The Role of Radiofrequency in Chronic Pain Management

Y L T N Mzoneli

Commentator: G Govender
Moderator: T Sommerville

Department of Anaesthetics
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INTRODUCTION

THE ROLE OF RADIOFREQUENCY IN CHRONIC PAIN MANAGEMENT

Chronic pain is still an enigma. It is complex, not fully understood and many physicians dispute that it is a disease; hence its treatment success remains poor.

The search for solutions to chronic pain management is ongoing and expanding. Management of chronic pain requires a multidisciplinary approach and follows the biopsychosocial model. The goal of management is to improve quality of life. The treatment modalities include drug therapy; surgery; psychotherapy; social work; physiotherapy; chiropractic techniques; acupuncture; interventional techniques like nerve blocks; epidurolysis; iontophoresis; stimulation therapy (transcutaneous nerve stimulation, spinal cord and brain stimulation) and radiofrequency procedures.

This talk will explore radiofrequency and its role as one of the interventional techniques to manage chronic pain.

There are two types of radiofrequency modalities currently used in pain medicine:
1. Continuous radiofrequency (CRF)
2. Pulsed radiofrequency (PRF)

HISTORY OF RADIOFREQUENCY

For many years heat has been used to relieve pain. In the 1970s CRF current was used to produce heat and cause thermal coagulation in the target nerve. As a result of neural destruction, the transmission of pain signal is disrupted. This is known as CRF/thermal RF or thermal ablation/lesioning.[1,2]

The idea of the second RF variation, namely PRF, was conceived during a scientific conference in Austria in 1995 at a meeting between a former Soviet-bloc scientist, Prof Ayrapetyan, Mr Rittman, an engineer for the company Radionics and Dr Sluitjer, an anaesthesiologist from the Netherlands, whilst discussing the mechanisms behind CRF treatment.

The Soviet-bloc professor, who was working on cellular changes induced by magnetic fields, challenged the conventional belief that pain relief after CRF was as a result of thermal tissue destruction, rather suggesting it could be secondary to strong magnetic fields induced by voltage fluctuations.[4]
The magnetic field idea was discussed with Mr E.R Cosman, a professor in physics and the then president of Radionics. (Radionics was the company that built RF generators and electrodes since the 1950s). Further work was done at Radionics to investigate this magnetic field hypothesis.

They found that the magnetic field strength around the electrode at the RF voltages and frequencies they used was about 1-2 Gauss (which is equivalent to the earth’s magnetic field) and therefore this hypothesis was discounted. Instead they found that the electric fields and currents were very large and were suspected likely agents to produce the clinical effects following RF treatment.\(^3\)

At the same time Dr Sluitjer came up with the suggestion that pulsing the current might work better. This resulted in the design of the first pulsed radiofrequency generator towards the end of 1995. This PRF generator was then sent to Dr Sluitjer who introduced it into clinical practice in February 1996.

That was the birth of the PRF concept, a minimally invasive, non-destructive technique to manage chronic pain. The first article on PRF by Sluitjer, Cosman, Rittman and van Kleef was published in the Pain Clinic Journal in 1998.\(^{3,4}\)

**BASIC PHYSICS OF RADIOFREQUENCY**

Radiofrequency techniques use high frequency alternating current in the 100-500 kHz range to burn or modulate the nociceptive pathways at various bodily sites.

The biological effects in tissues during radiofrequency treatment are presumed to be due to:

a) Thermal effects as in CRF  
b) High intensity electrical fields in PRF  
c) Or both\(^5\)

The RF system comprises:

a) A RF generator  
b) A ground (dispersive) plate with large surface area  
c) A needle (active/lesion) electrode which is insulated except at the tip for a distance of 2-10mm  
d) A thermocouple to monitor temperature
The tissues of the body to complete the circuit

Fig 1: *Diagram of RF system* [27]

The RF generator produces alternating current at 500 kHz which results in a concentrated alternating electrical field at the non-insulated tip of the electrode. The electrical field causes electrons and molecules to oscillate in the tissues near the electrode. These molecular oscillations and resistance to current flow by tissues produces heat which can be represented by isotherm lines around the electrode.

The temperature of the heat produced can be monitored by a thermocouple. The temperature achieved in the tissues can be increased by increasing the amplitude of the applied current [9]. The geometry of the electric field lines and isotherm lines around the electrode tip can be seen in Fig 2 below.

Fig 2: *Electric field and isotherm lines around the electrode tip* [27]
It can be appreciated from Fig 2 that the temperature and density of the electric field become progressively less with increasing distances from the electrode.

CRF utilises a constant output of high frequency electric current to produce temperatures between 60° - 80°C, resulting in thermal ablation of the target nerve. For the lesion to be optimally effective the electrode must be parallel to the nerve.[7] Fig 3

![Diagram showing needle path across and along nerve](image)

**Fig 3:** The heat energy forms an ellipsoidal shape around the electrode.[7]

The magnitude of tissue destruction is related to the temperature of the tissues, the size of the electrode, the duration of the procedure, tissue vascularity and conductivity of the surrounding tissues.[8]

The concept of PRF is to deliver high intensity electric field current to a target tissue with minimal heat production to modify neurons at the functional level.

In PRF the same 500 kHz current is delivered in short bursts for 20 msec twice per second interspersed with a silent phase lasting 480 msec. The long silent phase allows for heat elimination, keeping the target tissue temperature below 42 °C.[2] (See fig 4)
The production of heat during these pulses depends on the power deposition which is illustrated by the following equation \[5\]

\[
\text{Power deposition} \propto (\text{voltage applied})^2 \times \text{exposure time} \times \text{Tissue resistivity}
\]

This relationship explains why pulsing the current allows the power output of the generator to be substantially increased. The voltage output in CRF ranges between 15-25 V whereas in PRF the voltage output is at 45 V. \[8\]

PRF can produce much stronger electrical fields than CRF. The electric field strength at the tip of electrode has been calculated to be as high as 185 000 V/m for an applied voltage of 45 V. However the intensity of this electric field wanes exponentially with increasing distance from the tip.\[9\]

\[Fig\ 4: \text{ from Springer images.com}\]
THE BIOLOGICAL EFFECTS OF RADIOFREQUENCY AND MECHANISM OF ACTION

The effects of radiofrequency on tissues are due to:

i. Thermal energy
ii. Electrical energy

Continuous radiofrequency (CRF)

The aim of CRF is neuroablation where the tissue temperature is raised to 60°C - 80°C to produce a thermal lesion resulting in the interruption of nociceptive afferent pathways that mediate the patient's symptoms.\(^1\)

The advantage of thermal lesioning is that the lesions are well circumscribed and predictable when compared with chemical neurolysis, although the size of the lesion may be larger due to differences in tissue impedance, for example proximity to bone.

Raising tissue temperature above 45°C - 50°C for just 20 sec will result in the destruction cellular structures and biomolecules.\(^9\)

Dieckmann et al studied the morphology of heat lesions in the brains of living animals. They observed progressive layers of charring, coagulative necrosis, liquefaction necrosis and demyelination, as temperature decreases with increasing distance from the electrode.

Podhajsky et al demonstrated extensive Wallerian degeneration of the axons and disruption of their myelin sheaths and epineurium following 80°C lesioning of the sciatic nerve.\(^10\)

The disadvantages of CRF/thermal ablation is that it produces irreversible non-selective destruction of nerve fibres, and therefore may result in deafferentiation syndrome, motor function loss as well as new onset neuritis leading to neuropathic pain.\(^11\)

Consequently a variant of RF which is pulsed has become more popular.

Pulsed radiofrequency (PRF)

The main objective is to have neuromodulatory effects on pain processing mechanisms and be non-destructive or minimally destructive.\(^11\)

The therapeutic effects are attributed to the large current density of up to \(10^3 - 10^5\) A/m\(^2\). These are very large compared to the biophysical levels of 10 A/m\(^2\) for normal transmembrane currents.\(^9\)
Initially it was thought that PRF has no tissue destructive effect because no histological lesions (axonotmesis or neurotmesis) were found on light microscopy, as well as there being no significant sensory loss following PRF.

However recent evidence, looking at nerves under the electron microscope after PRF treatment, demonstrates that there is ultrastructural damage. Erdine et al demonstrated cellular damage at microscopic level when they evaluated 279 axons in PRF group vs 265 axons in a sham control group. There was disruption of mitochondrial membranes, microtubules and microfilaments. This damage increased progressively from A-β fibres to A-δ fibres and was maximal in C-fibres and this is consistent with the predicted inner electric field calculations.[13]

The exact mechanism by which PRF controls pain is not yet clear. It is believed that it is related to the high electric fields. There are hypotheses based on the experimental observations of its biologic effects on tissues.

The high electric fields cause charges on molecular structures and thus induce high transmembrane potentials (Um) on the neurons or cells. The transmembrane potentials generated are proportional to the electric field strength and radius of the nerve but inversely proportional to the frequency of intrinsic RF current and can be represented by the equation below.

\[
(Um) \propto \frac{\text{Amplitude of electric field} \times \text{Radius of target nerve}}{\text{Frequency of intrinsic RF current}}
\]

The changes or disruption in the ion channel conductances across the neuronal membrane alter the Nernst concentration gradients, resulting in alterations of the membrane resting and threshold potentials of the C-fibres that mediate pain. Therefore the dysfunctional hyperactive spontaneously firing neurons may be rectified and modified.[5,9]

When very high transmembrane potentials in the magnitude of 0.1-1 V are generated they may cause membrane deformation, the creation of pores and even rupture of the cell membranes. This effect is known as electroporation.[9]

The effects of Um at lower electrical energy is believed to induce long-term depression (LTD) of synaptic transmission. The induced LTD by membrane rectification antagonises the long-term potentiation which is purported to underlie chronic pain states.[5]

Another theory on how PRF produces its antinociceptive effect is via a pathway that involves c-Fos and ATF-3 genes. The increased expression of c-Fos in the laminae I and II of the dorsal horn after PRF application to dorsal root ganglion is a marker of neuronal activity.
C-Fos has been used for almost 2 decades as a neurobiologic marker in pain research. It was hypothesized that c-Fos expressing neurons may be inhibitory interneurons that produce inhibitory neurotransmitters that reduce pain like glycine, GABA and dynorphin.

However, there is new evidence showing that C-fos expression is not specific for nociceptive pathways\(^7\).

The upregulation of ATF-3 (activating transcription factor 3) appears to be restricted to stimulated A-δ and C-fibres.\(^2\) However the role of these molecular markers in the effects of PRF remains unclear.

More recently (in 2009) Hagiwara et al demonstrated that PRF may enhance the descending noradrenergic and serotonergic inhibitory pathways which are involved in the modulation of neuropathic pain.

Electric fields have effects not only on neurons but other cell lines as well. A few studies prompted by the positive results seen in intra-articular and intradiscal PRF show that electric fields have immunomodulatory effects by attenuating release of proinflammatory cytokines such as IL-1b, IL-6, TNFa and IL-8 from human neutrophils.\(^{14}\)

**CLINICAL APPLICATIONS**

Radiofrequency has been used for more than four decades to manage various chronic pain syndromes such as trigeminal neuralgia, back pain and complex regional pain syndrome. It has been regarded as minimally invasive when compared to surgery.

RF is practised by specially trained neurosurgeons, orthopaedic surgeons, pain physicians and interventional radiologists. Procedures are done under real time fluoroscopic, CT or ultrasound guidance for peripheral sensory nerves.

**Spinal or axial pain**

The bulk of RF research has been performed in patients with spinal pain, most commonly cervical and lumbosacral pain (LBP). The cause of spinal related pain could be:

a. Strain on the muscles and biomechanics of the spine

b. Degenerative changes:
   i. Facet joints
   ii. Osteophyte formation
   iii. Sacroiliac joint arthritis
c. Discogenic pain (bulging, herniated or degenerated disc)
d. Radiculopathy
e. Central spinal pain or myelopathy

![Diagram of vertebral column showing normal and degenerative discs.](image)

*Causes of back pain* \(^{[28]}\)

The diagnosis of the origin of pain in spinal pain is complex because an obvious pathological finding on MRI may be asymptomatic and, on the other end of the scale, the nociceptive focus may look completely normal on imaging.

Therefore good clinical assessment and diagnostic local anaesthetic blocks are indispensible tools in the diagnosis of pain generators. \(^{[11,17]}\)

Accurate determination of the cause of pain prior to RF treatment will predict the success or failure of treatment. For example central pain following cord injury does not respond to RF. \(^{[12]}\) The algorithm on how to diagnose spinal pain can be found from IASP guidelines.

**Cervical Region**

There are currently 2 accepted uses of RF treatment in the cervical region:

i. CRF/PRF targeting the medial branch of the dorsal ramus – for facet joint disease.

ii. PRF treatment of dorsal root ganglion (DRG) - to manage cervical radicular pain.
RF for facet or zygapophyseal joint pain

The facet or zygapophyseal or Z-joints are postulated to account for 50-60% of chronic cervical pain. They are innervated by the medial branch of the dorsal ramus of the spinal nerves above and below the joint.

Patients suitable for medial branch RF treatment are selected on the basis of a positive response to two diagnostic local anaesthetic blocks. CRF has been used successfully for medial branch neurotomy to denervate cervical-z joints, providing intermediate to long term pain relief.

The RCT done by Lord et al, comparing RF-facet denervation with a sham intervention for patients suffering chronic neck pain following whiplash injury, found that the median duration of complete pain relief was 7 months in the experiment group compared with 8 days in the control group. Although other literature seems to confirm this, a large prospective RCT is required to make the findings generalisable.

The use of PRF to treat cervical facet joints seems to result in shorter mean pain relief duration of approximately 4 months compared to 7 months following CRF z-joint denervation.

RF for cervical radicular pain

Cervical radicular pain is commonly caused by irritation or injury of C-spine nerve roots. Experimental work has shown that there is spontaneous and enhanced dorsal root ganglion (DRG) activity in subjects with radicular pain. These sustained DRG discharges are closely linked to sensitisation of the spinal dorsal horn cells resulting in the state of hyperalgesia.

Based on these observations the DRG has been one of the prime targets for neuroablative or neuromodulatory pain therapy. CRF treatment adjacent to the cervical DRG for radicular pain management as was first described by van Kleef in the early 1990s became less popular due to the high risk of new onset neuritis and loss of muscle strength in the hand as well.

When the new variant (PRF) came into practice, being a less painful and a non- or minimally neurodestructive technique, it has become the treatment of choice to perform DRG neuromodulation.
In a double-blind sham controlled RCT, van Zundert et al reported that at 3 months the PRF arm of the study had significantly better outcome and the need for pain medication was significantly reduced after 6 months. There were no complications reported.\[16\]

**Lumbosacral region**

The accepted applications of RF treatment in lower back pain are:

i. RF lumbar facet denervation
ii. PRF treatment of the DRG for lumbosacral radicular pain
iii. Nerve root RF

**RF for lumbar zygapophyseal pain**

The treatment of lumbar facet or zygapophyseal (L-Z) joint pain using RF denervation is the most studied indication for RF in pain medicine.

There is strong evidence supporting RF facet joint denervation especially with regards to short-term and intermediate term relief for lumbar facet joint pain. One RCT done by Tekin et al in 2007 comparing RF and PRF treatment of L-Z joints revealed that the techniques have comparable results but the duration of the effect is longer in the CRF group.\[18\]

Van Boxem et al looked at 5 RCTs on RF for lower back pain. They concluded that in general, after careful selection of patients, RF therapy of the L-Z joint might be effective with a number needed to treat (NNT) between 1.1 and 1.5.\[15\]

The problem with most patients showing no benefit are poor technique, suboptimal needle position, poor patient selection and not performing a prior LA diagnostic block of the medial nerve branch by the attending physician.\[17\]
It can be appreciated, in figure 5, the expertise and precision required to get the needle in the right spot.

![Figure 5](image_url)

**Fig 5 A) Lumbar facet joint anatomy showing the medial branch  
B) The oblique X-ray of L4/L5 facet joint with the needles in place for RF denervation of L3/4 medial branches. Needles are seen end on. Hard outlines show “Scotty dogs”**

**RF for lumbar radicular pain**

This is the most common LBP presentation seen in pain management facilities. Since the DRG represents the first structure of pain modulation, targeting it to treat neuropathic pain makes sense. CRF in managing neuropathic pain is now relatively contraindicated. There is consensus that PRF is the treatment of choice for DRG, radiculopathy and peripheral nerve lesions.\(^5,8,22\)

Indications for lumbar DRG PRF include lumbosacral radiculopathy due to disc herniation, osteophytes, spinal stenosis and neurogenic claudication.\(^{11,22}\)

A retrospective study was described of 54 patients who underwent PRF; they were divided into 3 groups based on the cause of their spinal pain: herniated disc vs spinal stenosis vs FBSS (failed back surgery syndrome). Treatment success was based on a numerical rating scale (NRS 1-10), global perceived effect, and reduction in medication at 30, 60, 90 and 180 days. Treatment success was 72.4% for disc herniation, 66.6% for spinal stenosis and 15.3% for FBSS with NNT of 1.38, 1.49 and 6.5 respectively.\(^{15}\)

Nerve root PRF compares favourably to nerve root steroid injection which may have devastating complications like paraplegia if particulate steroids are injected into a vessel that is a major supplier to the spinal cord.\(^8,11\)
Radiofrequency and the Sacroiliac joint

The sacroiliac joint (SIJ) has been found to be the primary source of pain and referred pain in the lower extremity in 10-30% of patients with lower back pain. The current evidence for RF treatment of SIJ is contradictory and limited but growing.

Vallejo and co-workers (2006), looking at a prospective case series on SIJ-PRF of lateral branches L4-S2 had positive results. Yin et al also reported success in 64% of their patients using sensory stimulation guided RF neurotomy for recalcitrant SIJ pain. However Ferrante, analysing a consecutive series of 50 patients who had SIJ RF denervation, showed poor results.\[15,22\]

This could be explained by dual innervation both anteriorly and posteriorly of the SIJ as well as varying levels of contribution, but targeting S1-S2 seems to give good results. Newer electrode designs are also improving the rate of success. The information regarding RF treatment of SIJ pain is starting to accumulate.

Radiofrequency for facial pain

Not all facial pain is trigeminal neuralgia; correct terminology and diagnosis is important in determining the choice of therapy and consequently its success. Trigeminal neuralgia is characterised by brief, episodic, sharp lancinating pain in the region of one or more trigeminal divisions, typically provoked by touch.

Trigeminal neuropathy is a constant, non-provokable, unremitting unilateral facial pain of variable intensity that tends to be associated with abnormal blink and jaw reflexes.

Trigeminal neuropathy results from more peripheral lesions whereas trigeminal neuralgia results from vascular compression, demyelination or any lesion at the root level.\[12\]

A systematic review (2004) of interventional techniques for treatment of trigeminal neuralgia which looked at 166 studies reporting on RF thermocoagulation, glycerol rhizolysis, balloon compression of the Gasserian ganglion and stereotactic radiosurgery, concluded that RF thermocoagulation offers the highest rates of pain relief which may last up to 5 - 10 years.

However it has its disadvantages which are paraesthesia, loss of facial sensation, masseter weakness and paralysis, decreased corneal reflex, keratitis and transient paralysis of CN III and IV.\[15\]
See figure below showing how some of the complications that may arise during CRF of Gasserian ganglion.

![Diagram of Gasserian ganglion complications](image)

- **b) Mislocation of the electrode**
- **c) Expansion of thermal energy to neighbouring neural structures**

PRF, because of its less neurodestructive nature, seemed a logical choice to treat trigeminal neuralgia but the case series have generated contradictory results. In those that did report pain relief, the duration of relief was short, ranging from 10-20 months compared to >5 years with CRF therapy. Balancing risks vs benefits, it may be worth the trouble to repeat a relatively complication-free procedure from time to time rather than having long-lasting analgesia with greater risk of complications.

Gasserian ganglion thermoablation is contraindicated for trigeminal neuropathy and breaking this rule invariably tends to lead to a dramatic increase in pain. PRF for this condition might be a good option but no evidence has been accumulated as yet.\(^\text{[12]}\)

Neuropathic facial pain secondary to postherpetic neuralgia is very difficult to treat because this form of pain centralises at an early stage. Hypocirculation of the hypothalamus has been documented at 2 months following the acute stage of the disease.

Therefore PRF is unlikely to work but may be tried whereas CRF of the ganglion is completely contraindicated.\(^\text{[2,5,15,20]}\)
Radiofrequency for peripheral nerves

Peripheral nerve damage can occur in a number of ways, for example post-surgery or crush injury, which results in ion channel modulation leading to nociceptor sensitisation, increased neuronal excitability and diminished central inhibition.

Pulsed radiofrequency use will probably have the greatest potential in managing peripheral nerve injury. CRF, which will cause further nerve destruction, seems counterintuitive.

PRF technique has been used in a number of peripheral nerves like
1. Occipital nerve for headaches
2. Suprascapular nerve
3. Intercostal nerves
4. Ilioinguinal and iliofemoral nerves

PRF has been evaluated as therapy for groin pain and orchialgia occurring spontaneously or following inguinal herniorrhaphy. Preliminary reports on PRF of the ilioinguinal and iliofemoral nerves have shown complete relief lasting up to 6 months.\(^{[24]}\)

Cohen and colleagues conducted a retrospective analysis of 46 patients with postsurgical thoracic pain and found that PRF of the DRG was more beneficial than pharmacologic therapy or PRF of the intercostal nerves.\(^{[21]}\)

PRF of the suprascapular nerve has shown some benefit for patients with shoulder pain who are not candidates for shoulder surgery; also for glenohumeral arthritis and frozen shoulder.\(^{[20]}\)

However most of the current information on peripheral nerve PRF is from case reports and series but higher level of evidence is still required.
CONCLUSION

Both CRF and PRF use high frequency alternating current to treat pain. The difference is that CRF uses heat to ablate the neural structure and PRF uses high electric current to modulate the tissues at the functional level. Its exact mechanism of action is not clear, but there are proposed hypotheses from experimental work.

There is good evidence supporting CRF to treat trigeminal neuralgia and facet joint disease, but the problem is the associated risks due to its neurodestructive mechanisms. Hence the move towards PRF with lesser side effects. PRF is technically easier, less painful and involves shorter treatment times because the needle does not have to be parallel to the nerve. It has shown promising results in a number of chronic pain syndromes but the evidence remains limited to support it according to EBM standards.

Most of the information regarding PRF is experimental; clinical evidence is not sufficient but it is slowly growing. The retarded pace at which this evidence is accumulating is due to a number of factors:

- Chronic pain on its own is very complex and much is still not well understood, therefore we are still fighting an unknown monster.
- The number of confounding variables in chronic pain and the interrelations with psychosocial factors. At times the situation is like what is called INUS in philosophy (insufficient nonredundant component of unnecessary sufficient complex).[25]
- The difficulty in defining the treatment ends that will properly define effectiveness when doing RCTs.[26]
- The division amongst pain physicians themselves, those that use mainly pharmacotherapy vs those that are interventionalists.

Pain medicine is one subspecialty where physicians have to integrate the best research evidence with clinical expertise and patient values – meaning patients’ unique preferences, concerns and the expectations that each patient brings to the clinical counter and which must be integrated into clinical decisions if we expect them to serve the patient.

Finally the lack of evidence and knowledge about PRF should fuel us as scientists/physicians to gather more information to refute or support the role of PRF in pain. After all, it is said that science is about discovering, recognising and changing paradigms.
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