

1 **Is Perfect the Enemy of Good? Weighing the Evidence for Biparametric MRI in**
2 **Prostate Cancer**

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43

44 **Abstract:** The role of multiparametric MRI in diagnosis, staging and treatment planning
45 for prostate cancer is well established. However there remain several challenges to
46 widespread adoption. One such challenge is the duration and cost the examination.
47 Abbreviated exams omitting contrast enhanced sequences may help address this challenge.
48 In this review, we will discuss the rationale for biparametric MRI (bpMRI) for detection
49 and characterization of clinically significant prostate cancer prior to biopsy and synthesize
50 the published literature. We will weigh up the advantages and disadvantages to this
51 approach and lay out a conceptual cost/benefit analysis regarding adoption of bpMRI.

52

53

54 **Introduction**

55 Prostate magnetic resonance imaging (MRI) has been utilized in assessment of prostate
56 cancers for decades, initially efforts were focused on staging known cancers and now on
57 detection and characterization.[1] This led to a significant expansion in the use of MRI in
58 prostate cancer.[2] [3] [4] The role of MRI in detection is to identify the clinically
59 significant lesions, which are defined as Gleason Grade (GG) group ≥ 2 , while leaving GG
60 1 or indolent lesions undetected. These major advances are possible based upon the
61 acquisition of a set of MR sequences (so-called multi-parametric or mpMRI). The four
62 sequences combine two with morphologic information (typically T1 (pre-contrast) and T2
63 weighted sequences) and two functional sequences namely-Diffusion-weighted imaging
64 (DWI)—and its counterpart, the apparent diffusion coefficient (ADC) map—plus pre- and
65 post-T1W images with dynamic I.V. gadolinium contrast enhanced (DCE) imaging. The
66 combination of these sequences provides information about different aspects of both tumor
67 morphology and biology such as cellular density (seen on DWI) and altered vascularization
68 (seen on DCE). It is now universally accepted radiological practice to interpret and report
69 Prostate multiparametric MRI using Prostate Imaging Reporting & Data System (PI-
70 RADS) v2.1 which incorporates the components of multiparametric MRI to a numerical
71 score signifying the likelihood of clinically significant cancer.[5]

72

73 The term “biparametric” (bp) has been used to refer to prostate MRIs which employ T2WI
74 and DWI sequences and omit the use of IV contrast. Thus, bpMRI excludes the IV injection
75 and acquisition of the post-contrast images. It thereby reduces the exam time and cost of
76 the contrast agent. The other advantages include increase patient acceptance due to the

77 avoidance of the IV administration and the avoidance of the Gadolinium itself. Intravenous
78 contrast administration also requires other associated resources such as preoperative lab
79 testing (specifically measurement of Glomerular Filtration Rate (GFR)), pharmacy costs
80 for storage, dosing and dispensing the contrast agents as well as the need for trained staff
81 to place, monitor and remove IV cannulas. Lastly, although gadolinium is generally
82 regarded as a very safe contrast agent with minimal toxicity or side effects, there have been
83 concerns regarding nephrogenic systemic fibrosis (NSF), now mitigated and more recently
84 concerns regarding deposition of gadolinium in the brain also with mitigation strategies.[6]
85 [7] [8] [9]

86

87 Given these factors, there is significant interest in abbreviated non-contrast MRI protocols.
88 In particular, the issues listed above have led many to question whether after the
89 elimination of gadolinium-based contrast enhanced sequences can still provide the required
90 information for prostate cancer detection. Over the past decade, numerous studies have
91 shown evidence to support the value of bpMRI in the assessment of both biopsy-naive men
92 and men with a prior negative prostate biopsy for potential cancerous prostate lesions.[10]
93 [11] In this review, we will describe the basis for bpMRI protocols, the evidence for and
94 against this approach, plausible applications and the implications of bpMRI from a
95 dissemination perspective.

96

97 **Multiparametric MRI**

98

99 There is now a wealth of prospective data supporting the ability of multiparametric MRI
100 to identify clinically significant cancer[12] [13] [14] and MRI-based diagnostic pathways
101 are widely acknowledged as superior to historical approaches which typically refer men
102 with a PSA above reference ranges for a sextant or systematic biopsy. [13] [15] [16] [12]
103 [17] [18]

104

105 Multiparametric MRI refers to MRIs which incorporate high resolution T2 & T1 weighted
106 MRI (T2W) sequences with functional sequences (DWI & DCE). The T2W sequences
107 provide morphologic details about the gland sub-structure internally- including zonal
108 anatomy, the location of the prostate pseudo capsule, and peri-prostatic structures. T1W
109 sequences are especially useful for detection of post biopsy hemorrhage within the prostate
110 gland or the seminal vesicles.

111

112 The peripheral zone is the site of origin of 75% prostate cancer.[19] The normal peripheral
113 zone appears of high signal intensity on T2W and tumors within the peripheral gland
114 appear as round or ill-defined hypointense (low signal) focal lesions. In addition to low T2
115 signal intensity, peripheral zone tumors typically exhibit restricted diffusion.[20] The
116 transition zone, is the site of origin of benign prostatic hyperplasia (BPH) and the remaining
117 25% of cancers. The MR findings seen in BPH are multifocal heterogeneous mixtures of
118 glandular nodules (T2 hyperintense) and intervening stromal tissue (T2 hypointense).
119 Cancers in the TZ, in contrast tend to demonstrate uniformly low T2 signal and a variety
120 of shapes such as lenticular non-circumscribed shape and can have blurred internal signal
121 described as “erased charcoal.” [21] [22] Therefore, stromal BPH can occasionally mimic

122 or obscure clinically significant cancer in the TZ as **these nodules are often highly**
123 **vascularized**. The central zone (CZ) and the anterior fibromuscular stroma (AFMS)
124 comprise the smallest portion of prostatic tissue and less than 5% of cancers originate
125 there—**however given lack of early enhancement in these two regions, the potential**
126 **for contrast enhanced sequences to identify tumor in these two sites is one potential**
127 **benefit of DCE sequences.**[5]

128

129 Both DWI and DCE sequences provide tissue characterization- namely cellularity and
130 vascularity respectively. DWI provides information on diffusion of water molecules in
131 tissue. In areas of cancer where the cells are tightly packed or dense they restrict the water
132 motion leading high signal on DWI and corresponding low ADC.[23] [24] [25] DWI can
133 qualitatively identify focal areas of restriction and the actual quantification using the ADC
134 value. Because loss of proliferative controls are a hallmark of aggressive tumors, areas of
135 restricted diffusion tend to harbor more aggressive tumors.[13] Low ADC values on MRI
136 (indicating restricted diffusion) indicate higher grade tumors. [14] [15] [26] ADC metrics
137 have been found to be inversely related to the Gleason grade, an established measure of
138 prostate tumor aggressiveness.[27] [28] [29]

139

140 The DWI is one of the most important contributors to the overall PI-RADS assessment and
141 must be combined with data from the T2W and DCE images.[20] [5] Just as diffusion
142 weighted sequences provide information about disordered cellular proliferation, contrast
143 enhanced sequences reveal tumor neovascularization, a process largely mediated by
144 increased androgen receptor expression seen in higher grade tumors.[30] **Therefore, even**

145 **taking into account the normal-age related changes of prostatic hyperplasia, prostate**
146 **cancer will often demonstrate focal and early enhancement compared to normal**
147 **gland tissue.**

148

149 It is now accepted radiological practice to interpret and report prostate MRI using PI-RADS
150 v2.1. This international standard provides an assessment of suspicious lesions from 1-5
151 with higher numbers indicating a higher probability of cancer.[20] T2 weighted images are
152 the key sequences for evaluation of the transition zone, whereas diffusion weighted
153 sequences are key for evaluation of the peripheral zone. The role of contrast enhancement
154 is limited to the evaluation of PI-RADS 3 (defined as: “the presence of clinically significant
155 cancer is equivocal”) lesions in the peripheral zone and has no formal role in TZ lesions.
156 Specifically, a PZ lesion which would otherwise be scored 3 in the peripheral zone based
157 on diffusion weighted sequences, but which exhibits early or focal contrast enhancement
158 would be scored 4 (defined as: “clinically significant prostate cancer is likely”).

159

160 *Barriers to MRI Dissemination*

161

162 Despite efforts to standardize prostate MRI, level-1 evidence of its role prior to biopsy, and
163 guidelines supporting its use,[31] [32] is still only used in a minority of men.[33] There
164 are many reasons for this in 2021, a major one being access to MR scanners. Due to the
165 high costs of the MR scanners and their operation, many healthcare systems across the
166 world have limited access. MRI utilization is carefully controlled and monitored, along
167 with insurance coverage. The limits vary and there are local and geographical differences

168 in the prioritization of clinical needs. There are also variations in the experience of
169 radiologists and lack of acceptance by referring physicians (Urologists, Radiation
170 Oncologists and other specialists).

171

172 While actual hospital MRI costs are difficult to accurately obtain and report, it is clear that
173 MR exams are charged at a premium in order to recoup the capital investment and relatively
174 high operational costs, given the technical training and skills required to both perform and
175 interpret the exam. These relatively fixed costs are resistant to change and will reflect the
176 level of acceptance by the insurance or third-party payors. Most MR exam times are
177 restricted to 30-40minutes per patient and any opportunity to reduce or speed up the exam
178 time can be very welcome.

179

180 The DCE sequence requires IV contrast and the exam or “table-time” as well as costs
181 associated with contrast can be modulated. In comparison to typical MR acquisition times
182 of around 30 minutes for an mpMRI, abbreviated protocols can allow for a reduction **in**
183 **acquisition time** to under 10 minutes.[11] **It should be noted that there is variability**
184 **due to specific protocols utilized and specific time savings related to elimination of**
185 **contrast sequences alone may less than the 20 minutes implied by this study. In the**
186 **study cited above, the authors utilized only axial T2W sequences and axial DWI. A 3**
187 **plane T2W and T1W sequence with a large field of view (to calculate volume, rule out**
188 **hemorrhage and assess for nodal and bony metastases) would not achieve such a**
189 **dramatic time savings. Because there are differences in the specific bpMRI protocols,**
190 **the amount of time and resources saved with this approach can vary.**

191

192 The second category of potential costs savings—reduction in pharmacy costs, and
193 associated resources required for contrast administration is also complex. While
194 eliminating contrast sequences may plausibly reduce costs related ordering, storing and
195 administering contrast agents, there are other mitigation strategies. For example, there was
196 a 2017 recommendation from the American College of Radiology which suggested that
197 evaluation of pre-procedural glomerular filtration rate (GFR) be made optional prior to
198 administration of macrocyclic contrast agents.[34] This has the potential for significant
199 costs savings in prostate imaging without needing to eliminate these sequences.[35]
200 Additionally, nearly all MRI facilities utilize Gadolinium contrast, so many of the costs
201 associated for storage and administration of contrast are fixed.

202

203 Although calculating the precise cost savings is difficult, and despite the presence of other
204 potential mitigation strategies to reduce the cost of MRI, it is likely that bpMRI protocols
205 do confer some cost savings. By reducing exam time, the number of MRIs per day can be
206 increased. This may increase revenue in fee for service settings, which may decrease the
207 depreciation time over which the equipment is “paid off” thereby spurring increased
208 investment in MRI scanners. This can subsequently offer the chance of lowering the
209 notable differences in health care access among some patients.[36] [33]

210

211 **Although a less intensive and shorter study duration is likely to save money in most**
212 **health systems, it is important to acknowledge that the financial benefits of adopting**
213 **of a bpMRI likely differ for different stakeholders and within different health**

214 **systems. For example, radiologists who practice in a fee for service setting may receive**
215 **credit for fewer MRIs if the total time to read a study is greater (possible with bpMRI)**
216 **and similarly, a greater number of biopsies performed in the setting of equivocal**
217 **bpMRI could raise costs for the health system at large while increasing revenue for**
218 **urologists who are paid on a per-biopsy basis.**

219

220

221 **Comparative Effectiveness of Multi-Parametric versus Bi-Parametric MRI**

222

223 *Review of current published investigations Comparing Multi- versus Bi-Parametric MRI*

224

225 One of the first studies to evaluate the relative contribution of DWI and DCE to prostate
226 MRI was performed by Yoshizako et al. and published in 2008.[37] Their team analyzed
227 preoperative MRIs on 35 men treated with radical prostatectomy for prostate cancer. The
228 accuracy of MRI for detecting *transition zone* cancer was compared using T2 only, T2 plus
229 diffusion weighted sequences, T2 plus contrast enhancement and all three sequences. The
230 accuracy of 64.3% increased to 69% percent when adding DCE alone, but to 83.3% when
231 adding DWI. Although both DWI and DCE sequences improved the accuracy of prostate
232 MRI, largest benefit was seen with the addition of diffusion weighted sequences and a
233 relatively smaller benefit was seen with the addition of contrast enhanced sequences.

234

235 A similar study comparing the relative contribution of diffusion weighted and contrast
236 enhanced sequences was performed by Kitajima et al, whose 2010 analysis of 53 sequential

237 men with suspected prostate cancer who received pre-biopsy MRI. The accuracy of MRI
238 for different MRI strategies was compared. [38] They reported that the addition of diffusion
239 weighted sequences and contrast enhanced sequences improve sensitivity, specificity and
240 accuracy compared to T2 weighted sequences alone. Although their ROC analysis showed
241 no significant difference between the AUC T2 weighted plus DWI versus all three
242 sequences (T2 plus DWI plus contrast enhanced sequences), the sensitivity and specificity
243 of the full multiparametric approach including both contrast-enhanced and diffusion
244 weighted sequences was superior to the biparametric approach. Likewise, a retrospective
245 study in radical prostatectomy patients by Taghipour et al found that DCE identified
246 clinically significant PCa in most equivocal PZ lesions, DCE being correct in increasing
247 the assessment category to PI-RADS 4 in 69% of cases that received a PI-RADS 3 score
248 based on DWI alone.[39]

249

250 Since that time, a small series mostly retrospective studies have assessed the relative
251 contribution of contrast enhanced sequences. A 2018 meta-analysis by Woo et al, pooled
252 the data from 24 studies comparing these two approaches. The study did not demonstrate
253 a benefit for multi-parametric over biparametric approach, however the studies exhibited a
254 large degree of heterogeneity, were mostly retrospective, and the MR techniques varied in
255 such as use of endorectal coil, Radiologist's experience and DCE temporal resolution as
256 well as the measure of truth or diagnostic accuracy (the studies varied in terms of the
257 reference standards for pathological evidence of prostate cancer with some using TRUS
258 versus transperineal biopsy, saturation versus targeted, and a minority using radical
259 prostatectomy specimens).[40]

260

261 Accuracy reported in other studies in the pre-diagnostic setting is similar and generally
262 comparable between the two approaches: Thestrup et al compared the accuracy of
263 biparametric versus multiparametric MRI in a series of men reviewed by two radiologists
264 at a single hospital. The authors compare of results generated using T2 and DWI only
265 versus multiparametric approach including IV contrast. They report sensitivity in the range
266 of 0.94 to 0.96 for biparametric and 0.93 to 1.00 for multiparametric protocols. The two
267 approaches were not significantly different in terms of accuracy. The rate of false negatives
268 was 0.49% for biparametric and 0.0% with mpMRI.[41] A similar two-institution study
269 was reported by Stanzone et al, AUC obtained from the ROC analysis were 0.91 and 0.93
270 for bpMRI and mpMRI, respectively.[42]

271

272 In one of the largest retrospective studies to date, Kuhl et al, reported their experience with
273 a prospective series of 542 men who were recruited for prostate MRI following negative
274 TRUS biopsies. Men received full multiparametric MRI studies and the radiologists
275 reviewed all images from an biparametric protocol prior to the full multiparametric series.
276 Men received an MRI guided biopsy and the biopsy results for the targeted lesions were
277 compared between the bi-parametric versus mpMRI. For the diagnosis of significant
278 prostate cancer using the abbreviated versus full protocols, the authors report sensitivities
279 of 93.9% (95% Confidence Interval (CI) 88.7 to 97.2) and 94.9% (95% CI 88.8 to 97.2),
280 respectively, and specificities of 87.6% (95% CI 83.9 to 90.7) and 84.8% (95% CI 80.1 to
281 88.2). The accuracy of the two tests was comparable. [11]

282

283 **In the Biparametric MRI for Detection of Prostate Cancer (BIDOC) Study, Boesen et**
284 **al, reported the results of a prospective single arm study which assigned biopsy-naïve**
285 **men with concern for prostate cancer (based on abnormal DRE or PSA >4ng/dl) to**
286 **receive bpMRI plus a systematic TRUS biopsy. They report an excellent negative**
287 **predictive value of negative bpMRI findings in ruling out significant prostate cancer**
288 **of 97% (95% CI, 95%-99%) supports the use of bpMRI as an initial screening test in**
289 **this population.[43] Similarly, in the IMPROD study, Merisaari et al report the**
290 **accuracy of bpMRI in a cohort of men who received radical prostatectomy.[44] While**
291 **there is necessarily bias related to the fact that this study only included men who**
292 **indeed had clinically significant cancer (based on the fact that they received radical**
293 **prostatectomy), the authors report that specificity of bpMRI findings of nearly 100%**
294 **once they included a margin of 10-12mm around the region of interest on bpMRI.**

295

296 Most recently Alabousi et al, performed a similar analysis pooling data from an
297 overlapping series of studies. This meta-analysis published in 2019 also found no
298 difference between the two approaches but commented on the large degree of heterogeneity
299 in the literature. [45]

300

301 *Prospective Studies Comparing Multi versus Biparametric MRI*

302 Imaging based comparative effectiveness trials are challenging as they present difficulties
303 with both blinding and allocation concealment. [46] [47] Thus prospective trials are not
304 straightforward. To date, multi- versus bi-parametric MRI studies have not been evaluated
305 in the context of a dedicated prospective clinical trial. With that said, reanalysis of trial

306 data from diagnostic studies has been performed to assess the relatively accuracy of bi-
307 versus multi-parametric MRI.

308

309 A series of retrospective analyses of prospective studies from the National Cancer Institute
310 were performed to assess the performance of MRI-based prostate cancer detection
311 strategies. Rais-Bahrami et al, (NCI) reviewed results from 149 men with no prior prostate
312 cancer diagnosis enrolled in a prospective trial, with mpMRI, followed by targeted biopsy
313 of lesions and standard 12-core biopsy. They did a sub-analysis of men with MR suspicious
314 lesions on both T2W and DWI MRI (defined as bpMRI positive) and found that bpMRI
315 positive lesions yielded an AUC of 0.8 with higher accuracy obtained in combination with
316 PSA. [48]

317

318 A separate validation study of 59 men at the NCI with no prior biopsy and referral for
319 elevated PSA > 4ng/mL compared the diagnostic accuracy of combining biparametric
320 “screen positive” lesions (visible lesion on DWI and T2W sequences) with PSA density
321 for predicting presence of significant disease. They report a sensitivity of 79.4% and 76.0%
322 respectively for detecting Gleason score 7 or higher lesions.[49] **It should be noted that**
323 **these results were obtained with relatively high-precision diagnosis by MRI guided**
324 **prostate biopsy and experienced radiologists.**

325

326 Similarly, a sub-analysis of the PROMIS trial data was used to compare bi- versus
327 multiparametric MRI. The prospective PROMIS trial was a diagnostic study that enrolled
328 576 men at 11 UK centres who received both transperineal mapping biopsies alongside

329 standard TRUS ultrasound guided 12 core biopsy.[12] In the sub-analysis Boisaily et al,
330 compared the diagnostic accuracy of MRI with and without contrast enhanced sequences.
331 Radiologists reported lesions on a 1-5 scale using first T2 alone, then T2 plus diffusion
332 weighted images then contrast enhanced images. They report no statistically significant
333 difference in diagnostic accuracy between the strategies of T2 + DWI versus T2 + DWI +
334 DCE. With that said, the DCE sequences did lead to scoring changes in a sizeable minority
335 of equivocal lesions—of 158 lesions scored 3/5 on biparametric MRI, 32 were downgraded
336 after addition of contrast sequences and 31 were upgraded to 4/5 or 5/5 with the addition
337 of contrast. [50]

338

339 Recently, the results of a large Swedish population-based screening trial using MRI were
340 published. This study randomized **1,532 men** with PSA above 3 ng/mL to receive either
341 standard transrectal ultrasound guided 12 or 10 core prostate biopsies, versus a bpMRI with
342 subsequent biopsy for PIRADS 3 or higher lesions. The authors report that the bpMRI
343 based strategy was non-inferior to standard biopsy using a noninferiority margin of 4% (p
344 <0.001 for noninferiority). Furthermore, the bpMRI strategy resulted in a lower percentage
345 of clinically insignificant cancer (4% versus 12% in the TRUS biopsy group).[51]

346

347 **Drawbacks of a Biparametric MRI Based Approach**

348

349 Although the ability of bpMRI to identify clinically significant cancer with similar
350 accuracy to multiparametric MRI is demonstrated in the above studies, there are
351 noteworthy limitations. For one, although the usefulness of DCE sequences in the PI-

352 RADSv2.1 is confined to a relatively “minor” case example of equivocal lesions on T2 and
353 DWI sequences, the number of PI-RADS 3 lesions is still a substantial portion of all pre-
354 diagnosis MRIs. Given an incidence of hundreds of thousands of new cases worldwide, a
355 findings of equivocal lesions in 20-30% of men represents a large group of men. As a result,
356 a bi-parametric MRI setup may trigger a need for an increased amount of documentation
357 and the tightening of follow-up and surveillance programs. By definition, bpMRI does not
358 carry any information from DCE. Any suspicious lesion in the PZ of the gland will be
359 assessed based on information provided by DWI/ADC primarily. Any lesion with a
360 suspicion score of PI-RADS 3 will not have the option to be upgraded to a PI-RADS 4;
361 subsequently, the probability of csPCa in those PI-RADS categories will likely change and
362 an extended diagnostic uncertainty will need to be accounted for by clinicians.
363 Nevertheless, under PI-RADSv2.1 guideline, the interpretation of TZ lesions will be
364 generally unchanged. Commentators have noted that a “safety net” is required for this
365 group which can included close follow-up with repeat MRI or proceeding directly to
366 biopsy. Thus bpMRI alone may raise the number of men receiving negative biopsies or
367 repeat MRI.[52] **Given that MRI-targeted biopsies themselves have a learning curve**
368 **and some degree of variability, both true-negative and false negative biopsies could**
369 **conceivably increase in number with bpMRI.**

370

371 Secondly, much of the work validating the MRI scoring systems and evaluating the
372 effectiveness of bpMRI has been done in centers of excellence with experienced GU
373 radiologists. Gatti et al, performed a noteworthy analysis of the accuracy of bi- versus
374 multi-parametric MRI which was stratified by radiologist experience. They report that

375 among radiologists with highest experience (over 1000 cases reported) there was no
376 difference between the multi- and bi-parametric MRI. In contrast, less experienced readers
377 needed the contrast enhanced sequences in order to boost sensitivity and to achieve high
378 AUCs.[53] While much of the initial research developing and validating MRI has been
379 performed in academic centers, the ability to translate this work into large scale practice
380 remains unproven and techniques to ensure quality are vital.[54] If contrast enhanced
381 sequences can shorten the learning curve then this may be a reason to retain these
382 sequences. **Another key factor is that less experienced radiologists using bpMRI may**
383 **require more time to read and score each study (especially equivocal studies). If this**
384 **is the case, then for a bpMRI, it is possible that the time-savings in the scanner itself**
385 **could be outweighed by the extra time required to read and score each study.**

386

387 **While the studies cited above and others support that bpMRI is not inferior to**
388 **mpMRI [44] [43] it is likely crucial to ensure there is high quality throughout the**
389 **diagnostic pathway (from referral to biopsy) including careful evaluation of clinical**
390 **factors and quality-assurance practices (including close monitoring of the proportion**
391 **of patients assigned to PIRADS-3). If the elimination of contrast enhanced sequences**
392 **leads to dramatic increases in the proportion of equivocal MRI reads then the benefit**
393 **of bpMRI could quickly be lost.**

394

395 **It should be kept in mind that many earlier studies comparing mpMRI and bpMRI**
396 **were performed prior to contemporary scoring systems (e.g. PI-RADS v2 and PI-**
397 **RADS v2.1). There is evidence that interrater agreement is higher using more modern**

398 **scoring system. Thus readers utilizing PI-RADS v2.1 may obtain even greater**
399 **concordance of mpMRI and bpMR, as shown in a recent study by Tamada et al.**
400 **[55](with the important caveat that PI-RADS v 2.1 does still require DCE sequences**
401 **for scoring some lesions).**

402

403 Lastly, there are specific clinical scenarios where contrast enhanced sequences are
404 required. For example, there is consensus on the importance of including contrast-enhanced
405 sequences in follow up after any prostate cancer therapy (e.g. after focal therapy).[56] It
406 may well be that the specific sequences utilized will ultimately be tailored to the clinical
407 scenario at hand with bpMRI utilized in a pre-diagnostic setting and a full MRI utilized
408 where necessary. Similar approaches to utilize less intense imaging protocols in specific
409 clinical settings are already utilized in other areas of medicine, for example, in the case of
410 using ultra low dose CT scans for follow up of patients with known kidney stones.[57]
411 There can also be technology based implication, which might demand a use of mpMRI.
412 MRI exams are especially susceptible to distortions from metallic materials; as a result,
413 patients with metal implants, such as a hip prosthesis, can be expected to have DWI result
414 in reduced diagnostic quality. Also, patients who received prostate treatment like hormonal
415 treatments, embolization, or focal therapy can harbor altered prostate morphology, making
416 an appropriate evaluation based on bpMRI challenging. **Similarly, a lower specificity can**
417 **be seen in men history of prostatitis—which typically have wedge shaped areas of**
418 **enhancement on mpMRI. In the case of prostate inflammation, it can be useful to**
419 **report this on pathology reports in order to address this potential confounder.**

420

421 **Along the same lines, men with high-risk prostate cancer are at risk for local invasion**
422 **and regional metastasis. There is evidence that a true multiparametric approach**
423 **including contrast enhanced sequences has greater ability to identify nodal metastases**
424 **and seminal vesicle invasion.[58] Thus for men with likely high risk or regional risk**
425 **group cancer the contrast enhanced sequences play a key role.**

426

427 **Can Biparametric MRI Improve Access?**

428

429 The ability to increase the number of MR exams within a given time period, while reducing
430 costs related to staffing (e.g. nursing and pharmacy) in MRI has significant implications
431 for access, costs and dissemination. In the United States, the performance of MRI for men
432 on active surveillance varies considerably from geographical region to region with far
433 greater use among wealthier, non-minority men in coastal cities.[59] [60] There is hope
434 that by reducing costs, bpMRI may increase the number of men who receive this test. This
435 would lower a socioeconomic barrier in access to care. There is extensive evidence that
436 that socioeconomic status and geography can increase disparities of care in cancer patients.
437 [61] [62] [63] [64] [65] Reducing these barriers to access and receipt of MRI would be
438 desirable and beneficial to many.

439

440 There is evidence supporting cost-effectiveness of pre-biopsy MRI strategy.[66] A recent
441 analysis from the University of Alabama compared typical costs and insurance
442 reimbursement for multi- versus bi-parametric MRI. They found that the profit achievable
443 with a biparametric strategy was \$510.44 versus \$638.74 for a mpMRI. When controlling

444 for the time required for the two studies, and taking into account that three biparametric
445 MRI studies can be performed within a 45 minute time window required multiparametric
446 MRI, the total increase in earnings for a typical 9 hour business day was \$10,710.9 using
447 a biparametric strategy.[67] Although few would argue that such considerations ought to
448 be the serious determinant of MRI strategy, the widespread adoption of prostate MRI
449 clearly depends on hospitals and radiology groups assessing the value of these two
450 approaches. **From a health systems perspective, the cost savings must be weighed
451 against the biopsies themselves: The reduction in unnecessary biopsies in men with
452 negative pre-biopsy MRI must be weighed against a potential need for more biopsies
453 in borderline cases of men with bpMRI. A recent study of Medicare insurance claims
454 for prostate biopsies reported a cost of \$1,750 for office biopsies and \$2,260 for those
455 performed in ambulatory surgical centers. [68]**

456

457 Broadly speaking, more expensive but more accurate diagnostic tests can yield cost savings
458 if they can avoid unnecessary procedures such as biopsies.[69] There is evidence that MRI
459 as an initial screening test to determine who gets biopsies can be cost-effective.[66] The
460 question of whether the additional marginal accuracy of multiparametric MRI can provide
461 value which outweighs the costs of this technique versus biparametric MRI has not yet
462 been answered. Various tools to improve standardization and quality of prostate MRI have
463 been proposed but ultimately the benefit of “guard rails” of contrast enhanced MRIs must
464 be weighed against the ability to provide these important tests to a far greater number of
465 men.

466

467 **Conclusion**

468

469 In conclusion, the data broadly support that biparametric MRI can approach the accuracy
470 of multiparametric MRI in high volume academic settings among expert radiologists with
471 extensive experience. The caveat is that prospective, generalizable community-based trials
472 are lacking and there remain specific use scenarios where mpMRI is necessary. There is
473 likely a conflict, between the potentially higher expertise required to accurately read and
474 report bpMRI and the stated goal of using bpMRI as a lever to support widespread
475 dissemination of prostate MRI. From a health systems perspective, the opportunity to
476 perform a larger number of MRIs in more settings and at lower costs must be weighed
477 against the potential for a greater number of equivocal results and the potentially steeper
478 learning curve with the bpMRI approach. While further evaluation of bpMRI in the
479 diagnostic pathway remains underway, the DCE component of a mpMRI exam remains an
480 integral part of most prostate MR exams.

481

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483

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