

Gruczoł krokowy - hipofrakcjonowanie, radiochirurgia

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Materials/Methods: In pDJDC plans, we use a beam set with 4-6 ports to the targets at the same level in the craniocaudal direction and employ another beam set for other targets using different port angles (9-12 angles in total). The couch moves fast during the intervals between the different beam sets. In 7 patients, 2 plans using the pDJDC and HDJ techniques were compared. Four of the 7 patients had multiple (n=2-6) distant metastases including those to the rib and lymph node and peritoneal dissemination. Two patients had esophageal cancer with 3 targets including a primary tumor and regional metastases. The other patient had 2 pleural disseminations from a thymic tumor. For multiple distant metastases, 25-40 Gy in 2- to 5-Gy fractions were prescribed for the planning target volumes at D50%. For esophageal cancer, 20-22 Gy in 2-Gy fractions were prescribed as boost plans. For thymic tumor, 60 Gy in 7.5-Gy fractions were prescribed. Conformity index, uniformity index (D5%/D95%), dose distribution in the lung, and beam-on time were evaluated using Wilcoxon signed-rank test.

Results: The median conformity index of all 7 patients was 3.0 for the pDIDC plans and 2.4 for the HDJ plans (p=.031). The median uniformity index of the planning target volume (n=25) for the 2 plans was 1.048 and 1.057, respectively (p=.10). For 5 patients with thoracic targets, the median of the mean lung dose was 2.6 Gy and 2.4 Gy, respectively (p=.63). The median V5Gy and V2OGy of the lung in the 5 patients were 11.8% and 8.5% (p=.63) and 1.6% and 2.1% (p=.32), respectively. The pDIDC plans reduced the beam-on time by 52% compared to the HDJ plans (median: 421 and 883 seconds, respectively, p=.03).

Conclusion: The pDJDC technique enables treatment of multiple targets in half time compared to the HDJ technique. The pDJDC plans were comparable to the HDJ plans in dose distribution except the conformity index. Author Disclosure: Y. Manabe: None. Y. Shibamoto: None. A. Torii: None. M. Niwa: None. T. Kondo: None. D. Okazaki: None. T. Murai: None. C. Sugie: None.

TU_15_3046

Oligometastases - New Era of Cancer Therapy?

A. Napieralska, W. Majewski, and L. Miszczyk; Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Gliwice, Poland

Purpose/Objective(s): The aim of the study is to evaluate treatment result of cancer patients (pts) with oligometastatic disease.
Additional identification of prognostic and predictive factors was also performed.

Materials/Methods: Inclusion criteria were: histological confirmation of cancer, one to three metastases (mets), except brain mets, stereotactic radiotherapy (SBRT) as local treatment of metastatic lesion, at least one follow-up (FU) visit. Group consisted of 542 consecutive cancer pts (186 female, 356 male; age 21-85, median 66) treated in 2004 – 2017 with SBRT due to 698 mets, including 241 lung (35%), 227 lymph node (32%), 106 bone (15%), 105 liver (15%) and 19 adrenal/soft tissue mets (3%). Median time to develop mets was 21 months after the primary diagnosis (range 0-315). Majority (91%) received primary radical treatment. SBRT total dose ranged from 6 to 60 Gy (median 36) delivered in fractions of 5 to 20 Gy (median 12). In statistical analysis Kaplan - Meier method, log rank test and multivariate Cox regression model were used.

Results: Follow-up (FU) ranged from 0.3 to 28.8 years (median 14.2) from primary diagnosis, from 0.3 to 17.2 years (median 6.6) from mets diagnosis and 0.1 to 9.8 years from mets SBRT (median 5.6). Five. 10., and 15-year overall survival (OS) was 81%, 61% and 46%, respectively. Local control after SBRT was achieved in 91% pts and remained stable to the end of PU in 80%. Other mets occurred in 51% of pts after SBRT. Multivariate analysis showed that time of mets detection (oligometastases vs oligorecurrence, p=0.000), age (p=0.03), type of treatment of primary tumor (radical vs palliative, p=0.000). location of mets

(p=0.002) and performance status (p=0.001) are significant factors influencing OS. Patients in oligometastatic group had 5-year OS from SBRT of 37% compared to 58% in oligorecurrence group (p=0.0003). Lung and gastrointestinal cancer pts are those who benefit the most from implementation of radical therapy in primary treatment (p=0.000 and 0.003, respectively). SBRT responders with liver and lymph node mets had better OS (p=0.0002 and 0.0099, respectively) and those with liver, bone and lung mets had improved PFS (p=0.0001, 0.011 and 0.003, respectively) compared to non-responders. Type of primary treatment (p=0.000), type of cancer (p=0.04) and performance status (p=0.02) were significant factors influencing PFS after SBRT in multivariate analysis. Type of cancer (p=0.006), location of mets (p=0.013) and presence of other than treated with SBRT mets (p=0.026) were significant factors influencing LC after SBRT in multivariate analysis. LC and PFS was better in pts with SBRT total dose over 50 Gy (p=0.008 and 0.0008, respectively).

Conclusion: Primary radical treatment of oligometastatic cancer pts in SBRT mets group improved OS and PFS, and should be applied in those in good performance status. Patients with oligometastases had inferior OS compared to oligorecurrence group.

Author Disclosure: A. Napieralska: None. W. Majewski: None. L. Miszczyk: None.

TU_16_3047

Consideration of Functional Status as a Tool to Predict Treatment Interruptions for Patients Receiving Palliative Radiation for Bone and Brain Metastases



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Purpose/Objective(s): Treatment interruptions are an infrequently studied topic in radiation therapy (RT). Minimizing interruptions is essential, as prolonged treatment courses predict for persistent regional disease and decreased owerall survival. To our knowledge, treatment interruptions have not yet been examined in patients receiving palliative radiation. Finding ways to predict for interruptions in this population can allow for increased treatment tolerance through methods such as hypofractionation. Kamofsky Performance Status (KPS) is a frequently used tool to quantify the functional status of cancer patients. However, its use in predicting palliative radiation treatment interruptions is unknown. This study investigated whether KPS, comorbidity, treatment location, or socioeconomic status (SES) are predictive of treatment interruptions in an ethnically diverse population.

Materials/Methods: This retrospective study included patients who received palliative radiation to the brain, spine, or bone between January 1°, 2016 and June 30°, 2016. Patients were treated either at a private academic hospital (PAH) or an adjacent safety-net hospital (SNH). Variables analyzed included treatment location, gender, socioeconomic status (SES), age, comorbidity (ACE-27 comorbidity index), and KPS score (stratified into good, fair, or poor). Patients were classified as having a major treatment interruption if they missed ≥ 2 treatments or ended RT prematurely. Univariable (UVA) and multivariable analyses (MVA) were performed by using the logistics regression model. Odds ratios (ORs) were estimated along with corresponding 95% confidence intervals and p-values. All p-values were two-sided.

Results: 124 patients were included in this study. 65.3% of patients were treated with palliative RT to the spine or bone, and 34.7% of patients were treated to the brain. 81.5% of patients were treated at the private academic hospital and 18.5% were treated at the safety-net hospital. 31.5% of patients had a good KPS score, 50.8% of patients had a fair KPS score, and

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Multi-Institutional Analysis of Prostate-Specific Antigen Kinetics Following Stereotactic Body Radiation Therapy

Naomi Jiang, MD

N. Jiang¹, C. R. King¹, A. T. Dang¹, Y. Yuan¹, S. P. Collins², S. Suy², C. A. Mantz³, L. Miszczyk⁴, A. Napieralska⁴, A. Namysl-Kaletka⁴, H. Bagshaw⁵, N. Prionas⁵, M.K. Buyyounouski⁵, Fang-I Chu¹, N. G. Nickols¹, D. Shabsovich¹, M. L. Steinberg¹, P. A. Kupelian¹, and A. U. Kishan¹

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SBRT for Prostate Cancer





Multi-Institutional Analysis of Prostate-Specific Antigen Kinetics Following Stereotactic Body Radiation Therapy

Naomi Jiang, MD

N. Jiang¹, C. R. King¹, A. T. Dang¹, Y. Yuan¹, S. P. Collins², S. Suy², C. A. Mantz³, L. Miszczyk⁴, A. Napieralska⁴, A. Namysl-Kaletka⁴, H. Bagshaw⁵, N. Prionas⁵, M.K. Buyyounouski⁵, Fang-I Chu¹, N. G. Nickols¹, D. Shabsovich¹, M. L. Steinberg¹, P. A. Kupelian¹, and A. U. Kishan¹

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PSA data was retrospectively collected from 5 different institutions

- 1062 low- and intermediate-risk PCa patients
- Treated with SBRT from 2004-2016
- 35-40 Gy in 5 fractions

Exclusion Criteria:

- Androgen deprivation therapy (ADT)
- <12 months of PSA data



	Low-Risk	Favorable Intermediate- Risk	Unfavorable Intermediate- Risk	Total	P-value
Median iPSA (IQR)	5.6 (4.4 – 6.9)	6.9 (5.1 – 9.4)	8.4 (5.4 – 11.2)	6.1 (4.8 – 8.3)	<0.001
Median nPSA (IQR)	0.2 (0.1 – 0.3)	0.2 (0.1 – 0.4)	0.2 (0.1 – 0.5)	0.2 (0.1 – 0.3)	0.06
≤ 0.5 ng/ml	489 (89%)	245 (82%)	159 (76%)	893 (84%)	<0.001
Biochemical Failure	2 (0.4%)	3 (1.2%)	7 (4.4%)	12 (1.3%)	<0.01
≤ 0.2 ng/ml	312 (57%)	152 (51%)	109 (52%)	573 (54%)	0.21
Biochemical Failure	1 (0.3%)	2 (1.3%)	2 (1.8%)	5 (0.9%)	0.16



- This is the largest study to date examining the PSA response after SBRT for low- and intermediate-risk PCa
- Results corroborate previously published SBRT PSA kinetics studies
- It is important to counsel patients regarding the benign PSA bounce phenomenon to decrease anxiety & unnecessary work-up
 - Occurs in about 1 in 4 patients
 - Long median time to bounce (18.1 months)
 - Large median bounce magnitude (0.52 ng/ml)
- Future Directions: Large-scale studies are needed to directly compare the PSA response of patients who receive SBRT versus other common treatment modalities





Erectile function after high-dose-rate brachytherapylike stereotactic body radiotherapy for organ-confined prostate cancer

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Sexual Health Inventory For Men (SHIM)

- Conclusion:
- Only <u>higher baseline SHIM score</u> and a <u>smaller pre-SBRT prostate volume</u> were correlated with improved long-term post-treatment erectile function post-SBRT
- Age as a continuous variable doesn't predict
 - (but age < 60 years borderline predicts significantly lower ED risk vs. whole group) (36% vs 64%)
- Testosterone level doesn't ever reach statistical significance, but at 6/7 evaluation points, the "not failed" group has a higher median T-level than "failed"
- No prostate, penile bulb or neurovascular bundle dosimetry variable had any significant measurable potency outcome correlation, nor did "risk group."
- This suggests that "patient factors" are more significant than "dosimetry factors" in predicting sexual QOL domain outcome post-SBRT.



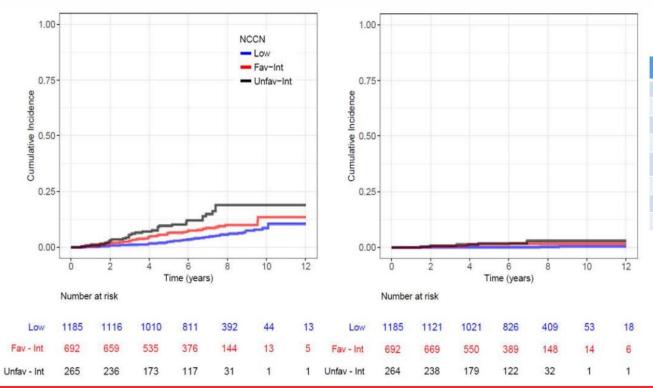
Long-Term Outcomes of Stereotactic Body Radiation Therapy for Low- and Intermediate-Risk Prostate Adenocarcinoma: A Multi-Institutional Consortium Study

A. U. Kishan¹, A. Katz², C. A. Mantz³, F. I. Chu¹, L. Appelbaum⁴, D. A. Loblaw⁵, I. D. Kaplan⁴, H. T. Pham⁶, M. K. Buyyounouski⁷, D. B. Fuller⁸, R. Meier⁹, S. P. Collins¹⁰, N. Shaverdian¹, A. T. Dang¹¹, Y. Yuan¹, H. P. Bagshaw⁷, N. D. Prionas¹², N. Nickols¹, M. L. Steinberg¹, and C. R. King¹

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BCR and DM Outcomes



Kaplan-Meier Estimates

7-Year BCR Rates

Low: 4.5%

Favorable Intermediate: 8.6% Unfavorable Intermediate: 14.9%

7-Year DM Rates

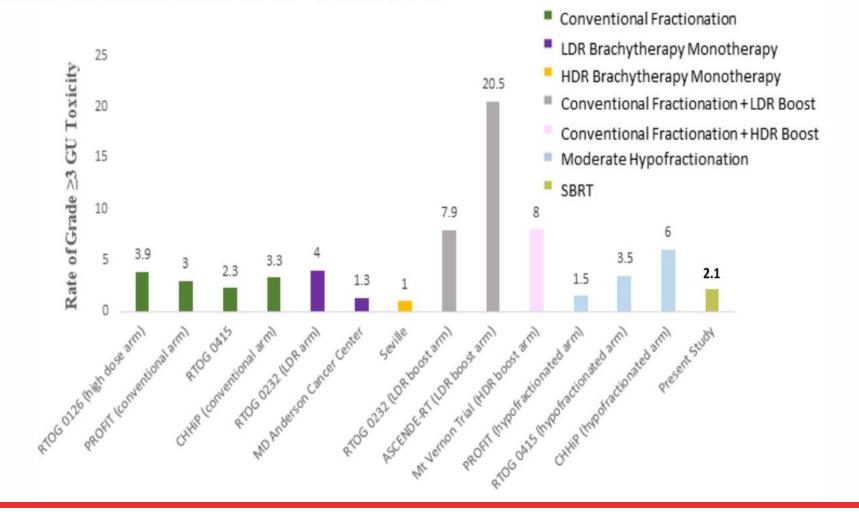
Low: 0.1%

Favorable Intermediate: 1.7%

Unfavorable Intermediate: 3.0%

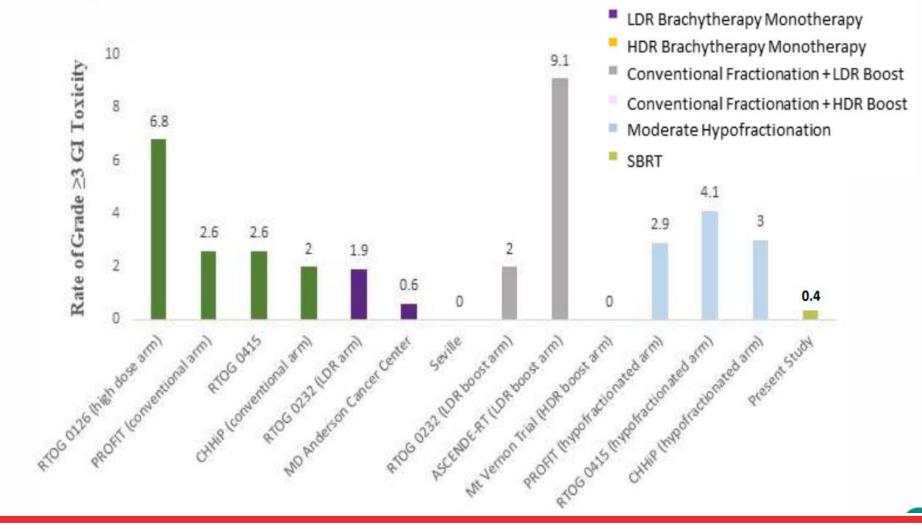


Comparative GU Toxicity





Comparative GI Toxicity



Conventional Fractionation



Conclusions

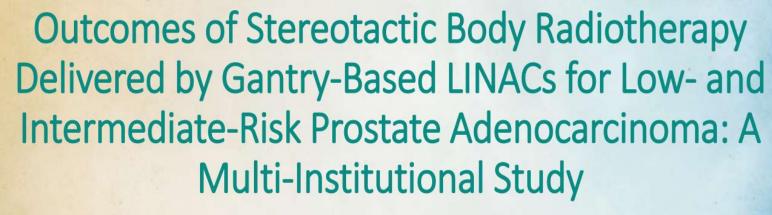
 The long-term safety and efficacy profile of SBRT compares favorably with other established radiotherapy modalities in the treatment of low- and intermediate-risk disease

 SBRT should be considered <u>a</u> standard of care option for low- and intermediate-risk PCa

Randomized data are forthcoming





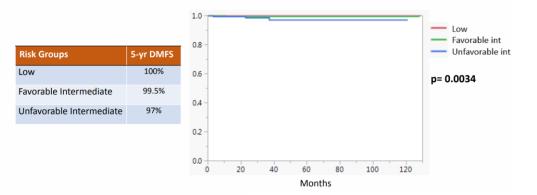


A. T. Dang, C. R. King, D. Shabsovich, C. A. Mantz, K. L. Stephans, D. A. Loblaw, P. Cheung, M. Scorsetti, L. Cozzi, A. S. DeNittis, Y. Wang, N. Nickols, P. A. Kupelian, M. L. Steinberg, and A. U. Kishan

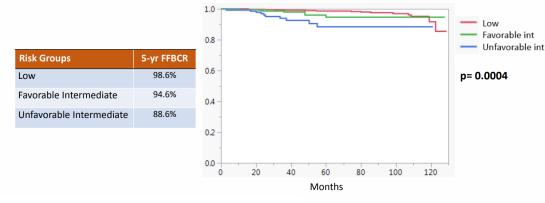




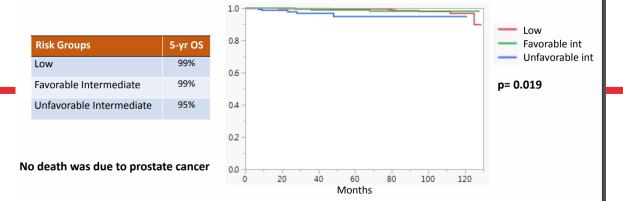
Results – Distant Metastasis-Free Survival



Results – BCR Free Survival



Results - Overall Survival



Stereotactic Body Radiation Therapy for Unfavorable Intermediate- and High-Risk Prostate Cancer: 3-year Outcomes of a Phase-II Trial

<u>Victor Macias</u>, MD, PhD (1,2); I. Barrera-Mellado, PhD (3); C. Marti, MD, PhD (1); A. Pont (4); A. Fernandez-Lara (1); P. Soria. MD, PhD (1).

- (1) Salamanca University Hospital. (2) Valladolid University Hospital.
- (3) University of Salamanca. (4) Hospital del Mar Research Institute. Spain.



Patient characteristics

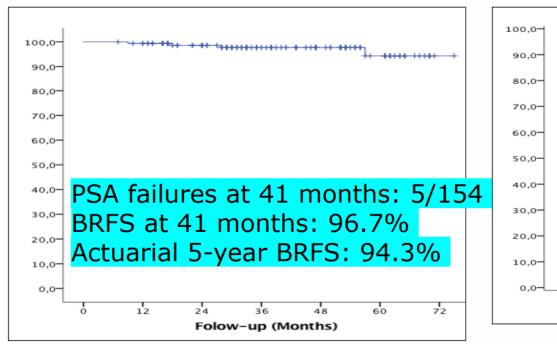
- 154 patients (9/2012 12/2017). Median age 71 (50-81).
- NCCN Low-risk: 29/154 (18.8%)
 Unfavorable Intermediate-, High-, Very high-risk: 91/154 (59.1%)
 Gleason 8-10: 18.1%; cT3: 19.7%; Mean PSA: 13.5 ng/ml (1.2 214 ng/ml)
- ADT: 72%; Long-term ADT (2-year LHRH analogue): 21.4%.
- Median follow-up: 41 months (9-76), 80% > 24 months
- Median irradiation time: 13 minutes (6-18).
 2/3 patients ≥ 100 miles round-trip drive.

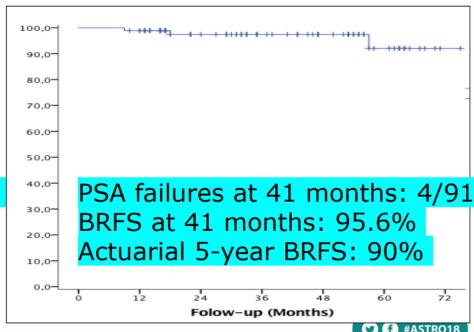


Biochemical Relapse Free Survival (nadir + 2 ng/ml)

Whole Series

Unfavorable Intermediate, High & Very High-Risk







- SBRT for unfavorable intermediate- and high-risk PCa is feasible and safe.
- Low rates of late urinary or rectal toxicity were observed.
- Its impact on health-related quality of life was mild and temporary.
- The 5-year biochemical relapse-free survival rate is encouraging (≥ 90%).
- SBRT for (unfavorable) High-Risk patients remains investigational until the outcomes over 5 years of follow-up and the findings of phase III trials validate these preliminary results.



Translating Discovery to Cure

Stereotactic body radiation therapy for locally recurrent prostatic carcinoma after prior therapeutic irradiation: Prostate-specific antigen response, disease-free survival, and toxicity

Donald Fuller (1), James Wurzer (2), Steven Bridge (1), Reza Shirazi (1), Jonathan Law (2), George Mardirossian (1)

(1) Genesis Healthcare Partners - San Diego; (2) Atlanticare - New Jersey



Stereotactic body radiation therapy for locally recurrent prostatic carcinoma after prior therapeutic irradiation:

Conclusions:

- PSA response kinetic is similar vs "de novo" RT, in spite of "conservative" dose (34 Gy/5 fx)
 - Except 24% relapse rapidly (≤ 2 years); consider "prostate-specific" PET/CT pre-salvage
- <u>5 yr. bRFS</u> 60% Comparable w HDR and w RP salvage series (UCSF(1), MSKCC(2), COH (3))
 - NOTE: 78% bRFS if PSA < 6.92 ng/mL at salvage (p=0.0001 versus higher PSA; Log-Rank)
- <u>Clinical Efficacy</u> is good to 5 years LRFS = 94%; DRFS = 89%;
- <u>ADT deferred > 5 yr = 69%</u>
- Toxicity GU is the main toxicity 8% G3+ (3% if ltd to "conventional" EBRT salvage)
 - GI toxicity is a NON issue in this study (0% G2+ GI toxicity)
 - ED Most had this PRE-salvage; ~80% of the rest lost it by 5 years POST-salvage
- Safe and effective: "HDR-like" SBRT salvage w this dose and these margins is ...
 - Our IRB has now approved sample n = 100



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Moderate hypofractionation for PCP



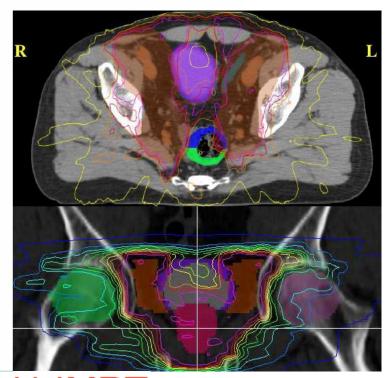
10-year Results of a Randomized Prospective Trial of Conventional Fractionated Versus Moderate Hypofractionated Radiation Therapy for Localized Prostate Cancer

Vladimir Avkshtol, MD; Tianyu Li, MS; Mark A. Hallman, MD, PhD; Richard E. Greenberg, MD; Robert A. Price, Jr, PhD; Robert G. Uzzo, MD; Charlie Ma, PhD; David Chen, MD; Daniel M. Geynisman, MD; Alan Pollack, MD, PhD; Eric M. Horwitz, MD



- Intermediate-risk prostate cancer:
 - Prescribed 4 months of ADT at the discretion of the treating physician
- High-risk prostate cancer:
 - Prescribed 2 years of ADT for all men
- CTV1: Prostate gland and proximal seminal vesicles
- CTV2: Distal seminal vesicles
- CTV3: Pelvic lymph nodes
 - Periprostatic, periseminal vesicle, external iliac, obturator, and internal iliac lymph nodes
- Intermediate-risk prostate cancer: CTV1 only
- High-risk prostate cancer: CTV1, 2, and 3

C-IMRT **76Gy in 38 fractions**



H-IMRT

70.2Gy in 26 fractions Df 2.7 Gy



Results: Disease Outcomes

Table 2. Disease Outcomes by Treatment Group

Outcome	5-year		10-year		UVA	MVA	
	C-IMRT %	H-IMRT %	C-IMRT %	H-IMRT %	P-value	HR	95% CI
BCDF	12%	17.4%	25.9%	30.6%	0.25	1.42	0.86 - 2.32
BF	9.1%	11.9%	21.2%	25.4%	0.5	1.26	0.74 - 2.2
Metastatic rate	4%	7.3%	5.3%	12.7%	0.06	2.12	0.97 - 4.63
os	92.7%	89.4%	78.4%	71.1%	0.16	1.43	0.93 – 2.19
PCSM	1.3%	2.7%	2.7%	4%	0.71	1.27	0.4 - 4.1

Biochemical and/or clinical failure (BCDF), biochemical failure (BF), overall survival (OS), prostate cancer specific mortality (PCSM)







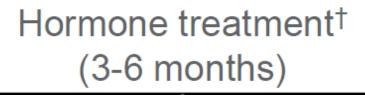
CHHiP

Changes in patient-reported outcomes from baseline up to 5 years in the CHHiP trial (Comparison of hypofractionated high-dose intensity-modulated radiotherapy schedules for prostate cancer) (CRUK/06/016)

John Staffurth*, Joanne Haviland*, Anna Wilkins, Isabel Syndikus, Vincent Khoo, David Bloomfield, Chris Parker, John Logue, Christopher Scrase, Alison Birtle, Zafar Malik, Miguel Panades, Chinnamani Eswar, John Graham, Martin Russell, Peter Kirkbride, Joe M O'Sullivan, Clare Cruickshank, David Dearnaley†, Emma Hall† on behalf of the CHHiP Trial Management Group

ASTRO October 2018



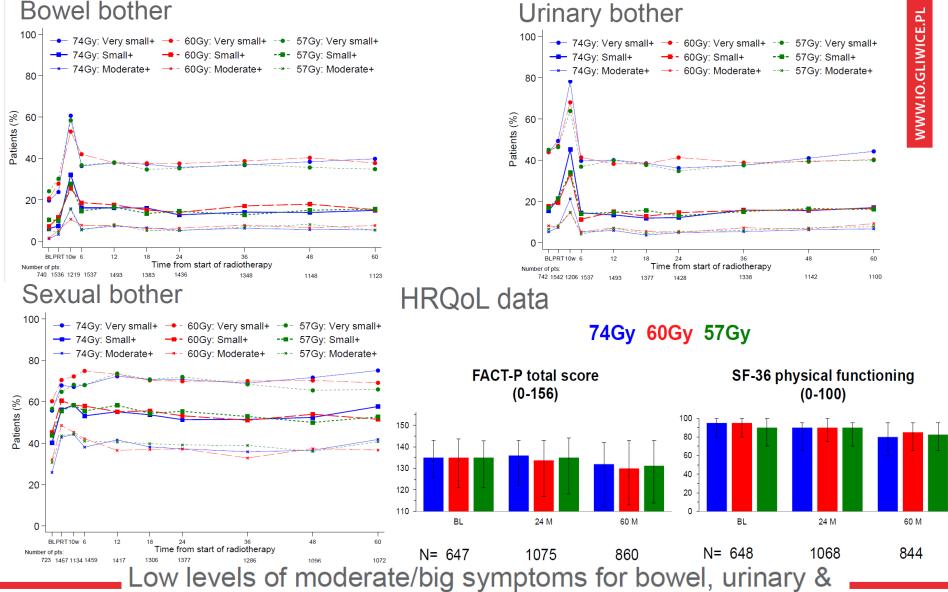


Clinical T1b-T3a, N0, M0
Risk of seminal vesicle involvement* ≤ 30%
PSA ≤ 30ng/ml

Randomise 1:1:1 N=2054 (%)

74Gy / 37f 7.4wks 60Gy / 20f 4wks 57Gy / 19f 3.8wks





sexual bother at 5 years in all schedules

Change in bowel or urinary symptoms up to 5 years similar between schedules

Rekomendacje ASTRO



Hypofractionated RT for Localized Prostate Cancer: An ASTRO, ASCO, and AUA Evidence-Based Guideline



Hypofractionated Radiation Therapy for Localized Prostate Cancer: Executive Summary of an ASTRO, ASCO, and AUA Evidence-Based

Scott C. Morgan MD, MSc, FRCPC *, Karen Hoffman MD, MHSc, MPH *, D. Andrew Loblaw MD, MSc, FRCPC, FASCO *, Hark K. Buyyounouski MD, MS ... Caroline Patton MA Daniel Barocas MD, MPH 5, Soren Bentzen DSc. PhD 5 Aichael Chang MD (), Jason Efstathiou MD, PhD (), Patrick Greany PhD (), Per Halvorsen MS (), Bridget F, Koontz MD (),

Introduction and Process

Scott Morgan, MD, MSc, FRCPC Division of Radiation Oncology The Ottawa Hospital and University of Ottawa Ottawa, Ontario, Canada



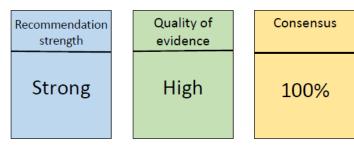
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KQ1 Recommendation Statements

<u>Prostate cancer control outcomes: Impact of risk</u> <u>stratification group</u>

 KQ1A: In men with <u>low-risk</u> prostate cancer who decline active surveillance and receive EBRT to the prostate with or without radiation to the seminal vesicles, <u>moderate hypofractionation should be</u> offered.



 KQ1B: In men with <u>intermediate-risk</u> prostate cancer receiving EBRT to the prostate with or without radiation to the seminal vesicles, <u>moderate</u> hypofractionation should be offered. Recommendation strength

Quality of evidence

Consensus
100%

Prostate cancer control outcomes: Impact of risk stratification group

 KQ1C: In men with <u>high-risk prostate</u> cancer receiving EBRT to the prostate, but not including pelvic lymph nodes, <u>moderate hypofractionation should be offered</u>.

Recommendation strength

Quality of evidence

Strong

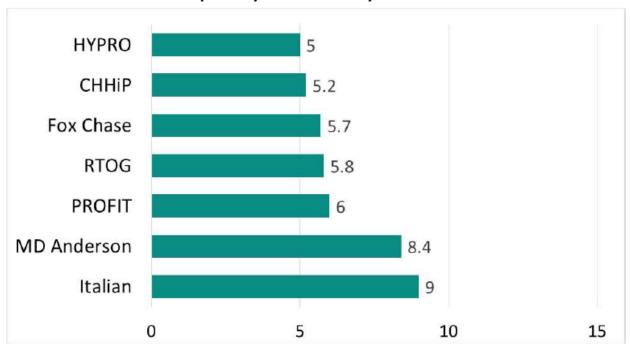
High

94%

Recommendations for or against the use of elective pelvic nodal EBRT in patients with high-risk cancer are beyond the scope of this quideline.

Moderate hypofxn provides similar <u>early</u> cancer control

Limited follow up beyond five years for most trials



Average life expectancy for a 65 year old man in the US is 19 years



KQ1E: Men should be counseled about the small increased risk of acute GI
toxicity with moderate hypofractionation. Moderately hypofractionated EBRT has
a similar risk of acute and late GU and late GI toxicity compared to conventionally
fractionated EBRT. However, physicians should discuss the limited follow-up
beyond five years for most existing RCTs evaluating moderate hypofractionation.

KQ2 Recommendation Statements

KQ2A: Regimens of 6000 cGy delivered in 20 fractions of 300 cGy and 7000 cGy delivered in 28 fractions of 250 cGy are suggested since they are supported by the largest evidentiary base. One optimal regimen cannot be determined since most of the multiple fractionation schemes evaluated in clinical trials have not been compared head to head.

Recommendation strength

Conditional

Quality of evidence

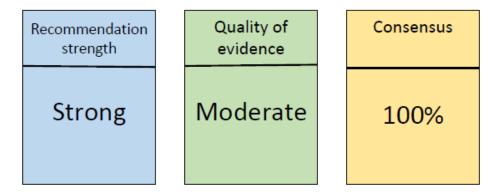
Moderate

Consensus

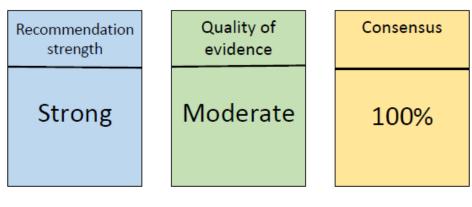
100%



 KQ7A: IGRT is universally recommended when delivering moderately or ultrahypofractionated EBRT.



 KQ8A: Non-modulated 3-D CRT techniques are not recommended when delivering moderately or ultrahypofractionated prostate EBRT.





Statement KQ4A

Ultrahypofractionated prostate EBRT of 3500 to 3625 cGy in 5 fractions of 700 to 725 cGy to the planning target volume may be offered to low- and intermediate-risk patients with prostate sizes less than 100 cm3. The key dose constraints in KQ5B should be followed.

- Strength of recommendation: Conditional
- Quality of evidence: Moderate
- Consensus: 88%



Rectal Dose Constraints: NRG GU005 (PI Rodney Ellis)

Structure	Moderate Hypofractionationation* Constraint	Ultrahypofractionation Constraint**
Rectum	D15% ≤75 Gy	D0.03cc ≤ 38.06 Gy
	D25% ≤ 70 Gy	D3cc ≤ 34.4 Gy
	D35% ≤ 65 Gy	D10% ≤ 32.63 Gy
	D50% ≤ 60 Gy	D20% ≤ 29 Gy
		D50% < 18.13 Gy
Bladder	D0.03cc ≤ 73.5 Gy	D0.03 ≤ 38.06 Gy
	D35% ≤ 70 Gy	D10% ≤ 18.12 Gy
	D50% ≤ 65 Gy	
	D90% ≤ 35 Gy	
Urethra		D0.03 ≤ 38.78 Gy





^{* 70} Gy in 28 factions; ** 36.25 Gy in 5 fractions

SABR of oligomets



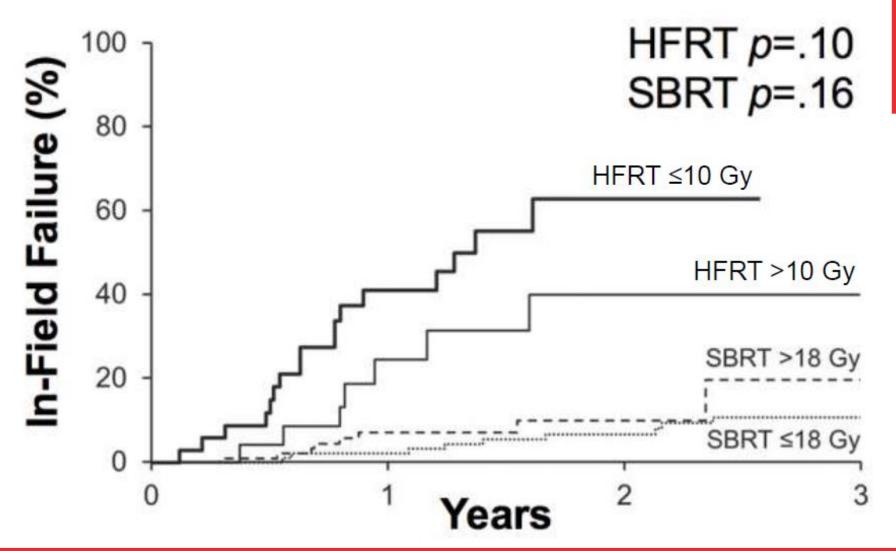


Stereotactic Body Versus Hypofractionated Radiation Therapy for Local Control of Prostate Cancer Bone Metastases

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Conclusions

- SBRT significantly improves in-field failure compared to HFRT for prostate cancer bone metastases
- No difference in biochemical failure, distant failure, or OS for metastases treated with SBRT
- Limitations: selection bias, heterogeneity of cohort





