

Restriction Spectrum Imaging as a quantitative biomarker for prostate cancer with reliable positive predictive value

Mariluz Rojo Domingo^{1,2}, Deondre D Do^{1,2}, Christopher C Conlin³, Aditya Bagrodia⁴, Tristan Barrett⁵, Madison T Baxter², Matthew Cooperberg⁶, Felix Feng⁷, Michael E Hahn³, Mukesh Harisinghani⁸, Gary Hollenberg⁹, Juan Javier-Desloges⁴, Karoline Kallis², Sophia Kamran¹⁰, Christopher J Kane⁴, Dimitri Kessler⁵, Joshua Kuperman², Kang-Lung Lee⁵, Jonathan Levine⁶, Michael A Liss¹¹, Daniel JA Margolis¹², Ian Matthews², Paul M Murphy³, Nabih Nakrour⁸, Michael Ohliger¹³, Courtney Ollison², Thomas Osinski¹⁴, Anthony James Pamatmat¹⁴, Isabella R Pompa⁸, Rebecca Rakow-Penner³, Jacob L Roberts⁴, Karan Santhosh¹⁵, Ahmed S Shabaik¹⁶, Yuze Song^{2,17}, David Song¹⁴, Clare M. Tempany⁸, Natasha Wehrli¹², Eric P. Weinberg⁹, Sean Woolen¹³, George Xu², Allison Y Zhong², Anders M Dale^{3,18,19}, Tyler M Seibert^{1,2,3}

¹Department of Bioengineering, University of California San Diego, La Jolla, CA, USA

²Department of Radiation Medicine, University of California San Diego, La Jolla, CA, USA

³Department of Radiology, University of California San Diego, La Jolla, CA, USA

⁴Department of Urology, University of California San Diego, La Jolla, CA, USA

⁵Department of Radiology, University of Cambridge, Cambridge, United Kingdom

⁶Department of Urology, University of California San Francisco, San Francisco, CA, USA

⁷Department of Radiation Oncology, University of California San Francisco, San Francisco, CA, USA

⁸Department of Radiology, Massachusetts General Hospital, Boston, MA, USA

⁹Department of Clinical Imaging Sciences, University of Rochester Medical Center, Rochester, NY, USA

¹⁰Department of Radiation Oncology, Massachusetts General Hospital, Boston, MA, USA

¹¹Department of Urology, University of Texas Health Sciences Center San Antonio, San Antonio, TX, USA

¹²Department of Radiology, Cornell University, Ithaca, NY, USA

¹³Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA, USA

¹⁴Department of Urology, University of Rochester Medical Center, Rochester, NY, USA

¹⁵Department of Computer Science, University of California San Diego, La Jolla, CA, USA

¹⁶Department of Pathology, University of California San Diego, La Jolla, CA, USA

¹⁷Department of Electrical and Computer Engineering, University of California San Diego, La Jolla, CA, USA

¹⁸Department of Neurosciences, University of California San Diego, La Jolla, CA, USA

¹⁹Halicioğlu Data Science Institute, University of California San Diego, La Jolla, CA, USA

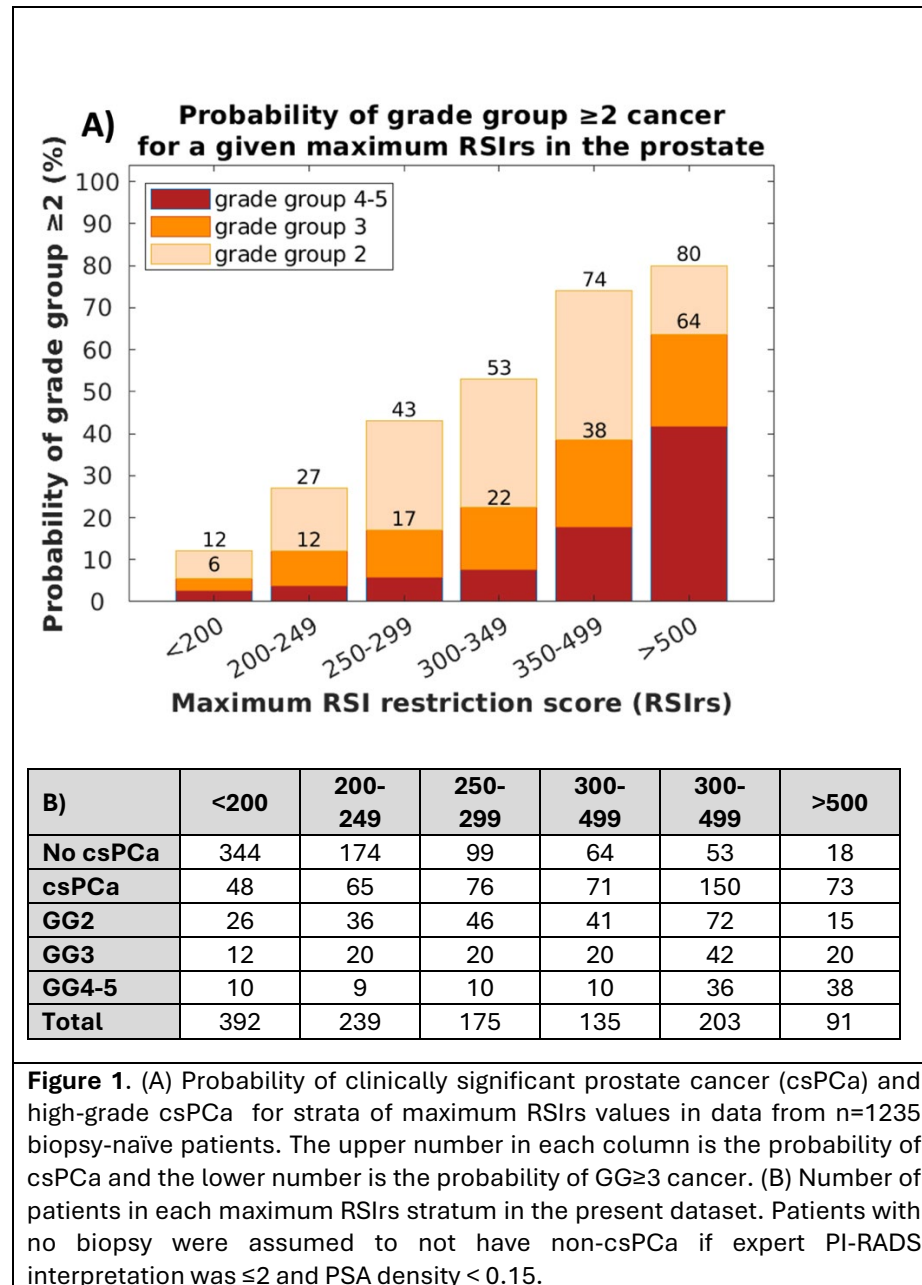
Background. Positive predictive value of PI-RADS for clinically significant prostate cancer (csPCa, grade group [GG]≥2) varies widely between institutions and radiologists. The Restriction Spectrum Imaging restriction score (RSIrs) is a metric derived from diffusion MRI that could be an objectively interpretable biomarker for csPCa. The goal of this study is to evaluate the performance of RSIrs for patient-level detection of csPCa in a large and heterogenous dataset, and to combine RSIrs with clinical and imaging parameters for csPCa detection.

Methods. In this retrospective study, 2845 patients were scanned for suspected or known csPCa at 7 centers. We calculated patient-level csPCa probability based on maximum RSIrs in the prostate, without relying on subjectively defined lesions. We used area under the ROC curve (AUC) to compare patient-level csPCa detection for RSIrs, ADC, and PI-RADS. Finally, we combined RSIrs with clinical risk factors via multivariable regression, training in a single-center cohort and testing in an independent, multi-center dataset.

Results. Among all patients (n=1892), probability of csPCa increased with higher RSIrs. GG≥4 csPCa was most common in patients with very high RSIrs. Among biopsy-naïve patients (n=877), AUCs for GG≥2 vs. non-csPCa were 0.73 (0.69-0.76), 0.54 (0.50-0.57), and 0.75 (0.71-0.78) for RSIrs, ADC, and PI-RADS, respectively. RSIrs significantly outperformed ADC ($p<0.01$) and was comparable to PI-RADS ($p=0.31$).

The combination of RSIs and PI-RADS outperformed either alone. Combining RSIs with PI-RADS, age, and PSA density in a multivariable model achieved the best discrimination of csPCa.

Conclusion. RSIs is an accurate and reliable quantitative biomarker that performs better than conventional ADC and comparably to expert-defined PI-RADS for patient-level detection of csPCa. RSIs provides objective estimates of probability of csPCa that do not require radiology expertise.



Funding Acknowledgements

This work was supported, in part, by the National Institutes of Health (NIH/NIBIB K08EB026503, NIH UL1TR000100), the American Society for Radiation Oncology, the Prostate Cancer Foundation (PCF20YOUN01), and the U.S. Department of Defense (DOD/CDMRP PC220278).

Conflicts of Interest Disclosure Statement

Tyler M. Seibert.

Honoraria from CorTechs Labs, Varian Medical Systems, WebMD, GE Healthcare, and Janssen; has an equity interest in CorTechs Labs, Inc, and serves on its scientific advisory board; and has received in-kind research support from GE Healthcare via a research agreement with the University of California, San Diego. These companies might potentially benefit from the research results. The terms of these arrangements have been reviewed and approved by the University of California, San Diego in accordance with its conflict-of-interest policies.

Michael E. Hahn

Honoraria from Multimodal Imaging Services Corporation and research funding from GE Healthcare.

Anders M. Dale

Founder of and holds equity in CorTechs Labs, Inc, and serves on its scientific advisory board; he also is a member of the scientific advisory board of Human Longevity, Inc, and receives funding through research agreements with GE Healthcare.

Rebecca Rakow-Penner

Consultant for Human Longevity Inc and Curemetric. She has the following stock options: Cortech Labs and Curemetrix: Stock options, consultant
Imagine Scientific, advisory board. SBIR
GE Healthcare, research agreement
Bayer consultant

Michael Liss

Founder/President of Oncobiomix with no relation to this manuscript.

Research reported in this publication was supported by the National Cancer Institute of the National Institutes of Health under Award Number R01CA279667. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Sean Woolen

Research grants paid to institution from Siemens Healthineers and General Electric