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Editorial

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Fast Magnetic Resonance Imaging as a Viable Method for Directing the Prostate Cancer Diagnostic Pathway

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Magnetic resonance imaging (MRI) has recently transformed the prostate cancer diagnostic pathway. Foundational studies include the verification PROMIS study [1], the randomised international PRECISION and multicentre Canadian trials [2,3], and head-to-head systematic versus MRI-directed biopsy studies [4,5]. Taken together, the evidence indicates that MRI before biopsy can allow one-third of men to avoid an immediate biopsy and reduce overdiagnoses, with 40% fewer clinically unimportant cancers and approximately 15% more clinically important cancers detected [6]. The MRI-directed biopsy strategy for prostate cancer diagnosis has received guideline endorsement [7].

This success has increased the demand for MRI scanner time and manpower resources, prompting the need to develop techniques that make MRI data acquisition and evaluation times faster. Promising strategies include MRI without contrast medium and imaging in the axial plane only. Systematic reviews of nonrandomised comparisons have suggested that MRI without contrast medium might be as accurate as MRI with contrast [8], albeit with some reservations [9]. A recent study of fast MRI (MRI without contrast medium in the axial plane only) performed on a 3-T scanner yielded promising results [10].

In this issue of *European Urology Oncology*, Russo et al [11] report the first randomised control study comparing multiparametric MRI (mpMRI) with fast MRI in directing the biopsy diagnosis of prostate cancer. The mpMRI approach used multiplanar imaging, contrast medium injection, and an endorectal receiver coil (ERC). The fast MRI was carried out in the axial plane without contrast medium and using a surface pelvic phased-array coil. Both approaches were performed at 1.5 T. There are two central results: (1) the ERC mpMRI biopsy approach had greater diagnostic yields for Gleason grade (GG) $\geq$2 cancers among men undergoing biopsy (32.7% vs 23.5%) with a mean difference of 9.2% (95% confidence interval [CI] −1.4% to 19.7%; p = 0.09); and (2) ERC mpMRI missed fewer GG $\geq$2 cancers (5.9% vs 16.7%), with a mean difference of 10.8% (95% CI −3.9% to 22.9%; p = 0.12). Of the ten GG $\geq$2 cancers missed by fast MRI, two were GG $\geq$3 cancers, whereas both cancers missed by ERC mpMRI were GG 2. The absence of statistical noninferiority led the investigators to conclude that monoplanar, non–contrast-enhanced MRI using a surface pelvic-phased array coil on a 1.5-T machine could be suitable for broader use to direct the prostate cancer diagnostic pathway. This bold idea requires greater scrutiny.

In this randomised noninferiority trial, the most crucial issue is the power of the study to supply the necessary statistical confidence on which the authors' assertion is based. Power calculations are usually undertaken on the basis of detection rates for the target conditions. Ideally, the detection rate/sensitivity is the proportion of men with GG $\geq$2 cancer who test positive on MRI when all the biopsy results are known. The latter is not true for this study, as many men did not undergo biopsy (18–24% of the men after negative MRI).

The investigators chose a literature detection rate/sensitivity of 90% for the power calculations [6]. If there is truly no difference between their version of standard ERC mpMRI and experimental non-ERC fast MRI in the ability to successfully detect GG $\geq$2 cancers (if both would success-

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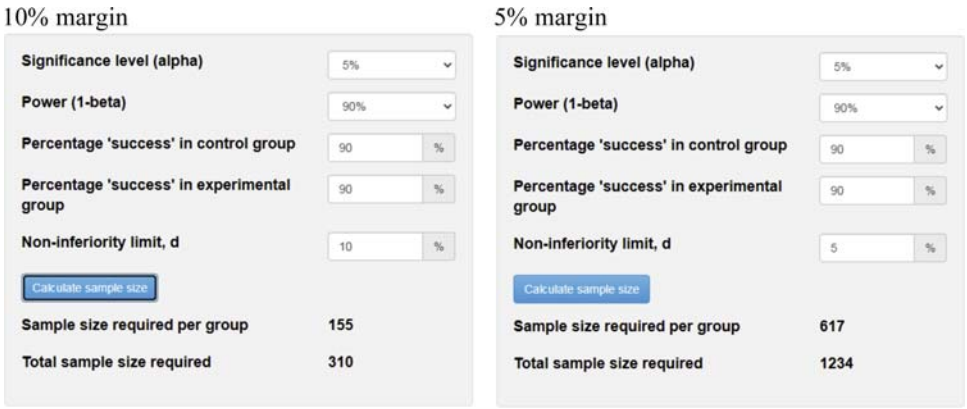

Fig. 1 – Power calculations for noninferiority based on 10% and 5% margins for detection sensitivity of 90%. Sealed Envelope Ltd. 2012. Power calculator for binary outcome non-inferiority trial. Available from: https://evaluation.sealedenvelope.com/power/binary-noninferior/.

fully detect 90% of the GG ≥2 cancers present), then 310 patients would be required to be 90% sure that the upper limit of a one-sided 95% CI excludes a difference in favour of the mpMRI group of >10%. That is, 155 patients per group would be needed (Fig. 1). Given this, we are perplexed by the reasoning that led the investigators to allocate two-thirds of the patients to the fast MRI group and one-third to the ERC mpMRI arm, thus going against the power calculator recommendations. This apportioning of the cohort makes the noninferiority finding less convincing.

Furthermore, many readers will ask how an almost 10% difference in diagnostic yield between ERC mpMRI and non-ERC fast MRI cannot be considered "clinically important". A noninferiority margin of 5% would strike a better balance for most urologists and patients, if we consider the standard of care to be the mpMRI-directed biopsy approach. A change from a 10% to a 5% noninferiority limit would quadruple the sample size (from 310 to 1234 men), and may have been the main impediment for an exploratory study (Fig. 1).

An important point to note is that ERC mpMRI is not the standard of care in most centres. It is highly likely that the greater detection of GG ≥2 cancers with mpMRI is not only because of the use of contrast medium, but also due to the additional use of the ERC and imaging in multiple planes. Other limitations of the study identified include its single-centre nature, no explicit quality assurance or quality control assessments, single observer assessments without documentation of intraobserver variability, and the greater proportion of indeterminate fast MRI scans requiring recall for ERC mpMRI (although the authors propose a viable alternative strategy based on using prostate-specific antigen density). Most importantly, the lack of long-term follow-up to verify if the diagnoses were correct, especially for MRI-negative cases who were not biopsied, make the sensitivity and specificity values reported unreliable.

The authors discuss their lower number of cases with Prostate Imaging-Reporting and Data System (PI-RADS) score 3 on ERC mpMRI (9/98, 9%) compared to fast-MRI (26/213, 12%) and indicate that this difference is lower than in the 4M study [10]. In the 4M study, the proportion of PI-RADS 3 cases was 11% for fast MRI and 8% for mpMRI technique. Thus, the differences are identical (3%). In addition, we should note that a direct comparison of the PI-RADS 3 rates between the current and 4M studies is invalid because of differences in technique. The 4M study was conducted without an ERC and on a 3-T machine, whereas Russo et al used an ERC on a 1.5-T machine for the mpMRI protocol.

The current trial by Russo et al [11] is therefore best considered as a promising step in exploring the role of monoplanar, noncontrast, 1.5-T, non-ERC MRI to direct the prostate biopsy pathway. This approach, however, needs further clinical testing and validation. Artificial intelligence methods that are trained on fast MRI sequences have recently shown good discriminatory power and an improvement in reader variability, and may be helpful in promoting the fast MRI approach [12]. Definitive investigations of fast MRI for directing the prostate cancer diagnostic pathway in prospective, multicentre, multiobserver settings would be welcomed.

Conflicts of interest: The authors have nothing to disclose.

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