Poster: Clinical track: Prostate

PO-0736

Tumour staging using MRI in prostate cancer: improvement of treatment decisions for radiotherapy

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Purpose or Objective: To assess and validate the incorporation of the multiparametric magnetic resonance imaging (mpMRI) tumor stage (mT-stage) to the conventional clinical tumor stage (cT-stage), in order to guide the radiotherapy (RT) treatment decisions in prostate cancer. In addition, to identify the clinical factors associated to the technique reliability.

Material and Methods: mpMRI was performed in 274 prostate cancer patients in order to refine the treatment decisions according to PSA, Gleason Score (GS) and cT-stage. Comparisons between the cT and mT-stage were performed, as well as the impact on the RT treatment prescription (target volume, doses and hormonal therapy [HT]) independently if it was finally performed. Changes in HT indication for intermediate risk with unfavourable factors were also analyzed. Until 2014, the unfavourable factors according to the initial criteria were a GS of 7 (4+3), or three unfavourable intermediate risk factors (T2b+PSA 10-20 ng/mL + GS 3+4), or T2c by digital rectal exam (DRE)/transrectal ultrasound (TRUS); more recently, unfavourable risk factors have been established according to Memorial Sloan Kettering Cancer Center (MSKCC) criteria: GS 4+3, or at least two intermediate-risk factors, or at least one intermediate-risk factor and a positive prostate biopsies (ppb) percentage greater than 50%. mpMRI validation was performed with pathological staging (n=90 patients finally decided to join surgery). To analyse the relationship between the reliability of mpMRI and the clinical variables, a univariate and multivariate logistic regression analysis was performed.

Results: The mpMRI upstaging range was 86-94% for any PSA value or GS. Following mpMRI, 32.8% of the patients (90/274) were assigned to a different risk group. Compared to cT-stage, mpMRI identified more intermediate-risk (46.4% vs. 59.5%) and high-risk (19.0% vs. 28.8%) prostate cancer patients. This resulted in a higher indication ($p<0.05$) of seminal vesicle irradiation (63.5% vs. 70.1%), inclusion of any extracapsular disease (T3-T4) within the target volume (1.8% vs. 18.2%), higher doses (65.3% vs. 88.3%) and more indication of HT associated to RT (45.6% vs. 62.4%), Table 1. Finally, decisions concerning RT were changed in 43.8% (initial criteria) or 52.5% (MSKCC criteria) of the patients, depending on the criteria applied to indicate HT in intermediate-risk patients. Global reliability of T-staging with DRE/TRUS was 8.8% (8/90), while it was 71.1% (64/90) for mpMRI. cT-stage was associated to a greater occurrence ($p<0.05$) of indication of inadequate RT treatments. mpMRI reliability was independent of PSA or GS or ppb percentage.

Table 1. Impact of mpMRI tumor staging on RT treatment prescription (target volume, doses and hormonal therapy).

Characteristics	DRE/TRUS n (%)	mpMRI n (%)	p value
T1-T2a	239 (87.2)	67 (24.5)	
T2b-T2c	30 (11.0)	157 (57.3)	<0.001
T3-T4	5 (1.8)	50 (18.2)	
Low-Risk (LR)	95 (34.7)	32 (11.7)	
Intermediate-Risk (IR)	127 (46.4)	163 (59.5)	<0.001
High-Risk (HR)	52 (19.0)	79 (28.8)	
Target volume			
VVSS prophylactic	174 (63.5)	192 (70.1)	<0.001
T3a+T3b+T4	5 (1.8)	50 (18.2)	
Doses			
Low	95 (34.7)	32 (11.7)	<0.001
High	179 (65.3)	242 (88.3)	
Hormonal Therapy			
HR and IR (Initial criteria)			
No	182 (66.4)	158 (57.7)	0.035
Yes	92 (33.6)	116 (42.3)	
HR and IR (MSKCC criteria)			
No	149 (54.4)	103 (37.6)	<0.001
Yes	125 (45.6)	171 (62.4)	
Hormonal Therapy in IR patients			
Initial criteria			
No	220 (80.3)	221 (80.7)	0.914
Yes	54 (19.7)	53 (19.3)	
MSKCC criteria			
No	180 (65.7)	144 (52.6)	0.002
Yes	94 (34.3)	130 (47.4)	
Hormonal Therapy in HR patients			
No	222 (81.0)	195 (71.2)	0.007
Yes	52 (19.0)	79 (28.8)	

VVSS seminal vesicles, *DRE/TRUS* digital rectal exam/transrectal ultrasound

Conclusion: mpMRI tumor staging significantly improved the RT treatment decisions in all prostate cancer risk groups. The magnitude of the impact on final RT treatment decisions will depend on the institution's clinical protocol for prostate cancer management.

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Predictors of PSA relapse in patients with intermediate risk prostate cancer treated with SBRT

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Purpose or Objective: SBRT has demonstrated favorable outcomes in selected patients with early stage localized prostate cancer. Treatment of patients with intermediate risk disease remains cautionary due to the heterogeneity within this population with respect to risk for occult extraprostatic disease. Here we report an analysis of PSA outcomes following SBRT for intermediate risk prostate cancer and identify disease specific risk factors for biochemical failure.

Material and Methods: Patients treated with SBRT at Georgetown University Hospital for intermediate risk prostate adenocarcinoma, with or without the use of androgen deprivation therapy (ADT), were included in this retrospective analysis. Treatment was delivered using CyberKnife® SBRT with doses of 35 Gy or 36.25 Gy in 5 fractions. PSA failure was defined as a rise > 2 ng/ml above nadir (ASTRO Phoenix definition) and analyzed using the Kaplan Meier method. A Cox proportional hazards model was generated using disease related covariates including T stage, primary gleason pattern, pretreatment PSA, number of positive cores, percent positive cores, maximum single core involvement in order to identify potential predictors of PSA relapse after SBRT. A logrank test was also used to compare patients classified as having favorable vs. unfavorable intermediate risk disease by previously reported criteria of primary gleason pattern 4, 50% cores involved, or ≥2 intermediate risk factors.

Results: Three hund;red and fifty three patients at a median age of 70 years (range, 46 to 90) received SBRT. ADT was initiated prior to SBRT in 16% of patients and the median pre-

treatment PSA was 7.2 ng/ml (range, 0.8 to 19.9). The overall 3-year biochemical relapse free survival (bRFS) was 93.9%. Cox regression identified primary gleason pattern as the only significant predictor of PSA relapse with a HR of 5.84 (1.92 to 17.8, 95% CI) for primary gleason pattern 4 vs. 3. There was no significant difference in bRFS between patients classified as having favorable vs. unfavorable intermediate risk disease, HR 0.39 (0.11 to 1.41, 95% CI). There were no significant benefits observed with respect to ADT in any subgroup.

Conclusion: Early PSA responses after SBRT for intermediate risk prostate adenocarcinoma compare favorably to those reported using other radiation therapy modalities. Primary gleason pattern 4 is predictive of less favorable bRFS, however early rates of PSA control are excellent compared to historical controls. The role of ADT in these patients is still unclear. The current evidence supports SBRT as a standard therapeutic option in intermediate risk disease.

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Hydrogel injection prevents long-term rectal toxicity after radiotherapy for prostate cancer

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Purpose or Objective: The aim of the study was to compare health-related quality of life (QoL) after external beam radiotherapy (RT) for prostate cancer with and without a hydrogel spacer.

Material and Methods: A group of 202 patients with the indication for treatment of the prostate +/- base of seminal vesicles without pelvic lymph nodes was treated in a single institution in the years 2010-2013. Depending on the patient's and responsible radiation oncologist's preference, 108 patients were selected for a hydrogel injection before the beginning of RT. The injection of 10 ml hydrogel was performed under transrectal ultrasound (TRUS) guidance after dissecting the space between prostate and rectum with a saline/lidocaine solution under local anaesthesia. Treatment was performed with a five-field IMRT or VMAT technique with daily ultrasound based image guidance. Only for patients with a spacer the prescription dose was increased from 76Gy to 78Gy, subsequently 80Gy. Patients were surveyed prospectively before RT (time A), at the last day of RT (time B), a median time of two months (time C) and seventeen months after RT (time D) using a validated questionnaire (Expanded Prostate Cancer Index Composite; comprising 50 items concerning urinary, bowel, sexual and hormonal domains). The multi-item scale scores were transformed lineary to a 0-100 scale, with higher scores representing better QoL. Baseline QoL assessment was available from 101 / 66 patients with / without a spacer. Responses to both the baseline and last (time D) questionnaire were available in 94 / 57 cases with / without a spacer.

Results: Apart from higher prescription doses in the spacer group, baseline patient characteristics were well balanced between patients with vs. without a spacer (Table). In particular, baseline QoL was comparable. Acute toxicity (corresponding to QoL changes at times B and C relative to baseline levels) did not differ significantly, with only a tendency for better scores in the spacer group. However, mean bowel bother scores >1 year after RT in comparison to baseline did not change for patients with a spacer (mean change of 0 points) in contrast to patients without a spacer (mean decrease of 7 points). Long-term mean urinary bother scores did not decrease in both groups. At time D, statistically significant differences were found in the function items "bloody stools", "painful bowel movements" and "frequency of bowel movements". Focusing on patients with no problem with bowel symptoms initially, 0% vs. 12% with vs. without a spacer reported a moderate/big problem with bowel symptoms >1 year after RT ($p<0.01$).

		with spacer	without spacer
patient age (years); median (range)		72 (49-82)	73 (53-85)
PTV (cm^3); median (range)		127 (37-335)	123 (36-300)
prescription dose to PTV ≤76Gy / 78Gy / 80Gy; %		64* / 26* / 10*	100* / 0* / 0*
PSA (ng/ml); median (range)		7.6 (2.3-83)	7.3 (1.8-94)
low/intermediate/high risk patients; %		33 / 37 / 30	33 / 42 / 26
urinary bother score; mean	before RT	84	79
	decrease at time B/C/D	18 / 14 / -1	21 / 17 / -2
bowel bother score; mean	before RT	94	93
	decrease at time B/C/D	14 / 3 / 0*	18 / 6 / 7*
sexual bother score; mean	before RT	66	66
	decrease at time B/C/D	6 / 12 / 12	9 / 19 / 17

*p<0.01 (significant differences between groups)
negative decrease corresponds to quality of life improvement

Conclusion: Though acute rectal symptoms are still reported, spacer injection is associated with a significant long-term benefit for patients after prostate cancer RT.

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IMRT versus 3D conformal radiotherapy when used in combination with I-125 prostate brachytherapy

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Purpose or Objective: To compare biochemical outcomes and toxicity of intensity modulated radiotherapy (IMRT) and three-dimensional conformal radiotherapy (3D-CRT) when used in combination with I-125 brachytherapy (BT) for the treatment of unfavorable-risk prostate cancer.

Material and Methods: A retrospective review was performed on 839 patients with localized prostate cancer who received external-beam radiotherapy (EBRT) following BT between 2003 and 2012. Patients were categorized into National Comprehensive Cancer Network risk groups: 616 were unfavorable intermediate-risk (Gleason score 4+3, or Gleason score 3+4 with positive biopsy core rate >1/3), and 223 were high-risk. Treatment begins with BT, followed 6 weeks later by 45 Gy/25 fractions of EBRT. EBRT was delivered via 3D-CRT in 616 men at first and via IMRT technique for 223 men after 2010. The prescription dose for I-125 was 100 Gy, up to 110 Gy after 2009. All patients underwent a CT scan for postplan dosimetry at day 30. The rectal volumes receiving doses higher than 30 Gy, 35 Gy, and 40Gy should be kept under 35%, 25%, and 15%, respectively. Neoadjuvant androgen deprivation therapy was given to 45% of patients. Biochemical failure was defined with the Phoenix criteria, and toxicity was graded according to the National Cancer Institute's Common Terminology Criteria for Adverse Events, prospectively collected. The median (range) follow-up was 7 (2-12) years for the entire cohort; 8.3 years for 3D-CRT, and 4.3 years for IMRT. The biological effective dose (BED) was calculated using an α/β of 2 Gy and the D90 values of the prostate on a day-30 CT scan. Comparisons were made by chi-square test and log-rank test.

Results: The total BED value of the prostate was higher in the IMRT group than in the 3D-CRT group (219 Gy2 vs. 209 Gy2, $p<0.001$). The 5-year actuarial freedom from biochemical failure for the IMRT group vs. the 3D-CRT group were 92.7% vs. 92.6% ($p=0.825$) for all; 95.4% vs. 95.1% for intermediate-risk, and 88.0% vs. 84.8% for high-risk group ($p=0.788$), respectively. Acute gastrointestinal (GI) grade 2+ toxicities occurred in 0.5% of the IMRT group and 2.7% of the 3D-CRT