Background: We present CADOnce\(^c\), a novel computerized decision support system for quantifying radiation therapy 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. CADOnce\(^c\) 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 spinecho 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. CADOnce\(^c\) 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.

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) CADOnce 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 ($A_{ch}/A_{cr}$, $A_{cr}/A_{ci}$, $A_{ch}/A_{cr}$, $(A_{ch} + A_{cr})/A_{ci}$) were quantified (see figure), (3) CADOnce 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: CADOnce\(^c\) is a new computerized decision support framework for quantitatively analyzing radiation therapy changes within the prostate. CADOnce\(^c\) comprises 4 distinct registration, segmentation, quantification, and classifier modules. On a small preliminary cohort of patient data, CADOnce\(^c\) 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.