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Letter to the Editor

Re: Thomas Bommelaere, Arnaud Villers, Philippe Puech, et al. Risk Estimation of Metastatic Recurrence After Prostatectomy: A Model Using Preoperative Magnetic Resonance Imaging and Targeted Biopsy. Eur Urol Open Sci 2022;41:24–34

Bommelaere et al. [1] report on their refined risk model for assessing the likelihood of metastatic recurrence of prostate cancer after radical surgery based on volume estimation of overall and high-grade disease at baseline, using combined multiparametric magnetic resonance imaging (mpMRI) and targeted biopsy outcomes. They should be congratulated for this innovative single-centre report and for their pioneering and systematic approach to the detection of prostate cancer. This is a mature cohort from a centre that has used mpMRI before targeted biopsy for more than a decade [2]. One limitation of the study could be in the validation of their model in other centres in the near future. This historic cohort presents another limitation linked to the temporality of its acquisition. More than one-third of the metastatic recurrences occurred within the first year, suggesting potential understaging at baseline. If prostate-specific membrane antigen positron emission tomography imaging had been introduced earlier, would the curves (Fig. 1 [1]) have taken a different shape, identifying rather than predicting spread of disease? The use of Harrell's C index is time-sensitive by definition [3], pairing each early event to another one and then comparing the predicted risk. It is therefore difficult to establish if the model reflects the possibility of detection of metastasis by a more performative clinical test at baseline or truly predicts its risk of occurrence. Nonetheless, the authors used the best approximation of volume and higher grade derived from mpMRI and targeted biopsy.

Using the threshold of 3.2 cm³ of Gleason pattern 4 or 5 reported previously by McNeal, the population is nearly split in two, with 40% classified as metastatic and 60% remaining under the detection capability of staging imaging. Such a divide probably indicates the limits of our current model of risk of prostate cancer based predominantly on volume and grade of disease. Beyond the proxy of margin status, some other biological mechanisms are probably in play. The histological taxonomy of prostate cancer based on morphology is probably limited in value, especially with the knowledge that 90% of men with prostate-specific antigen of <15 ng/ml harbour Gleason 7 disease on high-density transperineal mapping biopsies [4]. As an illustration, this

study detected a metastatic event after radical surgery in nearly 15% of patients harbouring only small-volume high-grade disease (0.5–1 cm³).

The attempt to risk-stratify prostate cancer via molecular taxonomy has also failed to demonstrate a single driver, with vast heterogeneity of the disease at this level of analysis [5]. In addition, while mpMRI-visible disease has been suggested as the dominant phenotype, the visibility phenomenon seems to be linked to molecular features of aggressiveness rather than an identifiable single molecular substrate [6]. Nevertheless, the authors of this study have demonstrated the importance of mpMRI and targeted biopsy, which should now be considered integral to contemporary risk models. In the future, a modified risk model might integrate molecular analyses from targeted biopsy tissue with a more refined quantitative assessment of multiparametric MRI parameters, each one detecting a set of different features of this heterogeneous disease [4].

Conflicts of interest: Claire Deleuze receives research support from EUSP. Louise Dickinson has nothing to disclose. Clement Orczyk is a proctor for Sonablate and a consultant for Varian and Imaging Medical.

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