

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository: <https://orca.cardiff.ac.uk/id/eprint/149596/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Liebert, Casril, Moroka, Naomi, Satish, Pranav, Freeman, Alex, Kelly, Daniel , Kirkham, Alex, Orczyk, Clement, Simpson, Benjamin S., Whitaker, Hayley C., Emberton, Mark and Norris, Joseph M. 2023. Diagnostic potential of radiological apical tumor involvement. *Journal of Robotic Surgery* 17 , pp. 705-706.
10.1007/s11701-022-01413-w

Publishers page: <http://dx.doi.org/10.1007/s11701-022-01413-w>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies. See <http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



Title: Diagnostic Potential of Radiological Apical Tumour Involvement

Casril Liebert¹, Naomi Morka¹, Pranav Satish¹, Alex Freeman², Daniel Kelly³, Alex Kirkham⁴, Clement Orczyk⁵, Benjamin S Simpson⁶, Hayley C Whitaker⁷, Mark Emberton^{5,7}, Joseph M Norris⁷

¹ University College London Medical School, London, UK

²Department of Pathology, University College London Hospitals NHS Foundation Trust, London, UK.

³School of Healthcare Sciences, Cardiff University, Cardiff, UK.

⁴Department of Radiology, University College London Hospitals NHS Foundation Trust, London, UK.

⁵Department of Urology, University College London Hospitals NHS Foundation Trust, London, UK.

⁶UCL Cancer Institute, University College London, London, UK.

⁷Division of Surgery and Interventional Science, University College London, London, UK.

Corresponding Author: Casril Liebert

University College London Medical School, London, United Kingdom.

74 Huntley Street, London, United Kingdom. WC1E 6DE.

Email: casril.liebert.19@ucl.ac.uk

ORCID ID: 0000-0002-6090-6731

Word count: 549

Ethics: No ethical considerations apply.

Conflicts of interest: Joseph M. Norris is funded by the Medical Research Council (MRC; grant MR/S00680X/1). Alex Freeman and Alex Kirkham have shares in Nuada Medical. Hayley Whitaker receives funding from Prostate Cancer UK, the Urology Foundation and Rosetrees Trust. Mark Emberton receives funding from NIHR53 i4i, MRC, Cancer Research UK, the Jon Moulton Charitable Foundation, Sonacare, Trod Medical, the Cancer Vaccine Institute, and Sophiris Biocorp for trials in prostate cancer, and acts as a consultant and/or trainer and proctor for Sonatherm, Angiodynamics, and Exact Imaging. The remaining authors have nothing to disclose.

We commend Veerman et al. for investigating the diagnostic performance of radiological apical tumour involvement (radATI) in preoperative prostate MRI and its impact on clinical outcomes in patients with localized prostate cancer (1). This retrospective study evaluated the diagnostic accuracy of MRI to detect pathological ATI (pathATI) in robot-assisted radical prostatectomy specimens. They found 2/56 (4%) of patients without radATI developed a biochemical recurrence (BCR) compared to 25/120 (21%) patients with radATI ($p = 0.003$). Multivariate analysis found patients with radATI more likely to have apical positive surgical margins (APSM) ($p = 0.004$). These findings have implications in predicting prostate cancer outcomes and further investigation of certain areas in this field would be valuable.

Firstly, we believe the author's acknowledgement of tumour location is an important step in the classification of prostate cancer. Tumour location has already been widely recognised in the study of breast and lung cancer, with increasing evidence indicating a similar presentation in the prostate (2). An important question that is under addressed is, what is it about apical tumours that carry additional risk? Variation in biology and morphology throughout the tumour may play a role in these differences. Additionally, higher rates of PSM due to incomplete surgical excision may contribute to increased recurrence risk in the apex. If this is the case, surgical management must be tailored by tumour location. RadATI detection of APSM, together with modifications in surgical techniques to reduce APSM may be necessary, as well as deploying adjuvant treatments to eliminate APSM. In addition, taxonomy may be warranted in categorising apical tumours based on morphology, volume, and grade. We are excited to see further progress in understanding the significance of prostate tumour location.

Secondly, literature suggests that a single APSM may be clinically insignificant on long-term outcomes (3,4). A study by Wadhwa et al. finds that APSMs lead to less BCR than PSM in other areas (5). On the contrary, the authors recommend radATI be treated with reduced apical nerve sparing to avoid APSM. We believe this approach may lead to overtreatment of radATI in the presence of an otherwise good prognosis. However, it is important to acknowledge the psychological distress PSM may have on patients, warranting the need for further treatment. In addition, Wadhwa's study has several limitations, such as the dataset details including any surgical technique, rather than focusing on specimens from robot-assisted surgery. Wadhwa also lacked important prognostic factors, such as tumour grade and amount of tumour at the margin.

We believe the extent of APSMs is a key prognostic factor and is found to be an independent predictor of BCR (6). Only extensive PSMs seem to significantly increase the risk of BCR, while focal APSMs have little effect. Most tumours in Veerman's study were clinically suspicious (63% with a PI-RADS 5) but the extensiveness was unknown. Consideration of the extent of PSM upon diagnosis would be an interesting topic for investigation. The authors may also wish to perform multivariable analysis for the effect of radATI on BCR.

The potential of MRI to predict ATI is exciting, however, future study may benefit from focus on the points highlighted here. We believe MRI may play a critical diagnostic and prognostic role for prostate cancer. Integrating MRI with other diagnostic techniques such as PSMA PET-CT, micro-ultrasound and PCA3 biomarkers could form a powerful toolkit in enhancing prognostication.

Bibliography:

1. Veerman H, Boellaard TN, van Leeuwen PJ, Vis AN, Bekers E, Hoeks C, et al. The detection rate of apical tumour involvement on preoperative MRI and its impact on clinical outcomes in patients with localized prostate cancer. *J Robot Surg*. 2021;
2. Satish P, Freeman A, Kelly D, Kirkham A, Orczyk C, Simpson BS, et al. Relationship of prostate cancer topography and tumour conspicuity on multiparametric magnetic resonance imaging: a protocol for a systematic review and meta-analysis. *BMJ Open*. 2022;12:50376.
3. Ohori M, Abbas F, Wheeler TM, Kattan MW, Scardino PT, Lerner SP. Pathological features and prognostic significance of prostate cancer in the apical section determined by whole mount histology. *J Urol*. 1999 Feb;161(2):500–4.
4. Blute ML, Bostwick DG, Bergstralh EJ, Slezak JM, Martin SK, Amling CL, et al. Anatomic site-specific positive margins in organconfined prostate cancer and its impact on outcome after radical prostatectomy. *Urology*. 1997 Nov 1;50(5):733–9.
5. Wadhwa H, Terris MK, Aronson WJ, Kane CJ, Amling CL, Cooperberg MR, et al. Long-term oncological outcomes of apical positive surgical margins at radical prostatectomy in the Shared Equal Access Regional Cancer Hospital cohort. *Prostate Cancer Prostatic Dis*. 2016 Oct 4;19(4):423–8.
6. Gautier M, Aude M, Gerjon H, Jerome R, Jean S, Arnauld V, et al. Risk of biochemical recurrence based on extent and location of positive surgical margins after robot-assisted laparoscopic radical prostatectomy. *BMC Cancer*. 2018 Dec 27;18(1):1–8.