CADOnc: A Computerized Decision Support System for Quantifying Radiation Therapy Changes in the Prostate via Multi-Parametric MRI

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Background: We present CADOnc©, a novel computerized segmentation, registration, and classification framework for quantifying changes in the prostate due to radiation therapy (RT) via multi-parametric MRI (Magnetic Resonance Spectroscopy, T2-weighted, Diffusion-weighted). Multi-parametric MRI has shown great potential in the early detection and staging of prostate cancer (CaP) [1]. Qualitative examination of such imaging is known to be difficult post-RT [1], with high inter- and intra-observer variability. There is thus a clear need for quantitative assessment of RT changes via multi-parametric MRI, in order to (a) identify residual disease, and (b) to identify new foci of cancer (local recurrence) within the prostate. CADOnc© provides a computerized solution to quantify (a) changes in specific multi-parametric MRI biomarkers in an automated manner, and to automatically quantify presence and extent of (b) residual disease, and (c) potentially new, recurrent tumors.

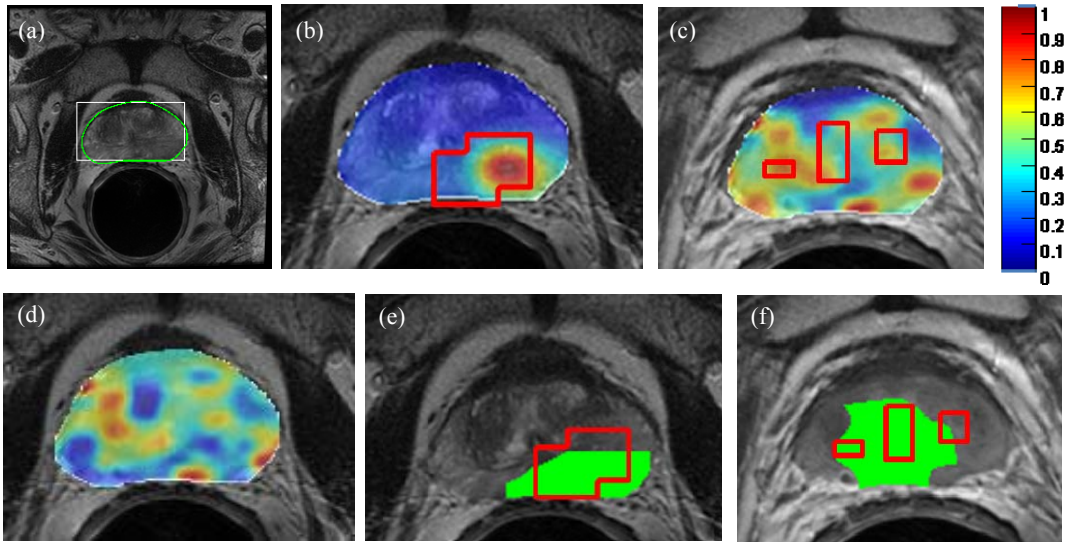
Methods: 7 *in vivo* patient datasets comprising both MRS and T2w MRI data were obtained. All patients underwent definitive external beam radiotherapy after initial MRI acquisition, with a mean interval of 5.4 months. Supplementary hormonal therapy had also been administered. Post RT, patients were reimaged via MRI. All MR imaging studies were performed in a whole-body MR scanner (Signa; GE), with a balloon-covered expandable endorectal coil for acquisition (parameters alongside). For MRS acquisition, a volume was selected via T2w MRI to maximize coverage of the gland without including the adjacent rectum and periprostatic fat. Spectroscopic data were acquired using a water- and lipid-suppressed double spin-echo point-resolved spectroscopy sequence (PRESS). PRESS imaging parameters were 1000/130 (TR/TE) with a 17-minute acquisition time. Spectral data were then apodized with a 1-Hz Gaussian function and Fourier transformed in the time domain and three spatial domains. The resultant data were zero-filled once in the time domain, after which the central 50% of each spectrum was extracted to obtain 512 data points. ADC maps were also calculated for those studies where DWI MRI was available. CADOnc© involves 4 distinct automated modules to analyze MR data: (i) Module 1 involves volumetric affine registration of pre- and post-RT MRI data via a spatially constrained mutual information (MI) similarity measure, thereby enabling quantitative per-pixel comparisons pre- and post-RT. (ii) Module 2 utilizes an automated prostate boundary delineation scheme for pre-RT T2w MRI [2], which makes use of a texture-classifier based Active Shape Model (ASM) algorithm. This prostate ROI delineation can also be utilized for post-RT T2w MRI (after registration), as well as ADC maps. (iii) Quantitative features which characterize texture and gradients on a per-pixel basis are derived from T2w MRI [6]. Metabolite quantification was used to characterize MRS data (area under choline, A_{ch}, creatine, A_{cr}, and citrate, A_{ci}, peaks) [1]. Note that citrate is known to be absent post-RT [1], and this was accounted for in our analysis. (iv) Module 4 integrates these descriptors into an automated unsupervised classification scheme [4], thereby allowing discrimination between different regions within the prostate.

Parameters	Pre-IMRT	Post-IMRT
Field Strength (T)	1.5	3
Matrix size	256 × 192	320 × 224
Slice thickness (mm)	3	3
TR (msec)	6000	6000
TE (msec)	100	95
	FSE	FSE

Results: Radiologist annotations of CaP and benign regions were obtained on a per-MRS voxel basis, and used as a ground truth surrogate for CaP extent. 4 studies were not utilized due to lack of sufficient labels. For all 3 studies considered: (1) CADOnc accurately identified regions of CaP on pre- and post-RT MRI (corroborated against ground truth), (2) Quantitative descriptor maps for T2w and ADC maps (where available), and metabolite peak areas and ratios (A_{ch},A_{cr},A_{ci}, A_{ch}/A_{cr}, $(A_{ch}+A_{cr})/A_{ci}$) were quantified (see figure), (3) CADOnc identified differences in A_{ch}/A_{cr}, T2w (intensities and texture) maps on post-RT MRI for diseased regions on pre-RT MRI, (4) Changes were identified for A_{ch}/A_{cr} and T2w (intensities and texture) maps to determine new foci of CaP on post-RT MRI.

Concluding Remarks: CADOnc© is a new computerized decision support framework for quantitatively analyzing radiation therapy changes within the prostate. CADOnc© comprises 4 distinct registration, segmentation, quantification, and classifier modules. On a small preliminary cohort of patient data, CADOnc© accurately quantified changes in specific multi-parametric MRI biomarkers, for both pre- and post-RT data. Further, quantitatively integrating these markers shows excellent utility in (1) predicting disease extent on pre-RT data, and (2) quantifying both residual and possible new foci of disease, post-RT.

References: [1] J. Kurhanewicz et al, *J Magn Reson Imaging*, 2002, v16(4), p. 451–63, [2] Anon, [3] Chan, I. et al, *Medical Physics*, 2003, v30(9): p. 2390-2398, [4] A.. Fred et al, *IEEE PAMI*, 2005, v27(6), p. 835-850.



(a) Initializing bounding box (white, via MRS) for automated ASM-based boundary delineation (result of capsule segmentation shown in green). (b) pre-IMRT Ch+Cr/Ci heatmap (from MRS), (c) post-IMRT Ch/Cr heatmap showing reduction in CaP and development of new cancer foci. (d) T2w MRI intensity difference heatmap. For heatmaps, red signifies areas of most change, blue of least change. Automated CADOnc detection result (green) via quantitative integration of T2w+MRS for (g) pre-IMRT, (h) post-IMRT data. Note that in (b)-(f) radiologist annotations of CaP regions are and are used as a surrogate for the ground truth, and are shown with a red outline.