In-bore MR-guided biopsy tissue genomics and focal therapy: Small series conclusions

Bernadette M. Greenwood, BSc., PG Cert., RT(R)(MR)(ARRT)
John F. Feller, MD
Rob Toth, PhD

INTRODUCTION AND OVERALL GOAL

Therapy planning and prognosis for prostate cancer are currently based primarily on Gleason Score and TNM staging[1]. Risk stratification of prostate cancer and treatment response may be influenced by predictive modeling based upon genomic profile of a tumor.

SPECIFIC AIMS

This HIPAA-compliant, IRB-exempt retrospective series illustrates the clinical utility of Decipher testing for potential risk stratification in prostate cancer patients seeking laser focal therapy for organ-confined Gleason 3+3, 3+4 or 4+3 cancer.

RATIONALE AND BACKGROUND

Ross and Cooperberg have described the utility of Decipher testing in post-prostatectomy specimens[2,3]. Radtke et al demonstrated that imaging genomics correlate well with final prostatectomy provided the target is hit. Our goal was to look at men in our laser focal therapy clinical trial to determine if the genomic status of their pre-treatment MRI-guided biopsy specimens could yield reliable prognostic information. Random, systematic biopsy specimens were not used because of their inherent lack of precision[4].

METHODS AND MATERIALS

20 men were identified from a Phase I clinical trial (NCT #02243033) who underwent laser focal therapy and had 6 month biopsy follow-up after treatment. All pre-treatment biopsy tissue underwent Decipher testing to obtain low, average or high risk level. The pre-treatment Decipher risk levels were then correlated with 6-month biopsy results.

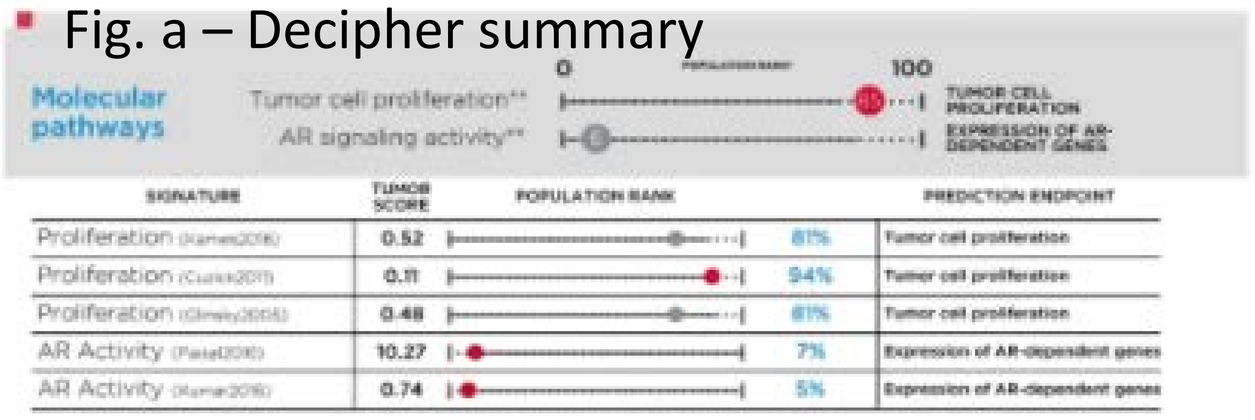
RESULTS

All sixteen of the men with low-risk genomics had negative six month biopsy. Of the four men who had positive biopsies one had low (0.39), one had average (0.54) and two had high (0.75 and 0.82) risk Decipher scores. We noted that the highest risk patient later developed metastatic colorectal cancer (Figs a-c). In this group of 20 men, 24% were Gleason Score 3+3, 62% were 3+4 and 14% were 4+3.

DISCUSSION AND CONCLUSION

Our observation suggests that a low Decipher score may be predictive of treatment response for laser focal therapy. More importantly, it also suggests the possibility of using tissue-based genomics for risk stratification in patients considering laser focal therapy for low or intermediate risk prostate cancer..

Fig. a – Decipher summary



SIGNATURE	TUMOR SCORE	POPULATION RANK	PREDICTION ENDPOINT
Proliferation (Kamal2016)	0.52	81%	Tumor cell proliferation
Proliferation (Cuzick2011)	0.11	94%	Tumor cell proliferation
Proliferation (Glinsky2005)	0.48	81%	Tumor cell proliferation
AR Activity (Patel2016)	10.27	7%	Expression of AR-dependent genes
AR Activity (Kamal2016)	0.74	5%	Expression of AR-dependent genes

Fig. b – key biomarkers

	biomarker	expression	percentile	zscore	class
→	ANP32B	3.370391	1	3.45216	High
	C9orf142	1.236049	1	4.163059	High
	RRAD	0.19541	0.998728	3.196028	High
	CKLF-CMTM1	1.158482	0.997455	3.371424	High
	NTHL1	0.233937	0.997455	3.255628	High
→	ALK	0.162726	0.997455	2.997586	High
	APOBEC3A	0.41545	0.996183	3.767725	High
→	S100A4	0.779056	0.996183	3.015152	High
	CENPW	0.613536	0.994911	3.091147	High
→	FANCF	0.538147	0.994911	2.646392	High
	IGFBP7	2.021744	0.993639	2.114304	-
	CCL13	0.322408	0.991094	3.47241	High
	MAD2L1	0.945228	0.991094	2.596222	High
	NRM	0.330491	0.989822	3.198333	High
→	SMUG1	0.562083	0.989822	2.57244	High
	CDCA3	0.26196	0.98855	2.544416	High
	FGF6	0.408567	0.984733	2.255954	High
→	MUTYH	0.334458	0.984733	2.338368	High
	PBK	0.051414	0.983461	2.5497	High
→	PCNA	1.05825	0.983461	2.182599	High

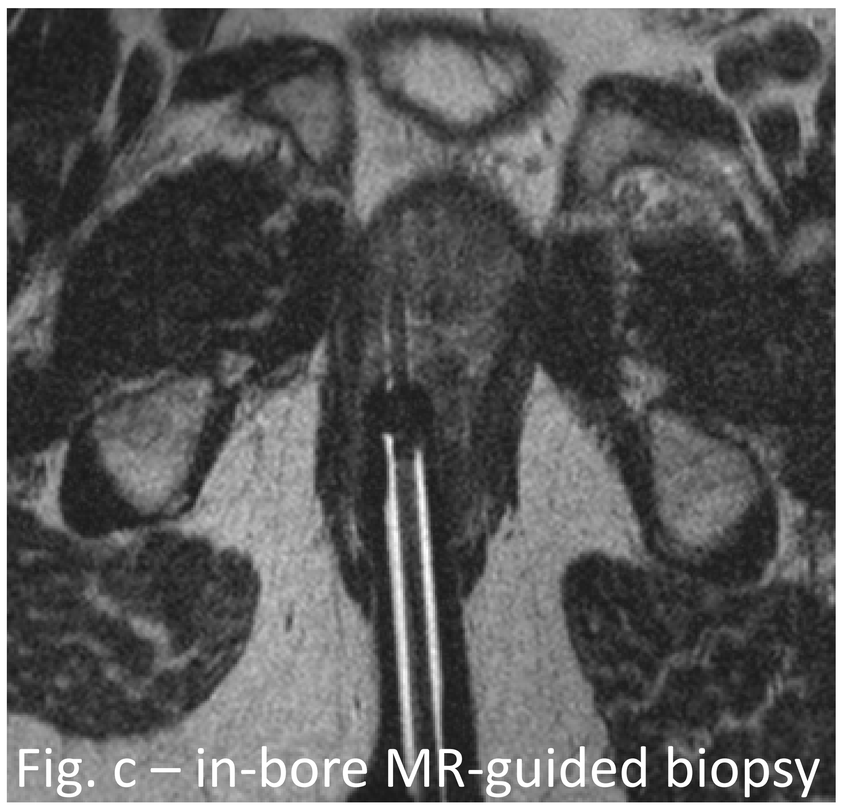


Fig. c – in-bore MR-guided biopsy

CASE SUMMARY:

- High Decipher V1 (0.82)
- ERG+
- High SYP, ANP32B (May play a role in cerebellar development and synaptogenesis)
- S100A4 is invasion gene
- High CLSPN, MCM6, PCNA -->RB1 loss
- High ALK which plays a role in neuron development and non-small cell lung cancer and large cell lymphoma
- Many genes playing role in oxidative DNA repair: PALB2, PCNA, NTHL1, FANCF, SMUG1
- GPX2 (96%0 is glutathione peroxidase family associated with colorectal cancer

REFERENCES

1. NCCN Guidelines Version 2.2017 Staging Prostate Cancer, https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf, accessed 6/22/2017
2. Ross AE, Den RB, Yousefi K, Trock BJ, Tosoian J, Davicioni E, Thompson DJ, Choeurng V, Haddad Z, Tran PT, Trabulsi EJ, Gomella LG, Lallas CD, Abdollah F, Feng FY, Klein EA, Dicker AP, Freedland SJ, Karnes RJ, Schaeffer EM. Efficacy of post-operative radiation in a prostatectomy cohort adjusted for clinical and genomic risk. Prostate Cancer Prostatic Dis. 2016 Sep;19(3):277-82.
3. Cooperberg MR, Davicioni E, Crisan A, Jenkins RB, Ghadessi M, Karnes RJ. Combined value of validated clinical and genomic risk stratification tools for predicting prostate cancer mortality in a high-risk prostatectomy cohort. Eur Urol. 2015 Feb;67(2):326-33.
4. Scattoni V, Maccagnano C, Capitanio U, Gallina A, Briganti A, Montorsi F. Random biopsy: when, how many and where to take the cores? World J Urol. 2014 Aug;32(4):859-69. doi: 10.1007/s00345-014-1335-0. Epub 2014 Jun 8. Review. PubMed PMID: 24908067.