# Rapid pre-biopsy MRI in patients with a clinical suspicion of prostate cancer: results of a controlled prospective registered IMPROD-trial

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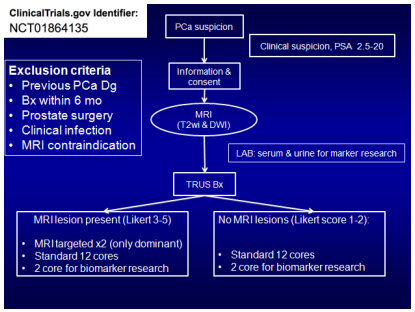
## PURPOSE

To investigate the accuracy and negative predictive value of a rapid biparametric MRI (bpMRI) and simple biopsy procedure in men with a clinical suspicion of prostate cancer (PCa), IMPROD= IMPROved prostate cancer Diagnosis – Combination of Magnetic Resonance Imaging and biomarkers.

## METHODS

Between March 2013 and February 2015, men with a clinical suspicion of PCa were enrolled to this prospective, controlled, registered (ClinicalTrials.gov Identifier NCT01864135) clinical trial (Figure 1).

**Figure 1**




**MRI Protocol:**

- 3T Verio (Siemens, Erlangen, Germany)
- only clinically available sequences & post-processing
- overall imaging time ~ 15 minutes
- **transversal T2w** (1): TR/TE 8640/101 ms, acquisition voxel size 0.6×0.6×3.0mm$^3$
- **sagittal T2w** (1): TR/TE 8640/101ms, acquisition voxel size 0.7×0.6×3.0mm$^3$
- **DWI**: Three separate acquisitions:
  - 1 (1): TR/TE 5543/80 ms, b values 0, 100, 200, 300, 500 s/mm$^2$, acquisition voxel size 2.0×2.0×3.0mm$^3$
  - 2. TR/TE 5000/87 ms, b values 0, 1500 s/mm$^2$, acquisition voxel size 2.0×2.0×5.0mm$^3$
  - 3. TR/TE 5000/87 ms, b values 0, 2000 s/mm$^2$, acquisition voxel size 2.0×2.0×5.0mm$^3$

**Reporting system:**

- One reader (IJ) using Likert scoring system: 1- significant cancer is highly unlikely to be present, 2- significant cancer is unlikely to be present, 3- significant cancer is equivocal, 4- significant cancer is likely to be present, 5- significant cancer is highly likely to be present.
- If Likert 3-5: DWI score for dominant Gleason grade 4 (circular ROI, size 21 mm$^2$) - ADC maps calculated using 5 b-values in the range of 0 to 500 s/mm$^2$: 0. not probable >850x10$^{-6}$ mm$^2$/s, 1. probable <850x10$^{-6}$ mm$^2$/s; 2. highly probable <750x10$^{-6}$ mm$^2$/s.

**Primary end point:**

- diagnostic accuracy of the following models for predicting PCa and clinically significant PCa (SPCa): 1. *blood model*: PSA, age, 5-alpha-reductase inhibitors use. 2. *visit model*: PSA, age, 5-alpha-reductase inhibitors use, digital rectal examination (DRE); 3. *TRUS model*: PSA, age, 5-alpha-reductase inhibitors use, DRE, TRUS findings, prostate volume (as measured by TRUS), PSA density. 4. *MRI model*: PSA, age, 5-alpha-reductase inhibitors use, DRE, TRUS findings, prostate volume (as defined by TRUS), PSA density, Likert score. 5. *MRI model including DWI score*: PSA, age, use of 5-alpha-reductase inhibitors, DRE, TRUS findings, prostate volume (as defined by TRUS), PSA density, Likert score, DWI score.

**Secondary end points**:

- prevalence of PCa, SPCa, and clinically insignificant PCa in the Likert score groups
- negative predictive values (NPV) of bpMRI
- detection rates of PCa, SPCa, and clinically insignificant PCa using targerted biopsy (TB) and systematic 12 core biopsy (SB)

**Prostate cancer risk groups:**

- *Definition no. 1* - Low risk (2): Biopsy Gleason score 3+3, Intermediate risk: Biopsy Gleason score 3+4, High risk: Biopsy Gleason score 4+3 or higher; *Definition no. 2* - Low risk (3): Biopsy Gleason score of 3+3 and/or 3+4 with < 50% of any core containing cancer and/or < 4 SB cores positive for cancer, Intermediate risk: Gleason score of 3+4 with ≥ 50% of any core containing and/or ≥ 4 SB cores positive for cancer, High risk: Gleason score of 4+3 or higher; *Definition no. 3*- Low risk: Biopsy Gleason score of 3+3 and/or 3+4, Intermediate risk: Biopsy Gleason score of 4+3, High risk: Biopsy Gleason score of 4+4 or higher. Clinically significant PCa was defined as intermediate and high risk PCa according to the definitions above.

**Statistical Methods:**

- logistic regression models were fitted, area under the curve (AUC)
- Chi-Square test was used to compare the proportion of low-, intermediate- and high-risk men among those upgraded based on TB compared with SB or wise verse.
- R version 3·2·0 (Vienna, Austria).

## RESULTS

In total, 175 men were prospectively enrolled. Fourteen men withdraw or were excluded from the analyses resulting in 161 out of 175 (92%) being included in the final analyses. Patient demographics are summarized in Table 1.

**Table 1**

| | All men | No prior biopsy cohort |
|---|---|---|
| n (% of total) | 161 | 134 (83.2%) |
| Age, mean (SD), years | 64.7 (6.4) | 64.7 (6.7) |
| PSA median (IQR), ng/mL | 7.5 (5.7-9.6) | 7.2 (5·4-9·3) |
| Prostate volume, median (IQR), cm$^3$ | 37.0 (27.5-49·0) | 38.0 (28.0-49.0) |
| Likert score, n (%) | | |
| - 1 | 30 (18.6%) | 26 (19.4%) |
| - 2 | 8 (5.0%) | 6 (4.5%) |
| - 3 | 24 (14.9%) | 20 (14.9%) |
| - 4 | 21 (13.0%) | 18 (13.4%) |
| - 5 | 78 (48.4%) | 64 (47.8%) |
| Men with anterior lesions, n (%) | 40 (24.8%) | 27 (20.1%) |

**Table 2 Results for primary end point**

| | benign vs. any PCa | Definition no. 1 [benign 3+3] vs. rest of PCa | Definition no. 2 [benign 3+3 3+4-low] vs. rest of PCa | Definition no. 3 [benign 3+3 3+4] vs. rest of PCa |
|---|---|---|---|---|
| Basic model | 0.66 (0.57-0.76) | 0.64 (0.56-0.73) | 0.69 (0.61-0.77) | 0.61 (0.51-0.72) |
| Visit model | 0.74 (0.66-0.82) | 0.74 (0.67-0.82) | 0.76 (0.69-0.83) | 0.66 (0.55-0.77) |
| TRUS model | 0.81 (0.74-0.87) | 0.83 (0.77-0.89) | 0.83 (0.77-0.90) | 0.72 (0.62-0.82) |
| MRI model | 0.91 (0.87-0.96) | 0.93 (0.89-0.97) | 0.92 (0.88-0.96) | 0.83 (0.77-0.90) |
| MRI&DWI model | 0.92 (0.88-0.96) | 0.93 (0.89-0.97) | 0.92 (0.88-0.96) | 0.85 (0.78-0.92) |

**Table 3 Prevalence of PCa, SPCa in the Likert score groups**

| | Likert score | | | | | |
|---|---|---|---|---|---|---|
| | 1 | 2 | 3 | 4 | 5 | Total |
| No Cancer | 24 (15%) | 6 (4%) | 17 (11%) | 4 (2%) | 4 (2%) | 55 (34%) |
| Gleason 3+3 | 4 (2%) | 0 (0%) | 6 (4%) | 6 (4%) | 7 (4%) | 23 (14%) |
| Gleason 3+4 | 2 (1%) | 2 (1%) | 0 (0%) | 7 (4%) | 34 (21%) | 45 (28%) |
| Gleason >3+4 | 0 (0%) | 0 (0%) | 1 (1%) | 4 (2%) | 33 (20%) | 38 (24%) |
| Total | 30 (19%) | 8 (5%) | 24 (15%) | 21 (13%) | 78 (48%) | 161 (100%) |

MRI and MRI&DWI models outperformed (p<0.05) all other models.

NPV of bpMRI (>Likert score 3) for SPCa was 90-100%. Performing biopsy only in men with Likert 3-5 would have resulted in a 24% (38/161) reduction in the number of men undergoing biopsy while missing 0-4 (0-3%) men with SPCa. The corresponding values for Likert 4-5 are 39% (62/161) and 1-5 (1-3%). The addition of SB to TB in men with Likert 3-5 (n=123) resulted in the upgrading of low risk to intermediate/high risk PCa in 8-12 men while 8-10 additional men were diagnosed with low risk PCa. In whole cohort (n=161), 25, 19, 16 men were upgraded to an intermediate/high risk PCa based on TB while 12, 14, 8 men based on SB (p<0.05).

## CONCLUSION

bpMRI, performed using a simple clinical MRI protocol, followed by TB in men with a clinical suspicion of PCa limits the number of unnecessary biopsy procedures.

## REFERENCES

1. Jambor I et al. J Magn Reson Imaging 2015; 41:1394-1404. 2. Filson CP, et al. Cancer 2016; 122: 884-92 3. Siddiqui MM, et al. JAMA 2015; 313: 390-7