Original Article

Comparison of Biparametric and Multiparametric Prostate Magnetic Resonance Imaging in Predicting Oncologic Outcomes After Radical Prostatectomy

Radikal Prostatektomi Sonrası Onkolojik Sonuçları Öngörmede Biparametrik ve Multiparametrik Prostat Manyetik Rezonans Görüntülemenin Karşılaştırılması

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ABSTRACT

Objective: This study aimed to evaluate the difference in predicting the pathological stage of retropubic radical prostatectomy (RRP) and biochemical recurrence (BCR) in patients with Prostate Imaging Reporting and Data System (PIRADS) scores of 3 and 4 on biparametric prostate magnetic resonance imaging (bpMRI) compared to patients who upgraded from PIRADS 3 to PIRADS 4 based on the contrast-enhanced PIRADS version 2.1.

Methods: This study evaluated 107 patients who underwent RRP and had preoperative multiparametric prostate magnetic resonance imaging (mpMRI) and were followed regularly. Group 1 included 31 patients evaluated as PIRADS 3 in both bpMRI and mpMRI, group 2 included 31 patients evaluated as PIRADS 3 in bpMRI and PIRADS 4 in mpMRI, and group 3 included 45 patients evaluated as PIRADS 4 without contrast. Comparisons were made between groups 1 and 2 and between groups 2 and 3.

Results: No significant difference was found between the groups in terms of demographic data, preoperative or postoperative radiology, and pathology findings. Extraprostatic extension positivity and BCR were more common in group 2 compared to group 1 although not significant. Multivariate regression analysis was performed to determine the risk factors in predicting BCR, which revealed the positivity of seminal vesicle invasion and high pathological stage in the pathology report as significant factors. Prostate-specific antigen (PSA) and PSA density were higher in group 3 than in group 2, but without significance.

Conclusions: This study revealed that mpMRI did not contribute in predicting BCR after RRP compared to bpMRI.

Keywords: Cancer, prostate magnetic resonance imaging, radical prostatectomy

ÖZ

Amaç: Biparametrik prostat manyetik rezonans görüntüleme (bpMRG) ile multiparametrik prostat manyetik rezonans görüntülemenin (mpMRG) Prostat Görüntüleme Raporlama ve Veri Sistemi (PIRADS) skoru 3-4 olan hastalarda retropubik radikal prostatektomi (RRP) patolojik evresi ve biyokimyasal nüksü (BKN) öngörmedeki etkisini kıyaslamaktır.

Yöntemler: Preoperatif mpMRG çekildikten sonra RRP uygulanan ve düzenli takipleri yapılan toplam 107 hasta değerlendirildi. Grup 1 hem bpMRG hem de mpMRG'de PIRADS 3 olarak değerlendirilen 31 hastadan, grup 2 bpMRG'de PIRADS 3 ve mpMRG'de PIRADS 4 olarak değerlendirilen 31 hastadan oluşturuldu. Grup 3 ise kontrastsız çekimde PIRADS 4 skoru alan 45 hastadan oluşuyordu. Grup 1 ve 2 ile grup 2 ve 3 arasında karşılaştırmalar yapıldı.

Bulgular: Demografik veriler, preoperatif/postoperatif radyoloji ve patoloji bulguları açısından gruplar arasında anlamlı fark yoktu. Anlamlı olmasa da ekstraprostatik yayılım (EPY) pozitifliği ve BKN grup 2'de grup 1'e göre daha sıktı. BKN, patoloji raporunda seminal vezikül invazyonu pozitifliği ve yüksek patolojik evreyi öngören risk faktörlerini belirlemek için çok değişkenli regresyon analizi yapıldı. Grup 2 ve 3 karşılaştırıldığında, prostat spesifik antijen (PSA) ve PSA dansitesi anlamlı olmasa da grup 3'te daha yüksekti.

Sonuçlar: Çalışmamızda mpMRG yöntemi bpMRG yöntemiyle karşılaştırıldığında, RRP sonrası BKN'yi öngörmede ek bir katkı sağlamadı.

Anahtar kelimeler: Kanser, prostat manyetik rezonans görüntüleme, radikal prostatektomi

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INTRODUCTION

Today, multiparametric prostate magnetic resonance imaging (mpMRI), which includes anatomical, functional T2-weighted imaging (T2WI), diffusion-weighted imaging (DWI), and dynamic contrast imaging (DCE), has an important place in every stage of prostate cancer (PCa) management. Interpretation varies a lot due to reader experience and differences in imaging quality. The Prostate Imaging Reporting and Data System (PIRADS) was announced in 2012[1]. The latest version, version 2.1, was released in 2019[2]. The current reporting system continues to evolve.

The current literature revealed controversial effects of DCE on mpMRI interpretation. Only the biparametric prostate magnetic resonance imaging (bpMRI) that uses multiplane T2WI and axial DWI is recommended as an alternative because mpMRI has several disadvantages[3]. The use of contrast and, accordingly, the acquisition of more images can lead to cost and labor loss due to prolonged time spent to acquire the images and interpret them. Additionally, renal function evaluation is required for each patient before the imaging. Gadolinium is retained in body tissues for years although acute gadolinium reactions are rare[4].

Lesions with PIRADS-3 can be classified as 4 with the contrast-enhanced examination. Apart from this distinction, it has no additional contribution to classification with bpMRI. This study aimed to compare the post-retropubic radical prostatectomy (RRP), and histopathological and oncological results of patients with PCa with different PIRADS scores in bpMRI and mpMRI.

MATERIALS and METHODS

Patients (n=107) with preoperative mpMRI taken from December 2016 to December 2019, indicated PIRADS-3 or -4, had undergone RRP with PCa diagnosis and were under regular outpatient follow-up were evaluated. The ethical permission for this study was approved by the locale Ethical Committee of the Istanbul Medeniyet University Goztepe Training and Research Hospital (decision no: 2020/0507, date: 02.09.2020). Patients who had mpMRI before RRP were included in the study if they had adequate quality MR images and had regular postoperative serum prostate-specific antigen (PSA) measurements. Patients without T2WI or apparent diffusion coefficient maps and patients who received radiotherapy, hormone therapy, or chemotherapy before imaging were excluded from the study. This study used two different MRI devices [1.5 Tesla GE Optima MR360 and MR450w (General Electric, Chicago, USA)]. Two

different gadolinium contrast agents were used for 3 years. Table 1 shows the MRI protocol used in the study. The mpMRI and bpMRI findings were re-reported by two experienced radiologists. Then, it was scored again on a five-point scale using the PIRADS v.2.1 criteria[2]. PSA density was defined as the ratio of PSA to prostate volume.

Patients evaluated as PIRADS-3 on both bpMRI and mpMRI were classified as group 1. Patients with PIRADS-3 on bpMRI and PIRADS-4 (3+1) on mpMRI were classified as group 2 (Figure 1). Patients with PIRADS-4 on both bpMRI and mpMRI were classified as group 3. The characteristics of lesions mapped after histopathological examination and lesions reported as PIRADS-3 or 4 detected on MRI were compared. The groups were also compared for oncological outcomes. Biochemical recurrence (BCR) was defined as two consecutive serum PSA values of >0.2 ng/mL.

Statistical Analysis

One-sample Kolmogorov-Smirnov test was performed to assess the normal distribution of quantitative variables of data. Mean ± standard deviation found in the variable with normal distribution and median values
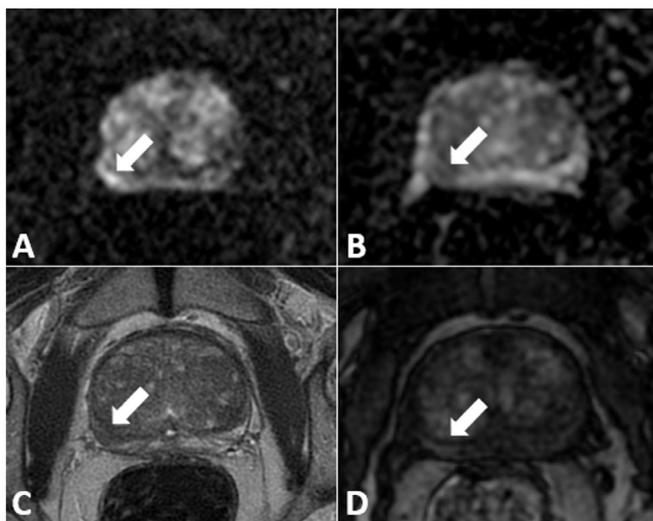
Figure 1. A case scored as PIRADS-4 both on bpMRI and mpMRI. **A.** High b value DWI (b1500), **B.** ADC, **C.** T2 weighted, **D.** T1-DCE perfusion sequences. The index lesion is marked with an arrow in the right peripheral zone.

PIRADS: Prostate Imaging Reporting and Data System, bpMRI: Biparametric prostate magnetic resonance imaging, mpMRI: Magnetic resonance imaging, DWI: Diffusion-weighted imaging, DCE: Dynamic contrast imaging

were recorded for the others. Quantitative values were compared with Student's t-test for normally distributed data, and the Mann-Whitney U test for non-normally distributed data. Fisher's Exact test and Pearson chi-square test were applied to determine the difference between the percentages of categorical variables. Binary logistic regression analysis was applied to obtain predicting factors for BCR following RRP. Multivariate logistic regression analysis was applied for data that were statistically significant in the univariate analysis. The statistical significance level was determined as p-values of <0.05. Statistical analysis was performed using the IBM SPSS version 22.0 package program.

RESULTS

Groups 1, 2, and 3 included 31, 31, and 45 patients, respectively. The mean follow-up period of our patients was 43.51±16 months. No statistically significant difference was found between the groups in terms of demographic data, histopathological findings, and preoperative/postoperative radiological findings (Table 2). Extraprostatic extension (EPE) positivity (19.4%, 38.7%, p=0.093) and BCR (6.5%, 19.4%, p=0.093, respectively) were lower in group 1 compared to group 2 although not significant (Table 2). Additionally, the tumor diameter reported in the pathology report was also shorter in group 1 compared to group 2 (p=0.077) (Table 2). Univariate regression analysis to determine the risk factors for predicting BCR revealed significant positivity of pathology reports for seminal vesicle invasion (SVI), high pathological stage, and EPE. The multivariate regression analysis indicated that the positivity of SVI and high pathological stage were significant factors (odds ratio: 13.961, 95% confidence interval: 1.224-159.277, p=0.034) (Table 3).

PSA at the time of diagnosis [9.1 (1.8), 18.4 (4.9), p=0.13] and PSA density [0.18 (0.02), 0.44 (0.13), p=0.105, respectively] were higher in group 3 than in group 2, but without significant difference (Table 2). Univariate regression analysis to determine the risk factors for predicting BCR revealed PSA value at the time of diagnosis, PSA density, pathological EPE positivity, pathological stage, and RRP International Society of Urological Pathology (ISUP) grade as significant factors. Multivariate regression analysis only revealed the pathological EPE positivity as significant (p=0.003) (Table 4).

DISCUSSION

Our study revealed no difference between the histopathological and early oncological results of patients with PCa who had different PIRADS scores based on bpMRI and mpMRI after RRP. The place of DCE in mpMRI remained a controversial issue in the current literature. DCE does not contribute to the overall assessment in the group of patients with low (PIRADS-1 or 2) or high (PIRADS-4 or 5) PIRADS scores. However, a positive DCE can increase the rating category from PIRADS-3 to 4[2]. Considerably, lesions identified as PIRADS (3+1) by contrast enhancement in the presence of suspicious cases may be a different form from PIRADS-4 lesions identified through bpMRI sequences in terms of clinically significant PCa (csPCa) detection[5]. Our study revealed no statistically significant difference between the group whose PIRADS score increased from 3 to 4 and the group that remained the same in terms of both histopathological features and BCR. No adverse effects were observed on the clinical course after RRP despite the increase detected in the imaging method.

Table 1. Multiparametric prostate MRI acquisition protocol used in the study.			
	T2W-FSE	**DWI**	**T1-DCE perfusion**
Plane	Axial + Coronal + Sagittal	Axial	Axial
Fat suppression	-	-	-
Repetition time (ms)	4413-5824	3445	4.1
Echo time (ms)	121.9	78	1.9
Flip angle (°)	160	90	12
Slice thickness (mm)	3	3	4
Field of view (mm)	200×200	240×240	240×192
Matrix (mm x mm)	320×320	96×96	160×160
NEX	2.5	2	0.78
Time interval after contrast injection (sec)	-	-	8-12 (40 phase)
b value (s/mm²)	-	50, 800, 1000, 1500	
T2W: T2 weighted, FSE: Fast spin echo, DWI: Diffusion-weighted imaging, DCE: Dynamic contrast enhanced			

Table 2. Demographic, clinical, preoperative, and postoperative radiology/pathology findings with follow-up.

	Group 1 (n=31)	Group 2 (n=31)	p-value	Group 2 (n=31)	Group 3 (n=45)	p-value
Age at diagnosis	63.1 (7.1)	64.7 (5.9)	0.352	64.7 (5.9)	65.7 (5.5)	0.431
Body mass index	28.4 (3.3)	27 (2.9)	0.087	27 (2.9)	26.6 (3.2)	0.541
Pack years of smoking	16.2 (3.2)	18.4 (2.8)	0.597	18.4 (2.8)	16 (2.5)	0.531
PSA (ng/mL)	10.5 (1.6)	9.1 (1.8)	0.567	9.1 (1.8)	18.4 (4.9)	0.131
Prostate volume detected at MRI	65.2 (46.6)	51.9 (27)	0.174	51.9 (27)	54.8 (28.9)	0.654
PSA density	0.19 (0.03)	0.18 (0.02)	0.662	0.18 (0.02)	0.44 (0.13)	0.105
Long axis of lesion (pathology)	17.3 (8.5)	21.5 (9.8)	0.077	21.5 (9.8)	22.4 (12.9)	0.763
Prostate volume (pathology)	63.4 (39.5)	52.3 (27.5)	0.206	52.3 (27.5)	57.8 (32)	0.442
Family history of PCa (n, %)	4 (12.9%)	6 (19.4%)	0.490	6 (19.4%)	5 (11.1%)	0.315
SVI + detected at MRI (n, %)	1 (3.2%)	3 (9.7%)	0.612	3 (9.7%)	4 (8.9%)	0.604
EPE positivity detected at MRI (n, %)	0	2 (6.5%)	0.492	2 (6.5%)	1 (2.2%)	0.563
LN + detected at MRI (n, %)	2 (6.5%)	2 (6.5%)	0.694	2 (6.5%)	6 (13.3%)	0.337
EPE positivity (n, %)	6 (19.4%)	12 (38.7%)	0.093	12 (38.7%)	21 (46.7%)	0.492
LN + (n, %)	0	1 (3.2%)	0.500	1 (3.2%)	0	0.408
pT2	25 (80.6%)	19 (61.3%)	0.093	19 (61.3%)	22 (48.9%)	0.286
pT3	6 (19.4%)	12 (38.2%)		12 (38.7%)	23 (51.1%)	
Biochemical recurrence (n, %)	2 (6.5%)	6 (19.4%)	0.130	6 (19.4%)	7 (15.6%)	0.666

PSA: Prostate-specific antigen, PCa: Prostate cancer, MRI: Magnetic resonance imaging, EPE: Extraprostatic extension, SVI: Seminal vesicle invasion

Table 3. Multivariate logistic regression analysis of predicting factors for biochemical recurrence following RRP (groups 1 and 2).

	Binary logistic regression (n=62)					
	Univariate model			Multivariate model		
	OR	95% CI	p-value	OR	95% CI	p-value
Age	1.037	0.919-1.169	0.557	-	-	-
BMI	0.787	0.588-1.054	0.108	-	-	-
Family history of PCa	0.714	0.078-6.538	0.766	-	-	-
PSA	1.050	0.990-1.115	0.106	-	-	-
Group 2 Ref: Group 1	3.480	0.644-18.810	0.147	-	-	-
PSA density	6.655	0.168-262.890	0.312	-	-	-
SVI	8.667	1.025-73.249	0.047	13.961	1.224-159.277	0.034
Capsular invasion	7.571	0.424-135.109	0.169	-	-	-
LN involvement	2.429	0.221-26.693	0.468	-	-	-
pT	5.256	1.103-25.049	0.037	7.020	1.210-40.714	0.030
RRP ISUP	1.665	0.854-3.245	0.134			-
EPE	5.256	1.103-25.049	0.037 -	-	-	-

BMI: Body mass index, PCa: Prostate cancer, PSA: Prostate-specific antigen, SVI: Seminal vesicle invasion, RRP: Retropubic radical prostatectomy, ISUP: International Society of Urological Pathology, EPE: Extraprostatic extension, OR: Odds ratio, CI: Confidence interval

Early identification of high-risk patients is crucial in managing patients with PCa. Preoperative detection of adverse pathologies, such as EPE, SVI, and high Gleason score in RRP, may influence the choice of surgical technique in high-risk patients and direct patients to multimodal treatments rather than surgery alone. A meta-analysis evaluating pre-PIRADS revealed that the use of functional imaging in combination with T2WI or

Table 4. Multivariate logistic regression analysis of predicting factors for biochemical recurrence following RRP (Groups 2 and 3).

	Binary logistic regression (n=76)					
	Univariate model			Multivariate model		
	OR	95% CI	p-value	OR	95% CI	p-value
Age	1.040	0.930-1.162	0.495	-	-	-
BMI	1.196	0.981-1.458	0.077	-	-	-
Family history of PCa	0.442	0.051-3.788	0.456	-	-	-
PSA	1.027	1.003-1.052	0.030	-	-	-
Group 3 Ref: Group 2	0.768	0.231-2.552	0.666	-	-	-
PSA density	2.161	1.023-4.564	0.044	-	-	-
SVI	2.109	0.362-12.283	0.406	-	-	-
Capsular invasion	11.273	0.940-135.235	0.056	-	-	-
LN involvement	1.727	0.308-9.700	0.535	-	-	-
pT	20.870	2.547-171.019	0.005	-	-	-
RRP ISUP	2.527	1.377-4.636	0.003	-	-	-
EPE	24.000	2.921-197.202	0.003	24.000	2.921-197.202	0.003

BMI: Body mass index, PCa: Prostate cancer, PSA: Prostate-specific antigen, SVI: Seminal vesicle invasion, RRP: Retropubic radical prostatectomy, ISUP: International Society of Urological Pathology, EPE: Extraprostatic extension, OR: Odds ratio, CI: Confidence interval

3T MRI increased the sensitivity for detecting EPE or SVI; however, the reader's experience was of paramount importance[6,7]. MRI is not recommended for local staging in low-risk patients because of its low sensitivity to microscopic EPE. However, MRI may still be useful for treatment planning[8]. In recent years, mpMRI has become an important tool in detecting patients with PCa having a high risk of adverse pathology[9,10]. A study comparing bpMRI and mpMRI in local staging revealed no clinically significant difference with DCE in estimating EPE. The authors concluded that the accuracy of local staging was similar in both bpMRI and mpMRI[11]. Our study group revealed that both bpMRI and mpMRI did not make an additional contribution in terms of EPE and SVI.

Few studies in the literature investigated the effect of bpMRI on BCR, and they all differ in terms of study design. Takeuchi et al.[12] investigated the effect of bpMRI PIRADS score on BCR after RRP. They grouped 25 patients as BCR and 101 patients as non-BCR. Univariate analysis revealed PSA, tumor volume, PIRADS score, ISUP grade, EPE, and positive surgical margin to be significantly associated with the development of BCR. Multivariate analysis revealed only ISUP grade and PIRADS score as independent predictors of BCR[12]. In the study by Park et al.[13], where the BCR rate was 13.3% (21/158), BCR was not detected in any patient with a PIRADS score of <4. Univariate analysis revealed that all parameters, except for SVI (p=0.254), were significant for BCR (p<0.05). Multivariate analysis revealed that the only independent

parameter for BCR was the PIRADS score (p<0.05)[13]. Our study revealed that pathological SVI positivity, high pathological stage, and EPE were significant factors for predicting BCR in univariate analysis between groups 1 and 2. Multivariate analysis revealed that pathological SVI positivity and high pathological stage were significant. PSA value, PSA density, pathological EPE positivity, pathological stage, and RRP ISUP grade were significant in univariate regression analysis between groups 2 and 3. Multivariate regression analysis revealed that only pathological EPE positivity was a significant factor. The factors affecting BCR might have differed since patients with PIRADS-5 lesions were excluded from our study and different groups were compared, although our results were similar to the literature. Our study performed mpMRI on all patients preoperatively, and bpMRI sequences were evaluated and re-scored on the same images. No difference was found between the two methods in predicting early oncological outcomes.

Therefore, bpMRI is not inferior to mpMRI in recognizing csPCa despite the relative superior sensitivity of mpMRI in the literature. Woo et al.[14] revealed that the performance of bpMRI in diagnosing PCa is comparable to mpMRI. Wang et al.[15] classified lesions of 109 patients who underwent prostate biopsy as DWI 3/DCE (-), DWI 3/DCE (+), and DWI 4/PIRADS-4 lesions. The contrast did not provide any additional benefit in detecting csPCa when evaluating DWI 3 lesions in the peripheral zone[15]. The frequency of PIRADS-3 lesions that upgraded to

PIRADS-4 using DCE-MRI remained unknown. Junker et al.[16] revealed that the absence of DCE changed PIRADS scores in 9.75% of patients. It increased the number of PIRADS-3 lesion number by 8.89% compared to mpMRI. BpMRI did not show significant differences in tumor detection rates and diagnostic accuracy[16]. Another study revealed that only 62 (16%) of 388 patients required a DCE sequence to score prostate lesions using PIRADS version 2[17]. Our study revealed that half of 62 patients were reported as PIRADS-4 with contrast-enhanced imaging. This change in the score may cause a difference in patient management before a biopsy. A meta-analysis of 13 studies involving patients with biopsy-diagnosed PCa revealed that lesions with PIRADSv2 scores of 3, 4, and 5 had mean positive predictive values of 12%, 48%, and 72%, respectively, for ISUP cancers of 2 and above; however, studies included in the meta-analysis had significant design heterogeneity[18]. A meta-analysis of 56 studies and 16,537 patients by Mazzone et al.[19] revealed that the positive predictive values for csPCa were 13%, 40%, and 69% for PIRADS-3, 4, and 5, respectively (p<0.001). Targeted biopsy failed to detect 6%, 6%, and 5% csPCa in PIRADS-3, 4, and 5 lesions, respectively. A PIRADS score of 3 or 4 in patients with suspected PCa may lead to differences in terms of MR fusion biopsy or standard biopsy, but it does not eliminate the need for biopsy.

The use of contrast-enhanced imaging methods is costly due to the necessity of using contrast material and the length of the exposure time[16]. In 2017, Porter et al.[20] modeled the potential cost of bpMRI versus mpMRI. The cost of bpMRI was $48.17 per image (duration 15 min) while mpMRI cost was $118.51 per image (duration 45 min)[20]. Choi et al.[21] revealed that bpMRI saves 10-15 min compared to mpMRI and that bpMRI time is approximately 30%-40% of the mpMRI time. Additionally, serious side effects, such as nephrogenic systemic fibrosis related to the use of contrast media, can be seen[22,23].

To our knowledge, our study is the first study to evaluate the effect of bpMRI on short-term BCR with subgroup analyses. BpMRI may become even more advantageous over mpMRI if the long-term oncological results are similar.

Our study had some limitations. The study was planned as a retrospective and single-center study. The number of patients was limited due to strict exclusion criteria. Additionally, our follow-up period for the evaluation of oncological results was quite limited. Thus, much longer follow-up periods are required to evaluate parameters, such as cancer-related survival and overall survival. Considering the similarity of short-term oncological results and histopathological parameters, the results of the imaging method using contrast material did not make any additional contribution to predicting patients' clinical course.

CONCLUSION

Our study revealed that mpMRI did not contribute any additional data when predicting BCR after RRP in PCa patients compared to bpMRI. Therefore, a long-term follow-up is needed to better evaluate oncological parameters.

Ethics

Ethics Committee Approval: The ethical permission for this study was approved by the local Ethical Committee of the Istanbul Medeniyet University Goztepe Training and Research Hospital (decision no: 2020/0507, date: 02.09.2020).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Author Contributions

Surgical and Medical Practices: O.E., N.G., M.B.D., T.T., Concept: O.E., A.I., M.C.C., A.Y., Design: O.E., A.I., M.C.C., A.Y., Data Collection and/or Processing: O.E., N.G., A.I., M.B.D., M.C.C., T.T., Analysis and/or Interpretation: N.G., M.B.D., T.T., Literature Search: O.E., M.C.C., T.T., Writing: O.E., N.G., A.I., M.C.C., A.Y.

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