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REVIEW ARTICLE

A comprehensive review of pulsed radiofrequency in the treatment of pain associated with different spinal conditions

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Objective: The objective of this review was to evaluate the efficacy of pulsed radiofrequency (PRF) treatment of pain associated with different spinal conditions. The mechanisms of action and biological effects are shortly discussed to provide the scientific basis for this radiofrequency modality.

Methods: We systematically searched for clinical studies on spinal clinical conditions using PRF. We searched the MEDLINE (PubMed) database. We classified the information in one table focusing on randomized controlled trials (RCTs) and other types of studies. Date of last electronic search was October 2016.

Results: We found four RCTs that evaluated the efficacy of PRF on cervical radicular pain and five observational studies. Two trials and three observational studies were conducted in patients with facet pain. For disc-related pathology, we found one RCT with PRF applied intradiscally and three RCTs for dorsal root ganglia PRF modulation lumbosacral

radicular pain. For sacroiliac joint pain, spondylolisthesis, malignancies and other minor spinal pathology, limited studies were conducted.

Conclusion: From the available evidence, the use of PRF to the dorsal root ganglion in cervical radicular pain is compelling. With regard to its lumbosacral counterpart, the use of PRF cannot be similarly advocated in view of the absence of standardization of PRF parameters, enrolment criteria and different methods in reporting results; but, the evidence is interesting. The use of PRF in lumbar facet pain was found to be less effective than conventional RF techniques. For the other different spinal conditions, we need further studies to assess the effectiveness of PRF.

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INTRODUCTION

Starting with the treatment of cardiac conduction abnormalities and for non-surgical tumour ablation, radiofrequency ablation (RFA) treatments have been used for over 50 years for a variety of medical conditions. Later, RFA was also used with thermal tissue ablation, gaining popularity in tumour ablation performed in several organs (liver, kidney, adrenal, spleen, prostate, bone and soft tissue, lung and breast). Percutaneous thermal tissue ablation is performed with radiofrequency (RF) current by transforming the patient into an electrical circuit with adhesive grounding pads on the thighs or back.¹

RFA is already used for the treatment of musculoskeletal pain.² The use of RFA for the treatment of pain of spinal origin was first described by Shealy³ and initially conducted

only by neurosurgeons. Some technical improvements, such as small diameter equipment and new generators that became available in the 1980s, allow the use of this tool by other types of specialists.

The idea of treating pain producing a heat lesion is simple: it is based on the interruption of a continuous nociceptive input by destroying the fibres conducting it. RF heat treatments began to be applied for a variety of pain syndromes: cervicogenic headaches,⁴ occipital neuralgia,⁵ cervical radicular pain,⁶ lumbar radicular pain,⁷ discogenic pain⁸ and pain associated with the sacroiliac joint (SIJ).⁹

The formation of heat is not the only outcome obtained with RF distribution. The tissue is also exposed to an electric field.

Biological effects of RF field have been investigated in Podhajsky *et al*, Higuchi *et al* and Cahana *et al*.^{10–12} These studies led to a search for new applications to apply RF without diffuse tissue damages,¹³ such as pulsed radiofrequency (PRF), a new method of applying RF without raising the temperature. In PRF, the output of the generator is cyclically interrupted. The initial parameters were two cycles of 20 ms each of active cycle. Nowadays, new different parameters are used, taking into account the new biological discoveries that are continuously published.^{14–19}

Pain is a survival mechanism that serves as a warning sign of ongoing or impending tissue damage. In Europe, the prevalence of chronic pain is 25–30%.²⁰

One out of three Americans experience chronic pain—more than the total number (of patients) are affected by heart disease, cancer and diabetes combined.²¹ About one-fifth of patients who report chronic pain have predominantly neuropathic pain.^{22,23}

“Pain” represents a final integrative package, the components of which consist of neurophysiological processes as well as contextual, psychological and sociocultural factors.²⁴ This is one reason for the discrepancies between preclinical studies (which measure increased tolerance to painful stimuli in animals), clinical studies (which assess efficacy) and clinical practice (which measures effectiveness). These factors and the neurophysiological differences between individuals may account for the differences in the clinical expression of the pathology that tends to correlate poorly with the intensity of pain for conditions such as back pain.

Initial clinical investigations²⁵ have shown that PRF could be used safely as an alternative method for ablation procedures in patients suffering from pain. The evidence of its efficacy in clinical practice for this technique, according to evidence-based medicine, is gradually growing.

The objective of this review was to analyze the existing literature on PRF in the treatment of pain associated with different spinal conditions and to determine what evidence is gained.

We systematically searched for studies reporting on spinal applications of PRF. We searched the MEDLINE database (PubMed) from 1980 to October 2016, using the free-text terms “pulsed radiofrequency”, “radiofrequency”, “spinal” and “spine” and combination of these with spine pathology and site.

INCLUSION CRITERIA

- Types of studies: Randomized Controlled Trials (RCTs), non-randomized observational studies, case reports and articles published to describe adverse effects
- Types of interventions: therapeutic spinal interventions using PRF performed with proper technique under image guidance (fluoroscopy, CT or MRI) were included.

Cervical radicular pain

Cervical radicular pain is defined as pain perceived by an arising in the upper limb caused by irritation of a cervical spinal nerve

or its roots. Approximately 1 person in 1000 suffers from chronic cervical radicular pain.²⁶ Van Kleef *et al*²⁷ first described RF treatment, adjacent to the cervical dorsal root ganglia (DRG).

We found four randomized trials on PRF treatment for cervical radicular pain.^{28–31} One study²⁸ reports that the effect of PRF group compared with sham at 3 months achieved a significantly better outcome. The other three studies^{29–31} concluded that PRF administered to a DRG might be as effective as transforaminal epidural steroid injection in terms of attenuating radicular pain caused by disc herniation, and its use would avoid the adverse effects of steroids. One other study²⁹ demonstrated that percutaneous nucleoplasty and PRF show significant pain improvement in patients with contained cervical disk herniation, but none is superior to the other. Combining cervical nerve root block and PRF appeared to be a safe and efficacious technique for cervical radicular pain. The combination therapy yielded better outcomes than either cervical nerve root block or PRF alone.

There are five observational studies^{32–36} about PRF on cervical radicular pain management. Despite lack of standardization of the enrolment criteria and different methods in reporting results, PRF can be considered a compelling treatment option.

In our opinion, PRF can be safely and efficaciously performed in the clinical practice, as conservative treatment option for cervical radicular pain, in accordance with the literature with good results.

Posterior degenerative spinal disease: facet pain

Facet joint pain, also known as zygapophysial joint pain, constitutes a substantial and frequent cause of mechanical spine pain. Predisposing factors for zygapophysial joint pain include spondylolisthesis/spondylosis, degenerative disc disease and advanced age. The reported prevalence rate varies widely in different studies, being heavily dependent on diagnostic criteria and selection methods. The diagnosis of lumbar facet joint pain is particularly difficult and may account for 15–45% of those patients experiencing chronic low back pain (LBP).³⁷

Two randomized trials on LBP, comparing PRF with RF denervation of facet joints, have been performed. The first study³⁸ showed that both treatment options have comparable results at 6 months, but the reduced pain scores were maintained at 1 year only for the RF group. The second study³⁹ showed that there was no significant difference between the RF and PRF groups in pain scores.

There are three observational studies^{40–42} about PRF in facet pain management. All studies reported good results on pain control.

The evaluation is limited by the absence of standardization of PRF parameters, and differences in enrolment criteria and method of reporting the results. The use of PRF in lumbar facet pain was found to be less effective than conventional RF.

It is our opinion that PRF should be used in clinical practice in selected patients. The reduced time of pain control, compared with RF, may suggest its use for patients awaiting spinal surgery. In the other clinical conditions, RF may be preferred owing to its longer efficacy maintenance.

Disc-related pathology

Chronic, persistent low back, lower extremity and radicular pain may be secondary to disc herniation, disc disruption, disc degeneration, spinal stenosis or post-lumbar surgery syndrome resulting in disc-related pain with or without radiculitis. Pain and disability in the low back spine and lower extremities following lumbar spine surgery has been hypothesized to be secondary to multiple causes including disc herniation, discogenic pain and spinal foramen stenosis along with inappropriate surgery.^{43,44}

Herniated lumbar disc is a displacement of disc material (nucleus pulposus or annulus fibrosus) beyond the intervertebral disc space. The prevalence of a symptomatic herniated lumbar disc is about 1–3% with the highest prevalence among people aged 30–50 years.^{45,46}

Disc herniation, discogenic pain, spinal foramen stenosis, radiculitis and post-surgery syndrome are managed with various types of PRF percutaneous interventional techniques including intradiscal PRF and DRG PRF modulation.

Intradiscal pulsed radiofrequency for discogenic pain
Starting with the first work made by Teixeira A and Sluijter ME⁴⁷ that proposes another treatment option for discogenic pain, intradiscal PRF, many other works have been published on this technique.

Based on the previous evidence of a randomized trial, comparing intradiscal-PRF with intradiscal electrothermal therapy⁴⁸ with good results, four observational studies have been carried out. All studies reported good pain results, evaluating the effectiveness of intradiscal PRF modulation in managing disc herniation, spinal stenosis and post-surgery pain.^{47–51}

Dorsal root ganglia pulsed radiofrequency modulation in disc herniation and radiculitis

A total of three randomized trials and seven observational studies^{33,52–61} evaluating PRF in managing disc herniation and radiculitis have been performed. All studies reported good pain results. In particular, clinical trials showed that PRF compared with placebo resulted in a better outcome and a substantial decrease in visual analogue scale score;⁵⁹ PRF compared with corticosteroids injection resulted in a higher number of patients with successful treatment results;⁶¹ and PRF + RFA and PRF alone both showed a successful reduction in pain intensity, with a better outcome in the PRF + RFA group.⁵⁵

However, the major issues concerning those studies were the lack of standardization of PRF parameters, enrolment criteria and heterogeneity in results reporting.

In our opinion, intradiscal therapy is a promising treatment, but further studies are needed to effectively validate it. DRG PRF modulation trials obtained good results and may be considered a good treatment option in clinical practice. However, some concern regarding intradiscal treatment invasiveness and potential derived issues remains.

Sacroiliac joint

SIJ pain is defined as pain localized in the region of the SIJ, reproducible by stress and specific provocation test, and reliably relieved by selective infiltration of the SI joint with a local anaesthetic. Depending on the diagnostic criteria used (clinical examination, intra-articular test blocks, medical imaging), the reported prevalence of SI pain among patients with axial LBP varies between 16% and 30%.⁶²

The SIJ is accepted as a potential source of low back and/or buttock pain with or without lower extremity pain.^{63,64} The SIJ receives innervation from the lumbosacral nerve roots.⁶⁵ Neurophysiological studies have demonstrated both nociceptive and proprioceptive afferent units in the SIJ.⁶⁶ There is still no universally accepted gold standard for the diagnosis of SIJ pain.

Two studies^{67,68} illustrate the effectiveness of PRF modulation in managing SIJ pain.

In our opinion, according to new preclinical evidences on PRF biological effects, applying PRF to SIJ may be a promising tool to pain palliation, but clinical trials are needed to confirm this hypothesis.

Spondylolisthesis

Degenerative spondylolisthesis is the slippage of one vertebral body over the one below due to degenerative changes in the spine especially facet joints degeneration and is a well-recognized source of low back and radicular lumbar pain.⁶⁹ A 2006 study by Belfi et al⁷⁰ reported a prevalence of 5.7% for spondylolysis and 3.1% for spondylolisthesis.

There is only one randomized prospective study⁷¹ for PRF treatment for spondylolisthesis reporting good pain palliation results, with a significant reduction of numeric rating scale compared with steroid + bupivacaine injection.

In our opinion, the evidence for PRF efficacy has yet to be confirmed by further studies.

Infection

Spinal infections and inflammatory conditions of the spinal cord are increasing,⁷² but PRF has never been evaluated for the treatment of pain associated with infections of the spine, except for the treatment of post-herpetic neuralgia.

One randomized prospective evaluation,⁷³ one case report,⁷⁴ and an article with a case series but with a different area of application of PRF⁷⁵ have been carried out (Table 1).

Considering the major trial,⁷³ short-term pain relief and an improvement of the quality of life was achieved by PRF treatment.

Table 1. Characteristics of trials and observational studies included in the review

Study	Year of publication	Number of patients	Site of treatment	Outcome	Study design
Van Zundert ³²	2003	18	Cervical radicular	72% of patients pain relief of 50% at 4 weeks	Observational
Van Zundert ²⁸	2007	23	Cervical radicular	At 3 months, the PRF group showed a significantly better outcome with regard to the global perceived effect (>50% improvement) and VAS (20 point pain reduction)	Trial PRF vs SHAM
Chao SC ³³	2008	49	Cervical radicular	55% of patients pain relief of 50% at 3 months	Observational
Choi GS ³⁵	2011	15	Cervical radicular	77.3% of patients pain relief of 50% at 3 months	Observational
Choi GS ³⁴	2012	21	Cervical radicular	66% of patients pain relief of 50% at 3 months; 71% of patients satisfied at 12 months	Observational
Yoon YM ³⁶	2014	22	Cervical radicular	68% success rate after 6 months	Observational
Wang F ³⁰	2016	62	Cervical radicular	At 1, 3 and 6 months of follow-up, the combined therapy achieved significantly lower NRS and higher GPE compared with CNRB or PRF alone group ($p < 0.001$)	Trial PRF + CNRB vs PRF alone vs CNRB
Halim W ²⁹	2016	34	Cervical radicular	Within 3 months, both PCN and PRF show significant pain improvement in patients with contained cervical disk herniation, but none is superior to the other	Trial vs PCN
Lee DG ³¹	2016	38	Cervical radicular	No statistically significant difference was observed between the PRF and TFESI groups in terms of VAS scores at any time during follow-up	Trial PRF vs TFESI
Mikeladze ⁴⁰	2003	114	Spondylosis/facet pain	59% patients respond favourably (pain reduction more than 50%)	Observational
Lindner R ⁴¹	2006	48	Spondylosis/facet pain	21/29 non-operated patients and 5/19 operated patients, the outcome was successful	Observational
Tekin I ³⁸	2007	20	Spondylosis/facet pain	PRF and CRF are effective but PRF is not as long lasting as CRF	Trial PRF vs CRF
Kroll HR ³⁹	2008	25	Spondylosis/facet pain	No significant difference between CRF and PRF, there was a greater improvement over time noted within the CRF group	Trial PRF vs CRF
Colini-Baldeschi ⁴²	2012	300	Spondylosis/facet pain	62% of patients reported good pain relief at 1 month	Observational
Teixeira A ⁴⁷	2006	8	Intradiscal	100% fall of the NRS score of at least 4 points at the 3-month follow-up	Observational
Rohof O ⁴⁹	2011	76	Intradiscal	38% of the patients had >50% pain reduction (3 months), 29% (12 months)	Observational

(Continued)

Table 1. (Continued)

Study	Year of publication	Number of patients	Site of treatment	Outcome	Study design
Fukui S ⁴⁸	2012	31	Intradiscal	The mean NRS was significantly improved from 7.2 ± 0.6 pre-treatment to 2.5 ± 0.9 in the disc PRF group, and from 7.5 ± 1.0 to 1.7 ± 1.5 in the IDET group (6 months)	Trial PRF vs IDET
Jung YJ ⁵⁰	2012	26	Intradiscal	Successful outcome in 58%, 50% and 42% patients, measured at 3, 6 and 12 months post-treatment	Observational
Fukui S ⁵¹	2013	23	Intradiscal	65.2% had >50% pain reduction, 12 months after treatment	Observational
Teixeira A ⁵²	2005	13	DRG in disc herniation and radiculitis	NRS fell from 7.83 to 2.25 over the first 2 weeks, followed by a gradual further fall to 0.27 at the final follow-up, 15.8 (11–23) months after the procedure	Observational
Martin DC ⁵³	2007	8	DRG in disc herniation and radiculitis	Treatment were effective from 2 to 12 months	Observational
Abejón D ⁵⁴	2007	54	DRG in disc herniation and radiculitis	A decrease in the NRS score was observed in patients with HD and SS, but not in those with FBSS	Observational
Chao SC ³³	2008	116	DRG in disc herniation and radiculitis	44 % of patients had pain relief of 50% or more at the follow-up period of 3 months	Observational
Simopoulos TT ⁵⁵	2008	76	DRG in disc herniation and radiculitis	70% of the patients treated with PRF and 82% treated with PRF + CRF had a successful reduction in pain intensity at 2 months	Trial vs PRF + CRF
Tsou HK ⁵⁷	2010	127	DRG in disc herniation and radiculitis	55.10% of patients had initial improvement $\geq 50\%$ at 3-month follow-up	Observational
Van Boxem K ⁵⁶	2011	60	DRG in disc herniation and radiculitis	The primary end point was achieved in 29.5% of all the PRF interventions. After 6 months, 50% pain relief was still present in 22.9% of the cases and after 12 months in 13.1% of the cases	Observational
Nagda JV ⁵⁸	2011	50	DRG in disc herniation and radiculitis	100% of patients were identified who received 50% pain relief or better after PRF and CRF	Observational PRF + CRF
Shanthanna H ⁵⁹	2014	31	DRG in disc herniation and radiculitis	6 of 16 patients in the PRF group and 3 of 15 in the placebo group showed a >50% decrease in VAS score	Trial vs SHAM
Koh W ⁶¹	2014	62	DRG in disc herniation and radiculitis	The number of patients with successful treatment results was higher in the PRF group at 2 months and 3 months	Trial vs corticosteroid injection
Van Boxem K ⁶⁰	2015	65	DRG in disc herniation and radiculitis	Clinical success was achieved in 56.9%, 52.3% and 55.4% of the patients at 6 weeks, 3 months and 6 months, respectively	Observational

(Continued)

Table 1. (Continued)

Study	Year of publication	Number of patients	Site of treatment	Outcome	Study design
Vallejo R ⁶⁷	2006	126	SIJ	72.7% of patients experienced “Good” (>50% reduction in VAS) or “Excellent” (>80% reduction in VAS) pain relief	Observational
Sluijter ME ⁶⁸	2008	1	SIJ	Successfully treated	Case report
Hashemi M ⁷¹	2014	8	Spondylolisthesis	PRF significantly reduced NRS at 6-month follow-up compared with steroid + bupivacaine	Trial PRF vs steroid + bupivacaine
Ke M ⁷³	2013	96	Post-herpetic neuralgia	Short-term pain relief, and improved quality of life	Trial PRF vs SHAM

CNRB, cervical nerve root block; CRF, continuous radiofrequency; DRG, dorsal root ganglia; FBSS, failed back surgery syndrome; HD, herniated disc; IDET, intradiscal electrothermal therapy; LBP, low back pain; NRS, numeric rating scale; PCN, percutaneous nucleoplasty; PRF, pulsed radiofrequency; SIJ, sacroiliac joint; SS, spinal stenosis; TFESI, transforaminal epidural steroid injections; VAS, visual analogue scale.

In our opinion, the evidence for PRF efficacy needs to be confirmed by further studies.

Malignancy

Although most often back pain has a benign origin, it can occasionally be caused by malignant cause including primitive or, most commonly, secondary involvement. 75% of vertebral body lesions are malignant, whereas benign lesions predominate in the posterior elements (70%).⁷⁶

In our opinion, based on a case series⁷⁷ and a case report,⁷⁸ the evidence for PRF has yet to be investigated.

Vertebral fracture

Our literature search yielded no further studies.

Ankylosing spondylitis

Our literature search yielded no further studies.

Cauda equina syndrome

Our literature search yielded no further studies.

COMPLICATIONS FROM PULSED RADIOFREQUENCY

Complications from PRF interventions (sacroiliac treatment, DRG neurotomy and intradiscal PRF) are exceedingly rare.

Most side effects such as local swelling, pain at the site of the needle insertion and pain in the extremities are short lived and self-limited. More serious complications may include neural trauma, injection into vessels, haematoma formation and sciatic nerve injury. Infectious complications including spondylodiscitis, intra-articular abscess, systemic infection, and even meningitis have been reported. In addition, minor complications such as light-headedness, flushing, sweating, nausea, hypotension, syncope have been reported.⁷⁹

DISCUSSION

Some well-conducted trials have been performed in spinal conditions such as cervical radicular pain, degenerative spondylosis and for disc herniation and radiculitis.^{38,39}

In conditions whereby RFA had already been established as an effective treatment, such as in facet denervation, PRF would prove to be of little benefit; but, in our opinion, it has to be considered as an alternative treatment because of its advantages over RFA. In fact, PRF is safer and reduces the risk of tissue damages. Furthermore, one recent study⁸⁰ showed that 80% of patients undergoing PRF treatment rejected spinal surgery in the short term and 76% in the long term. Patients also reported a very high level of satisfaction (84% satisfied/very satisfied), demonstrating that a less invasive approach like PRF could result in a better option for the patient.

PRF has been demonstrated to be a safe and effective procedure for a variety of conditions, being a less invasive alternative to surgical intervention, but more evidence is required.

Some authors⁸¹ found some possible predictive factors for successful outcomes of PRF treatment in patients with lumbosacral radicular pain. PRF adjacent to the DRG showed better results in patients aged around 50 years old, with limited disability and after a positive diagnostic nerve root block. A combination of all these factors creates a fair predictive value. This is important to explain to patients their future outcome after treatment. In particular, in our opinion, it is very important to have a correct pain test (nerve root block) to confirm imaging data and clinical suspicion, even if this is not always easy to perform in clinical practice.

In our opinion, some of the questions regarding the effective “PRF dose” (e.g. time of energy delivery) remained unanswered and may be one of the main reasons for controversial results in some studies. Notably, optimization of the electrical parameters of the RF and duration of PRF treatment requires further clinical studies to achieve a tailored standardized protocol for each condition, possibly improving the outcome of this technique. Some information about the “appropriate PRF dose” may emerge from preclinical studies considering the effect of PRF on tissue cultures. In the past three years, new PRF biological effects have been proposed based on preclinical models, adding new perspectives to existing models: electric fields have demonstrated

effects on immune modulation, integrating the inflammatory component to the pre-existent neurosignaling background. Some studies showed that proinflammatory cytokines, such as interleukin-1b, tumor necrosis factor- α and interleukin-6 are attenuated by electric fields.^{82,83} However, these effects are, at the moment, only postulated and need to be confirmed *in vivo* with future research.

Every PRF treatment is performed under imaging guidance (CT, X-ray or ultrasound), which makes the procedure safe and precise. This treatment could be part of the everyday clinical activity of non-vascular interventional radiologists.

The studies mentioned above use different kinds of imaging guide modalities (ultrasound, CT and more frequently fluoroscopy) that have recognized different peculiarity (precision, radiation dose, cost-effectiveness and availability).

The kind of imaging guidance varies from different parameters (equipment availability, costs, specific experience and expertise of physicians, anatomical site and patient age). Currently, there is no evidence about the best imaging technique to guide these procedures. CT is considered the imaging guidance that permits the most precise needle positioning. On the other hand, CT is afflicted by a high cost per single procedure and the lack of a dedicated CT for interventional purpose in the majority of medical centre. Moreover, radiation exposure could be considered relatively high even if recent advances on CT software have dramatically reduced radiation dose.

Ultrasound presents the advantage of a high availability in almost every centre and the absence of radiation exposure, but is still conditioned by the experience of physicians. Almost every anatomical site could be reached by experienced ultrasound physicians, but some concerns remain about the direct visualization of some anatomical structures (e.g. spinal nerve roots).

X-ray fluoroscopy is indubitably the imaging guidance most used in clinical practice. Availability and costs are advantageous. Radiation exposure and lack of direct visualization of spinal nerve roots still represent a disadvantage for the use of this technique.

In our opinion, CT guide shows the major advantages over other guided techniques to date.

CONCLUSION

The results of the comprehensive review of the literature for PRF treatment in the management of different spinal pain condition are summarized below:

- for cervical radicular pain, the evidence is compelling.
- For posterior degenerative spinal disease: facet pain, the evidence is limited. PRF in lumbar facet pain was found to be less effective than conventional RF.
- For disc-related pathology, the evidence is interesting.
- For an SIJ, the evidence is promising.
- For spondylolisthesis, the evidence has yet to be confirmed.
- For infection, the evidence needs to be confirmed.
- For malignancy, the evidence has yet to be investigated.

In conclusion, there is enough evidence to use PRF for cervical radicular pain, the same evidence of efficacy has yet to be proved for disc-related pathology, while in other spinal conditions, more investigation has to be performed. This review reveals the huge heterogeneity of the studies regarding the dosage, time of application of the PRF and the image guidance (fluoroscopy, CT, ultrasound *etc.*), which makes it even more difficult to compare. We need further well-conducted trials to confirm this preliminary consideration and to extend the real efficacy of this technique.

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