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Microneedling of Irradiated Amniotic Gel versus Platelet Rich Plasma Gel in the Treatment of Atrophic Post Acne Scars

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Abstract

Background: Post-acne scarring remains a current challenge to prevent and treat despite advancement in acne treatment. There are two types of scars, atrophic and hypertrophic scars, depending on whether there is a net loss or gain of collagen. **Objective:** The main objectives of this study were to compare the efficacy of using microneedling combined with either plasma gel or amniotic fluid gel in treatment of atrophic post acne scars with clinical and histological evaluation. **Methods**: This study included Twenty-three cases with atrophic post acne scars. The treated area on the face was divided equally into two halves. Before the procedure, we applied thick layer of local anesthetic cream for approximately 45 to 60 minutes. Microneedling using dermapen combined with irradiated amniotic gel topically was applied to left side of the face and platelet rich plasma gel was applied to the right side**.** Patients received four sessions with 3 weeks interval between sessions. Clinical examination with histopathological analysis was carried out one month after the last session. **Results**: There was a significant increase in the improvement percentage of acne scars on right side (dermarpen and platelet rich plasma gel) than left side of face (dermapen and irradiated amniotic gel). Histologically, improvement of character of collagen and elastic fibers was noticed, especially on right side. Meanwhile**,** a significant increase in epidermal thickness on both sides of face was detected**. Conclusion**: Dermapen combined with either plasma gel or amniotic gel are promising effective therapeutic modalities for atrophic acne scars. However, combination of platelet rich plasma gel with dermapen has a higher therapeutic efficacy than that of amniotic gel with dermapen.

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Keywords

Post Acne Scars, Irradiation, Amniotic Gel, PRP

1. Introduction

Post-acne scarring remains a common problem despite the advances in the treatment of acne [1]. The pathogenesis of acne scars may be related to reduced degradation of inflammatory mediators, collagen fibers, and subcutaneous fat, which ultimately leads to reduced or increased collagen deposition [2]. Atrophic acne scars are more common than hypertrophic scars. There are 3 main types of atrophic scars: icepick, boxcar, and rolling scars [3].

Plasma gel is one of PRP (Platelets rich plasma) formulation having desirable biological or medical properties, deriving from an initial blood composition that comprises proteins in a gelled state as a result of thermal heating and cooling treatment. It contains numerous growth factors and cytokines in addition to being rich in fibrin and coagulated proteins [4].

The amnion is the innermost layer of fetal membranes, which forms a sac filled with the amniotic fluid, thus surrounding and protecting the embryo. The amniotic epithelial cells produce numerous cytokines and factors known to promote cell proliferation and differentiation [5].

Almost all growth factors are large hydrophilic molecules so, they penetrate the epidermis in very low quantities. Accordingly, cutaneous application should be accompanied with transdermal delivery systems [6].

Microneedling results in release of various growth factors leading to neocollagenesis and elastin deposition at the epidermal/dermal junction with thickening of the epidermal stratum spinosum [7].

The aim of the present study is to compare the efficacy of the irradiated amniotic gel and PRP gel both combined with microneedling in treatment of post acne scars.

2. Materials and Methods

This prospective split-face study included 23 cases, with facial atrophic post acne scars. Detailed consents with explained information about the treatment were informed and signed by all patients. The experimental design of this study concerned the ethical standard declared in the 18th World Medical Association (WMA), Helsinki, Finland (June 1964) and its later amendments, and approved by Institutional Review Board of Faculty of Medicine Zagazig University (approved code IRB#:6545-25-11-2020).

The excluded subjects had active acne, herpes labials, Pregnancy, lactation immunosuppression, bleeding or coagulation disorders, hepatic or renal failure and uncontrolled diabetes.

2.1. Procedures of the Treatment

The treated area on the face was divided equally into two halves by an imaginary

midline. Before the procedure, targeted areas were disinfected by alcohol swab, and a thick layer of local anesthetic cream (eutectic mixture of lidocaine and prilocaine, EMLA cream, APP pharmaceuticals, Fresenius Kabi, USA) was applied for approximately 45 to 60 minutes. The microneedling procedure was done using dermapen (My M length of microneedle 0.25 - 2.5 mm, depth 2 mm needle no 12 needles, width 2 cm diameter) in the horizontal, vertical and oblique directions. The PRP gel (1 - 2 ml) was applied to right side of the face and amniotic gel (1 - 2 ml) on the left side. The treated areas were left to dry for 30 minutes.

2.2. Procurement of Amniotic Gel

Investigational samples of a premade amniotic gel product were obtained from amniotic tissue laboratory, Egyptian Atomic Energy Authority, Cairo, Egypt. This product contains a liquefied extract of human amniotic membrane and sterilized by gamma irradiation.

2.3. Plasma Gel Preparation

After preparation of PRP [8], it will be put in syringes the syringes were placed (1 minute) in a hot water path (60 - 100˚C), then (1 minute) in a cold path (8 - 0˚C) for transforming plasma into viscous gel.

Scaring improvement was rated using the Goodman and Baron scale [9]. An improvement by two grades is considered excellent, one grade is rated as good and no change is labeled as a poor response. Sessions needed are four sessions, three weeks' duration is required between sessions.

2.4. Clinical Evaluation

Clinical response was assessed after 3 months of starting the treatment (1 month after the end of sessions). The clinical improvement in atrophic acne scars appearance was estimated and evaluated based on global aesthetic improvement scale (GAIS score) Goodman and Baron Scale, patients' self-satisfaction assessment (poor, fair, good, very good, excellent). Adverse effects, including erythema, edema, crusting, pigmentary changes, ecchymosis and scarring, were examined at each visit.

2.5. Histopathological Examination

Three mm punch biopsies were taken from patients at baseline and months after the final session. Biopsies were stained by hematoxylin and eosin (H&E), Van Gieson stain for elastic fibers, Masson Trichrome for collagen and (ki-67) cellular marker for proliferation, and can be used in immunohistochemistry. The slides were examined for histopathological results.

3. Results

The demographic and clinical data of the patients are summarized in **Table 1**.

With regard to the clinical grading of post acne scars according to Goodman and Baron scale, there was no statistically significant difference between both sides of the face before treatments.

Table 1. The demographic and clinical data of studied patients.

	N	%
Age per years		
Mean ± SD (Range)	23.3 ± 2.67 (19 - 30)	
Sex		
Females	15	65.2
Males	8	34.8
Family history		
Negative	7	30.4
Positive	16	69.6
Clinical characteristics	N	%
Lesion duration per years		
Mean ± SD (Range)	4.13 ± 1.632 (1 - 7)	
Skin photo types		
II	2	8.7
III	13	56.5
IV	8	34.8
Types of atrophy		
Rolling	15	65.2
Icepick	17	73.9
Boxcar	18	78.3
Previous treatment		
Yes	23	100.0

Table 2. Clinical grading of Goodman and Baron scale before and after treatment with amniotic gel combined with microneedling (left side).

Goodman and Baron scale	Amniotic Gel Combined with Microneedling				^{Mc}p
	Before		After		
	n.	%	n.	%	
Grade 1	0	0.0	8	34..8	0.008
Grade 2	7	30.4	12	52.2	0.332
Grade 3	10	43.5	3	13.0	0.092
Grade 4	6	26.1	0	0.0	0.031

Goodman and Baron scale had been improved significantly after being treated

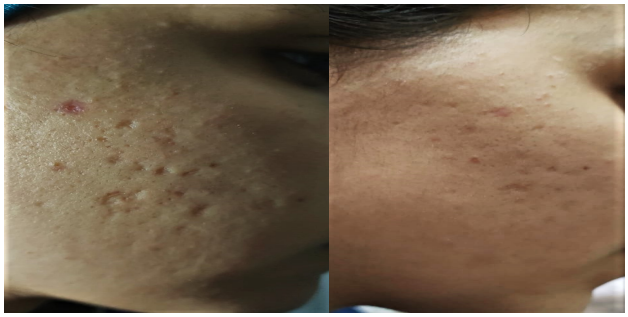
with Amniotic Gel Combined with Microneedling, where 34.8% of cases become grade 1 after treatment. All grade 4 cases improved after treatment p = 0.031 (Table 2).

Table 3 showed that the Goodman and Baron scale had been improved significantly after being treated with PRP gel combined with microneedling, where 69.6% of cases become grade 1 after treatment. In addition, decline of grade 3 to be (8.7%) after treatment compared to (47.8%) before treatment, the difference is statistically significant p = 0.022. Moreover, all grade 4 improved after treatment (p = 0.008).

Table 3. Clinical grading Goodman and Baron scale before and after treatment with Platelet Rich Plasma Gel Combined with Microneedling (right side).

Goodman and Baron scale	Platelet Rich Plasma Gel Combined with Microneedling				^{Mc}p
	Pre		Post		
	n.	%	n.	%	
Grade 1	0	0.0	16	69.6	0.0001
Grade 2	4	17.4	5	21.7	0.99
Grade 3	11	47.8	2	8.7	0.022
Grade 4	8	34.8	0	0.0	0.008

(A) (B)



(C) (D)

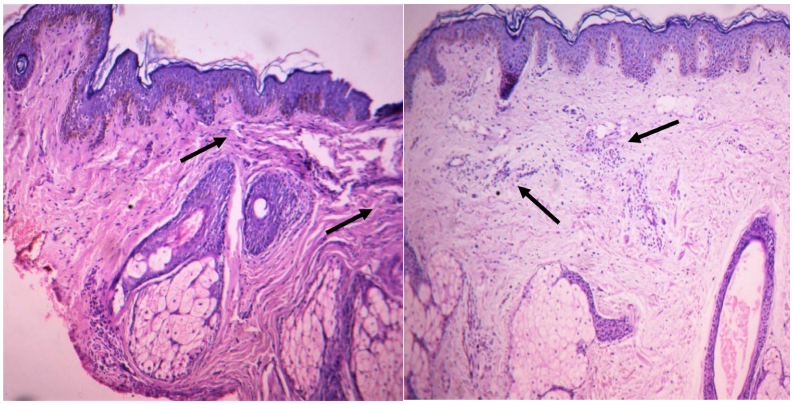
Figure 1. Female patient 23 years old with atrophic acne scars: (A) left side of face at baseline and (B) clinical appearance 1 months after last session of amniotic fluid gel with microneedling showing good improvement; (C) right side of face at baseline and (D) clinical appearance 1 months after last session of plasma gel with microneedling showing very good improvement.

However, after treatment grade 1 was significantly higher in right side which was treated with Platelet Rich Plasma Gel combined with microneedling than left side (34.8%) which was treated with Amniotic Gel combined with microneedling, p = 0.018. In contrast, grade 2 was significantly lower (21.7%) at right side than left side (52.2%), p = 0.032 (Figure 1).

Regarding GAIS score, grade 1 was significantly higher in right side which was treated than left side (13.0%) which reached (60.9%) with PRP gel combined with microneedling treated with amniotic gel combined with microneedling, p = 0.0007. However, the difference between GAIS score in both sides was statistically insignificant.

Post treatment swelling was significantly higher in right side (91.3%) than left side (52.2%), p = 0.003. However, the difference of other complications between both treatments was statistically insignificant.

3.1. Histopathological Evaluation



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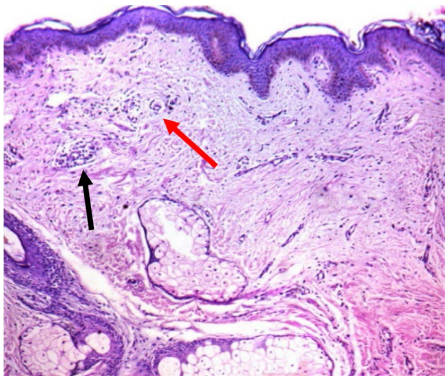
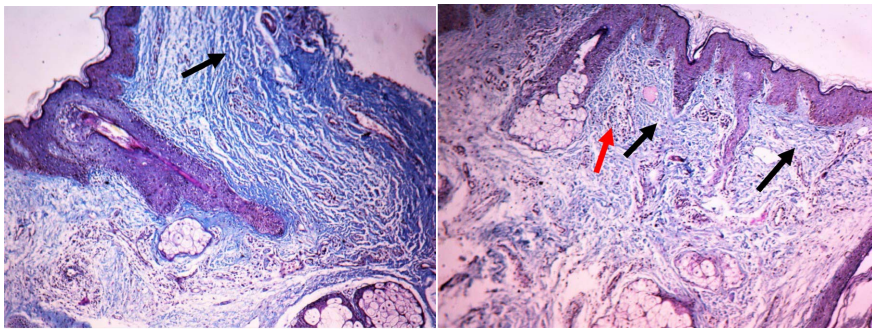
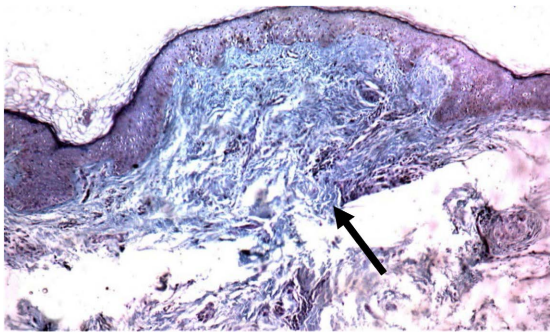


(C)

Figure 2. (A) Pretreated biopsies showing thickened crumbled collagen bundles in papillary and reticular dermis and align parallel to the surface of epidermis (black arrow) with vertically placed blood vessels (H&E, 100X). (B) Post-treated biopsies with PRP gel showing new thin collagen fibers formation, fibroblastic proliferation and inflammatory cells (black arrow) (H&E, 100X). (C) Post treated biopsies with amniotic gel showing similar result as PRP with new thin collagen fibers formation (red arrow), fibroblastic proliferation and inflammatory cells (black arrow) (H&E, 100X).



(A) (B)



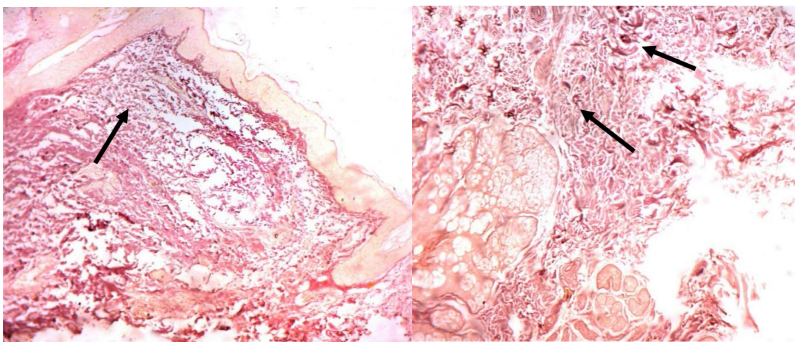
(C)

Figure 3. (A) Pretreated biopsies showing thickened collagen bundles (green color) in papillary and reticular dermis (Masson trichrome, 200X). (B) Post treated biopsies with PRP gel showing new thin fibers of collagen (stained blue) (black arrows) with inflammatory infiltrates and new vessels formation (red arrow), (Masson trichrome, 200X). (C) Post treated biopsies with (AF) gel showing still thickened collagen bundles in papillary and reticular dermis (black arrow) (Masson trichrome, 200X).

Pretreatment biopsies showed atrophic changes in epidermis, thickened disorganized collagen bundles in papillary and reticular dermis and vertical arranged blood vessels.

After treatment, biopsies from PRP gel treated side showed collagen remodeling with presence of normal thin collagen fibers and new blood vessel formation.

In amniotic gel treated side there was no marked improvement with still presence of thickened crumbled collagen bundles and vertical located blood vessels (**Figures 2-4**).



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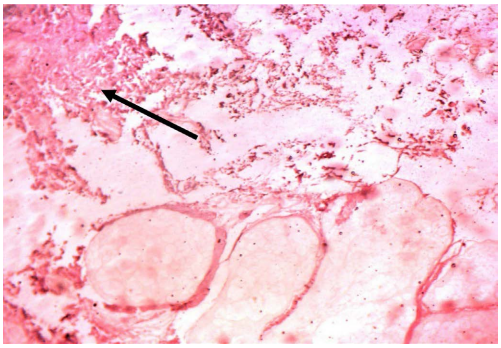
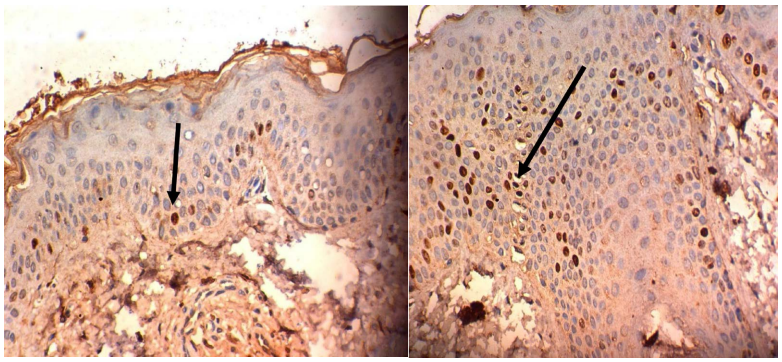


(C)

Figure 4. (A) Pretreated biopsies showing thickened crumbled collagen bundles (black arrow) (Van Geison, 100X). (B) Post treated biopsies with PRP gel showing new thin fibers of collagen (stained red) with few elastin fibers formation (stained black), (Van Geison, 200X). (C) Post treated biopsies with (AF) gel showing still thickened collagen bundles arranged parallel to the surface (black arrow) (Van Geison, 200X).

3.2. KI 67 Findings



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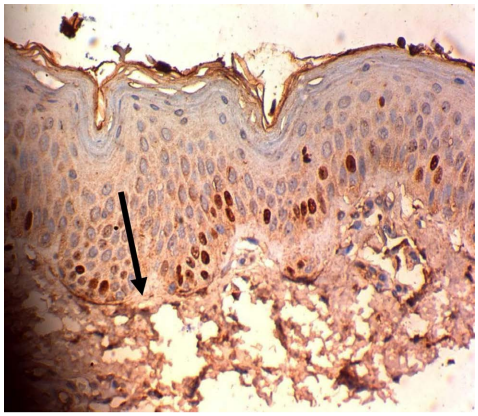

(C)

Figure 5. (A) Ki67 expression in pretreated biopsy showing focal mild nuclear staining in very few parabasal keratinocytes with Ki67 (400X). (B) Ki 67 stain in post treated biopsies with PRP gel showing that the proportion of cells expressing Ki67 antigen dramatically increase basal, parabasal, and intermediate zones of keratinocytes, (Ki67, 400X). (C) Ki 67 staining in post treated biopsies with (AF) gel showing nuclear expression in few basal and parabasal cells (Ki 67, 400X).

Pretreatment biopsies showed focal expression in very few basal keratinocytes. In PRP treated sides, there was a significant increase in basal and para basal cells. Amniotic gel treated side showed mild expression of KI67 in basal and para basal keratinocytes (**Figure 5**).

4. Discussion

Acne scaring is caused by deficient wound healing during inflammatory stage of acne and may be associated with psychological effects [10]. In the current study, the severity of acne scarring was assessed before and after treatment using Goodman and Baron grading system. The right side of the face which was treated with plasma gel combined with microneedling had been improved after treatment as 69.6% of cases become grade 1 after treatment. In addition, decline of grade 3 to be (8.7%) after treatment compared to (47.8%) before treatment, the difference was statistically significant ($p = 0.022$). Moreover, all grade 4 improved after treatment ($p = 0.008$).

The left side of the face which was treated with amniotic gel combined with microneedling had been improved after treatment where 34.8% of cases become grade 1 after treatment. All grade 4 cases improved after treatment ($p = 0.031$).

In the present study there was non-significant difference between the two sides of the face as regards baseline clinical grading according to Goodman and Baron Scale then after treatment, there was a significant difference between the 2 sides of the face as grade 1 was significantly higher in right side (69.6%) which was treated with plasma gel combined with microneedling than left side (34.8%) which was treated with amniotic gel combined with microneedling, $p = 0.018$. However, grade 2 was significantly lower (21.7%) at right side than left side (52.2%), $p = 0.032$.

The global aesthetic improvement scale (GAIS) was used to evaluate two modalities used in treatment of the post acne scar. It showed a significant difference between the two sides of the face as score1 (excellent improvement) of GAIS score was significantly higher in right side (60.9%), than left side (13.0%), $p = 0.0007$.

The obtained result of right side of the face which was treated with Plasma gel with microneedling are higher than those of Nassar *et al*. [11] who treated acne scars of 26 patients as Scar subcision which was done 1st on both sides of the face. Plasma gel injection was done on the right side and PRP injection was done on the left side.

The sessions were done monthly for 4 months. The results of right side of the face which was treated by subcision with plasma gel according to GAIS score were as follows score 1 (excellent improvement) (38.5%), score 2 (very good improvement) (19.2%) score 3 (good improvement) (15.4%) and score 4 (poor improvement) (26.9%). As for the results of the present study of right side of the face, they were as follows, score 1. (60.9%) score 2 (21.7%), score 3 (13.0%) and score 4 (4.3%).

Elfar and Hasby [12] treated atrophic postacne scars of 60 patients. The patients

were divided into three groups with 20 patients being treated with intradermal injection of plasma gel, 20 patients treated with dermaroller, and 20 patients subjected to combined plasma gel and dermarollar. The results of the cases who were treated with plasma gel with microneedling after one month from end of treatment were as follows, 30% of patients had excellent improvement 40%, of patients had very good improvement, 20% of patients had good improvement and 10% of patients had poor improvement.

In the current study, the results of right side of the face were as follows, 60.9% of patients had excellent improvement, 21.7% of patients had very good improvement, 13% of patients had good improvement and 4.3% of patients had poor improvement. Comparing to the obtained result of right side of the face which was treated with Plasma gel with microneedling, the obtained results are higher than those results.

El-Domyati *et al.* [13] had conducted his split face study on 10 cases with atrophic post acne scars received five sessions of microneedling, with 2 weeks interval on both sides of the face. Then, Amniotic fluid derived mesenchymal stem cell conditioned media (AF-MSC-CM) was topically applied to right side of the face after microneedling. 1 month after the end of sessions, there was a highly significant increase in improvement percentage of right side (65.40 ± 11.34) vs. left side of face which was treated by dermarollar (38.60 ± 9.02; P & lt; 0.001). By grading the improvement percentage, a significant difference was also noticed on left side of face (DR) as they had moderate improvement in 80% and good improvement in 20% of patients (p = 0.008). Meanwhile, a significant difference was also noticed on the right side of the face (DR and AF-MSC-CM) as they showed moderate improvement in 20%, good improvement in 60%, and very good improvement in 20% of patients (p = 0.003). In the present study the results of left side of the face are 13% of patients had excellent improvement, 47.8% of patients had very good improvement, 30.4% of patients had good improvement and 8.7% of patients had poor improvement.

In comparison with the results of left side of face which was treated with amniotic gel with microneedling, our results are similar to those results. Regarding histopathology, our histopathological results of the left side are similar to that reported by El-Domyati *et al.* who demonstrated that both sides of face showed increase in deposition of collagen bundles, which became more fine and organized with decreased interfibrillary spaces. Improved characters of collagen bundles were better noticed on right side (amoiotic gel with microneedling) vs. left side of the face (microneedling only). After treatment, the content of abnormal elastic tissues decreased, with the appearance of the newly synthesized elastic fibers, which appeared fine and well organized, especially on right side of face.

From histopathological point of view, the current results are more or less similar to that of Elfar and Hasby, who demonstrated that after the end of therapeutic procedures of different studied groups, the dermal collagen showed more condensed collagen. There was also a decrease in the perivascular inflammatory cell

infiltrates to be (+1), (+2), and (+1) in groups A (plasma gel injection), B (Dermapen), and C (Dermapen with plasma gel), respectively.

5. Conclusion

Dermapen combined with either plasma gel or amniotic gel are promising effective therapeutic modalities for atrophic acne scars. However, combination of PRP gel with dermapen has a higher therapeutic efficacy than amniotic gel with dermapen.

Authors' Contributions

NA performed the research and analyzed the data, SA performed histopathological analysis, NR provided the work plan and experimental design of the research and the procurement of the amniotic gel, TE performed clinical investigations and follow up. and HD shared in data analysis and manuscript writing. All authors had read and approved the final manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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