T2-weighted imaging, together with single shot echo-planar DWI were performed in the axial plane with b value of 700s/mm^2 (TR/TE 3800/71ms, slice thickness/gap 4/0.8mm, NEX 12, matrix 128x128, ASSET 2). MRI was obtained prior to EBRT (*Pre-RT$_0$ MRI*), and during 5 sessions of MRI-guided HDR-BT with intracavitary ring and tandem applicator *in situ* (*Post-RT$_{1\text{-}5}$ MRI*). Regions of interest around the tumor were drawn on ADC maps by an experienced radiologist with reference to the T2-weighted images, and the mean ADC (x 10^{-3}mm^2/s) calculated. T2 intensity of tumor (*T2-Tumor*), psoas muscle (*T2-Psoas*), and *T2-Tumor* /*T2-Psoas* (*T2-Ratio*) were calculated for normalization. Patients were categorized as complete response (CR) versus partial response (PR) after completion of therapy. Paired student t-test was used to compare *Pre-RT$_0$ T2-Ratio*, and ADC to the final *Post-RT$_5$* values, and to determine whether *Pre-RT*, mid-treatment *Post-RT$_1$*, and percentage change (*Post-RT$_1$ – Pre-RT$_0$*) differed between the CR and PR groups. Subgroup analysis was performed to determine whether the *Pre-RT$_0$* ADC varied by histology and tumor size.

Results: 2/21 patients were excluded, as no abnormal T2 signal was present after EBRT. 4/19 (21%) patients were classified as PR (3 adenocarcinoma, 1 squamous ca.), and 15/19 were classified as CR (15 squamous ca.) [Figs. 1,2]. The mean *Pre-RT$_0$* ADC was 1.08 (range: 0.91-1.66) with significant difference between the mean *Pre-RT$_0$* ADC of CR and PR groups (1.03 vs. 1.22, *p=0.046*). Subgroup analysis showed that *Pre-RT$_0$* ADC did not vary based on tumor size (<5 vs. >5 cm), however, there was a difference in the ADC between squamous and adenocarcinoma histology (1.03 vs. 1.31, *p=0.005*). In comparing *post-RT$_5$* to *Pre-RT$_0$* parameters, both *T2-Ratio* and ADC demonstrated a significant change with treatment; (2.4 vs. 2.0, *p*=0.01, 15% change) and (1.07 vs. 1.58, *p*<0.001, 50% change) respectively, and no difference in *T2-Psoas* signal (286 vs. 256, *p*=0.25) was identified. Mid-treatment *Post-RT$_1$* ADC, mid-treatment *Post-RT$_1$ T2-Ratio*, and percentage change from pre-therapy values for *Post-RT$_1$* ADC and *T2-Ratio* were not different between CR and PR groups and did not correlate with outcome (*p=0.98, 0.32,0.21,0.72* respectively).

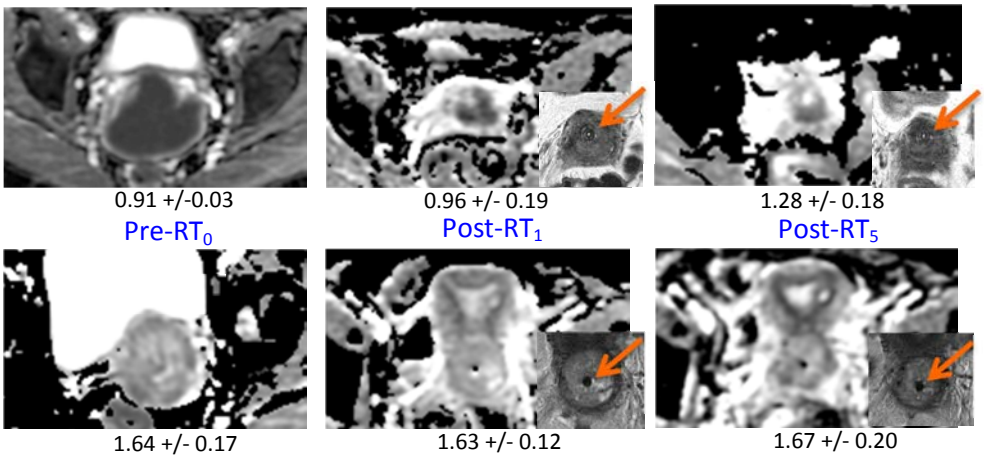

Fig. 1: ADC maps in 33 y.o with Stage IIB squamous ca. The mass has decreased in size after EBRT with *Post-RT$_1$* ADC (x 10^{-3}mm^2/s) of 0.96 during first HDR-BT session. During the fifth session, mass has decreased further in size. *Post-RT$_5$* ADC has increased to 1.28. Patient was considered CR after therapy. No significant artifacts in DWI with applicator in situ (arrow on T2 image).

Fig. 2: ADC maps in 62 y.o with Stage IIB adenocarcinoma. The mass has decreased in size after EBRT with *Post-RT$_1$* ADC (x 10^{-3}mm^2/s) unchanged at 1.63 during first HDR-BT session. During the fifth session, size has decreased slightly, but *Post-RT$_5$* ADC remains stable at 1.67. Patient was considered PR after therapy completion. No significant artifacts in DWI with applicator in situ (arrow on T2 image).

Conclusion: This study demonstrates the feasibility of DWI in treatment planning for patients undergoing HDR-BT with brachytherapy applicator *in-situ*. Both ADC and *T2-Ratio* reliably indicate treatment response, although ADC shows a wider dynamic range. Only pre-therapy ADC was statistically different between the CR and PR groups, with no outcome information provided by either ADC or *T2-Ratio*. Studies with large cohorts are needed to establish threshold values in defining residual disease at the time of brachytherapy and correlation with outcomes based on ADC.

References: 1) Haack S et al. *Acta Oncologica*. 2010;49:978-983 **2)** Somoye G et al. *Eur Radiol* 2012;22:2319-2327