We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

186,000

200M

Download

154
Countries delivered to

Our authors are among the

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us? Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.

For more information visit www.intechopen.com



Application of Radiofrequency in Pain Management

Suleyman Deniz, Omer Bakal and Gokhan Inangil

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/100803

Abstract

The application of radiofrequency is a treatment for many clinical conditions such as trigeminal neuralgia, complex regional pain syndrome, chronic postsurgical pain, cancer pain, hyperhidrosis and facet joint pain requiring ablation of different nerve locations. In this procedure, a constant high-frequency, high-temperature electrical current is applied to target tissue. Sluijter has achieved significant pain relief using radiofrequency current at a temperature below 42°C that produced strong electromagnetic field with no thermal lesion and referred as pulsed radiofrequency. The use of pulsed radiofrequency is a non-neurodestructive and therefore less painful technique, and it serves as an alternative method to continuous radiofrequency. Many studies have demonstrated favorable outcomes with pulsed radiofrequency compared to continuous radiofrequency.

This chapter suggests the use of continuous and pulsed radiofrequency with a minimally invasive procedure for patients with chronic pain as an alternative to surgical treatment and it might be an additional option among nonsurgical treatment methods.

Keywords: pain, treatment, pulsed radiofrequency, minimally invasive surgical procedures, continuous

1. Introduction

The application of radiofrequency (RF) electrical signals to neural tissue with an RF lesion generator and RF electrodes inserted into the tissue is common to treat pain [1] and other diseases such as atrial fibrillation [2], malignant liver tumors [3], intermediate and large bone tumors [4] and varicose veins [5]. The basis of this method is to generate enough RF heating power in the tissue to raise the temperature above 45–50°C which is referred as the "lethal temperature", as the tissue exposed to these temperatures for 20 s or more are known to be destroyed by the heat [1].



The earliest RF lesion generators and electrodes were built by Cosman et al. in the early 1950s. They used continuous-wave RF with 0.1–1 mHz frequency and therefore referred as continuous RF lesioning [6, 7]. The basic principles and properties such as shape and size of heat lesions caused by for different electrode geometries and temperatures are well described today [8].

Recently, another RF method is especially used for pain treatment in which short pulses of RF signals are applied to the neural tissue through the RF electrode. This method is referred as pulsed RF lesioning [9].

While continuous RF used power sources with 0.1–1 mHz frequency range to produce RF heat lesion, pulsed RF signals have pulse durations ranging from 10 to 30 ms, and pulse repetition rates ranging from 1 to 8 Hz (pulses per second) [1]. Pulsed RF which produces a lesion to nerve tissue by transmission of high-voltage current through thermocouple probe has been used as a non- or minimally neurodestructive technique alternative to heat lesions because the average tissue temperature rise is less than continuous RF with the same voltage [1, 10–14]. Sluijter has achieved significant pain relief using radiofrequency current at a temperature below 42°C that produced strong electromagnetic field with no thermal lesion [9–11].

The objective of this book chapter is to explain the physics, operating principles, the mechanism of action, contraindications, complications and evaluation of efficacy of pulsed RF and continuous RF therapies in chronic pain management, in addition discussion of examples of clinical procedures.

2. The physics and operating principles of radiofrequency

RF lesioning is based on the principle of a very-high-frequency current passage down a 27G thermocouple probe which is inserted through a special 22G fully insulated cannula except for its tip. The current passes down the thermocouple probe and heats the surrounding tissues to a temperature controlled by the operator. The location of the nerve is achieved by a stimulating current with the thermocouple probe, and with a destructive current a circumscribed lesion is created. The lesion is shaped like a match with a diameter of about 2–4 mm [1, 11, 12].

The cannula, placed close to the targeted nerve to be lesioned, is usually confirmed under X-ray. Then, stylet of cannula is removed and replaced by the thermocouple probe. The operator initially attempts to seek the nerve by low-voltage stimulation at a frequency of 50 Hz, aiming the strongest sensory stimulation at the lowest possible voltage. The cannula needs to be within 3 mm of the nerve in order to create an adequate lesion and a maximum stimulation level of around 0.6 V would indicate this. The operator should always ensure that the cannula is not dangerously close to any motor nerve when trying to lesion a sensory nerve [1, 10–12].

When the operator is satisfied that the needle is in a safe place, a radiofrequency current (about 300–500 kHz) is passed through the thermocouple probe. The current heats up the surrounding tissues and produces a lesion in the targeted nerve. At a temperature of below 44–50°C, no permanent neurological damage will occur; thus, for practical purposes, when we mention

lesion size, we mean the volume of tissue within the 44–50°C. In all cell types, the heating of tissue above 44–50°C for several minutes will indeed result in cell death [1, 10–12].

In order to eliminate any possibility of a heat lesion being produced, Sluijter suggested a radiofrequency technique which uses a temperature of no greater than 42°C and which utilises the strong electric field generated by the passage of the radiofrequency current to achieve pain relief [12]. In order to apply an electric field to the tissues, without raising the tip temperature above 42°C, the radiofrequency current can be applied in a pulsed fashion. The "silent" period between pulses allows for the dissipation of heat produced during the active cycle [12]. Cosman and Sluijter have modified the standard lesion generator to deliver radiofrequency current bursts of 45 V at a repetition rate of 2 Hz with each burst 20 ms long; the rest period is therefore 480 msec. This is defined as pulsed RF [10–12, 15, 16].

The resistance to the current flow can be measured and it is useful in certain procedures since it indicates the position of the needle tip. The impedans will be 400 Ω in extradural tissues and measuring a 200 will warn operator that the tip is passed to the cerebrospinal fluid (CSF) and a 800 Ω impedans will indicate when the tip enters CSF during percutaneuous cordotomy. Similarly, during procedures with intervertebral disc, an impedans is very high and it falls below 200 Ω while nucleus pulposus impedans of nucleus pulposus is reached [1, 10–12].

3. Mechanism of action of radiofrequency

Continuous RF lesioning involves the passage of a very high frequency which causes destruction by heat. It is simple and clear. Efficacy of pulsed RF has been clinically documented and has been used for chronic pain conditions for the last 20 years, but its mechanism of action is not fully understood [10-14]. It has been suggested to alter gene expression in neurons, by means of neuromodulation [1, 11, 17-23]. Stimulation of serotonergic and noradrenergic systems and induction of descending pathways have also been proposed [22]. There is no clinical evidence of any nerve damage with pulsed RF [11, 12, 19, 22, 23]. Higuchi et al. have presented experimental evidence that pulsed RF applied to the rat cervical dorsal root ganglion causes upregulation of the immediate early gene c-fos immunoreactivity in the laminae I & II of the dorsal horn [18]. Hamann et al. applied pulsed RF to the sciatic nerve or the L5 dorsal root ganglion in the rat. They studied the expression of activating transmission factor 3 (ATF3), an early intermediate gene expressed in response to cell stress. They also reported a trend downregulation of CGRP expression [24]. Hamann et al., pointing out the lack of laboratory evidence for this phenomenon, felt that this may be due to changes induced in the function of the Schwann cells [24]. Electric fields have demonstrated effects on immune modulation, as there are studies that show proinflammatory cytokines, such as interleukin (IL)-1b, TNF-alpha and IL-6, are attenuated by electric fields [25]. Upregulation of adenosine A2A receptor density has also been observed in human neutrophils treated with generated electric fields, and this appeared to be associated with inhibition of the catabolic cytokines, such as TNF-alpha, IL-6 and IL-8 [26].

In an animal study evaluating the histologic effects of continuous RF at 67°C and pulsed RF applied adjacent to rabbit dorsal root ganglia (DRG), Erdine et al. found mitochondrial degeneration and a loss of nuclear membrane integrity in the continuous, but not in the pulsed group [27]. Another histopathologic study, comparing the effects of continuous RF and pulsed RF delivered at 42°C on the rat DRG and sciatic nerve, showed no structural changes aside from transient endoneurial edema and collagen deposition [28]. In addition, Hagiwara et al. more recently demonstrated that pulsed RF may actually enhance the descending noradrenergic and serotonergic inhibitory pathways, which are intimately involved in the modulation of neuropathic pain [22]. Pulsed RF may be useful and continuous RF is contraindicated, e.g., in neuropathic pain and it is safe in locations where continuous RF may be potentially hazardous, e.g., DRG lesioning. It is virtually painless as no heat is generated [10–12].

Sluijter describes four phases in a pulsed RF treatment procedure:

- **a.** A stunning phase, which provides immediate relief.
- **b.** A phase of post procedure discomfort, which may last for up to 3 weeks.
- **c.** A phase of beneficial clinical effect, which has a variable duration.
- **d.** A phase of recurrence of pain, we are still in the early days but many cases record 4–24 months of relief [11, 12].

4. Contraindications of radiofrequency

Gauci does not recommend the use of both continuous and pulsed RF in patients with psychological overlay, drug dependency and total body pain [12]. Continuous RF treatment is also contraindicated in all nerve that carries motor fibers [1, 10–13].

Pulsed RF therapy seems ineffective in some diseases and would be contraindicated. Whereas according to some studies, pulsed RF appears to be ineffective in our opinion; one of the reasons for this is the insufficient "pulsed RF dose" applied. For example, in a study the anti-allodynic effects of pulsed RF was significantly greater when pulsed RF exposure was increased from 2 to 6 min [29]. Therefore, there also exist unresolved questions regarding the effective "pulsed RF dose" based on voltage settings and duration of pulsed RF treatment, which require further clinical studies in order to confirm.

5. Complications of radiofrequency

The high temperature applied with continuous RF is neurodestructive and is usually characterized by a period of discomfort, including hypoanesthesia and a neuritis-like reaction [1, 10–14]. Sometimes pain may potentially worsen due to nerve regeneration and may lead to neuroma formation. Other complications such as hematoma, numbness, transitory diplopia, meningitis, Horner's syndrome and urinary retention may occur [12–14, 16, 17, 19, 30, 31].

In the publication of Cahana et al., it is stated that there is documentation of more than 1200 patients who have been treated with pulsed RF and no neurological complication was reported [23]. In a recent clinical study on patients with premature ejaculation, pulsed RF was performed to dorsal nerves of penis and no functional disorder that indicates a nerve lesion was determined [19]. We have not observed such a complication in our clinical experience.

6. Procedure for application of radiofrequency

The applications of continuous and pulsed RF in our department were made in operating room. Before procedure, prothrombin time and platelet counts were checked. Following a peripheral IV route, the patients were monitorized with ECG, oxygen saturation and non-invasive arterial blood pressure and sedated with 0.02 mg/kg IV midazolam. Following subcutaneous local anesthetic infiltration, a RF lesion generator was used for continuous and pulsed RF thermal ablation. A 22-gauge, 5–15 cm, RF cannula with a 2–10 mm active-pinned tip (with matching electrode) is advanced to the target tissue. The electrode of the RF device is placed on the cannula, and the impedance is seen to be between 200–400 Ω . In order to check the position of the cannula neurophysiologically, paresthesia is observed with 50 Hz sensory stimulation at 0.3–0.5 V and lack of motor contraction with 2 Hz motor stimulation at 0.9–1.5 V. After this neurophysiological testing, continuous RF thermal coagulation is applied at 60–80°C for 60–120 s. Pulsed RF thermal coagulation is applied at 42°C for 120–600 s. Following thermal coagulation, 2 ml of 2% lidocaine is applied through the cannula. All patients are monitored for potential complications following 2 h after the procedure. Patients were discharged home on the same day.

7. Applications of radiofrequency treatment

- **a.** Radiofrequency facet joint denervation
 - *Cervical facet joint denervation* [12, 32–35]

Target: Medial branch of the cervical posterior primary ramus

Required equipment: Mobile C-arm fluoroscopic X-ray systems, RF lesion generator, the cannula (a 22-gauge, 5 cm length, 2–4 mm active-curved tip (with matching electrode) of the RF, the grounding line

Patient position: Supine and the X-ray tube "looks" at the side opposite to that being treated (C2–C5), prone (C6–C7)

View: Lateral-oblique view of the cervical spine (C2–C5), postero-anterior-oblique view of the cervical spine (C6–C7)

Treatment modality: Continuous RF (80°C for 60 s), pulsed RF (42°C for 120–360 s)

Thoracic facet joint denervation [12, 32, 34, 35]

Target: Medial branch of the thoracic posterior primary ramus

Required equipment: Mobile C-arm fluoroscopic X-ray systems, RF lesion generator, the cannula (a 22-gauge, 5-10 cm length, 2-4 mm active-curved tip (with matching electrode) of the RF, the grounding line

Patient position: Prone

View: Postero-anterior view of the thoracic spine

Treatment modality: Continuous RF (80–85°C for 60 s), pulsed RF (42°C for 120–360 s)

• Lumbar facet joint denervation [12, 32, 34–36]

Target: Medial branch of the lumbar posterior primary ramus (eye of the Scottie dog, L1–L4), the junction between the superior articular process and the upper surface of the lateral part of the sacrum (L5), just lateral to the sacral foramen (S1–S3)

Required equipment: Mobile C-arm fluoroscopic X-ray systems, RF lesion generator, the cannula (a 22-gauge, 10-15 cm length, 5 mm active-pinned tip (with matching electrode) of the RF, the grounding line

Patient position: Prone

View: Postero-anterior-oblique view of the lumbar spine (tunnel vision)

Treatment modality: Continuous RF (85°C for 60 s), pulsed RF (42°C for 180–360 s)

- Radiofrequency dorsal root ganglion
 - Cervical DRG pulsed RF/continuous RF [12, 34, 35, 37]

Target: Typical cervical DRG (C3–C6)

Required equipment: Mobile C-arm fluoroscopic X-ray systems, RF lesion generator, the cannula (a 22-gauge, 5-10 cm length, 2 mm active-curved tip (with matching electrode) of the RF, the grounding line

Patient position: Supine and the X-ray tube "looks" at the side opposite to that being treated (C1–C6), prone (C7–C8)

View: Lateral-oblique view of the cervical spine (C2–C5), postero-anterior-oblique view of the cervical spine (C6–C7)

Treatment modality: Pulsed RF (42°C for 120 s), continuous RF (65°C for 60 s) (do not carry out C1–C2)

Attention: The vertebral artery may lie in needle path. Careful! (C1–C2)

• Thoracic DRG pulsed RF/continuous RF [12, 34, 38–40]

Information: Effective in the treatment of chronic thoracic postherpetic neuralgia and chronic postsurgical thoracic pain

Target: Thoracic DRG

Required equipment: Mobile C-arm fluoroscopic X-ray systems, RF lesion generator, the cannula (a 22-gauge, 10 cm length, 2 mm active-curved tip (with matching electrode) of the RF, the grounding line

Patient position: Prone

View: Postero-anterior-oblique view of the thoracic spine, angle your beam slightly cranially (T1–6), angle your beam slightly caudally (T7–12)

Treatment modality: Pulsed RF (42°C for 120 s), continuous RF (67°C for 60 s)

Attention: Pneumothorax! Careful!

• Lumbar DRG pulsed RF/continuous RF [12, 27, 41–43]

Information: Effective in the treatment of chronic post-amputation stump pain and complex regional pain syndrome

Target: Lumbar DRG

Required equipment: Mobile C-arm fluoroscopic X-ray systems, RF lesion generator, the cannula (a 22-gauge, 10-15 cm length, 2 mm active-pinned tip (with matching electrode) of the RF, the grounding line

Patient position: Prone

View: Postero-anterior-oblique view of the lumbar spine (no double end plate) (chin of the dog)

Treatment modality: Pulsed RF (42°C for 120 s), continuous RF (50–65°C for 60 s)

- Radiofrequency sympathetic nervous system
 - *Sphenopalatine ganglion pulsed RF/continuous RF* [12, 44–47]

Information: Effective in the treatment of posttraumatic headache, chronic face and head pain and cluster headaches

Target: Pterygopalatine fossa, pterygomaxillary fissure

Required equipment: Mobile C-arm fluoroscopic X-ray systems, RF lesion generator, the cannula (a 22-gauge, 5 cm length, 2 mm active-pinned tip (with matching electrode) of the RF, the grounding line

Patient position: Supine and the X-ray tube "looks" at opposite to the treated side

View: Lateral-oblique X-ray view of skull to show pterygomaxillary fissure

Treatment modality: Pulsed RF (42°C for 120–240 s), continuous RF (60–90°C for 60–90

• Superior cervical ganglion pulsed RF/continuous RF [12, 48]

Information: Effective in the treatment of tinnitus and atypical face pain

Target: The superior cervical sympathetic ganglion is formed by the coalescence of the upper four cervical sympathetic ganglia. It is situated at the level of C3, postero-medial to the carotid sheath and to the internal jugular vein

Required equipment: Mobile C-arm fluoroscopic X-ray systems, RF lesion generator, the cannula (a 22-gauge, 5-10 cm length, 2 mm active-curved tip (with matching electrode) of the RF, the grounding line

Patient position: Prone

View: Lateral-oblique X-ray view of the cervical spine

Treatment modality: Pulsed RF (42°C for 120 s), continuous RF (70–75°C for 60 s)

• Stellate ganglion pulsed RF/continuous RF [12, 49–51]

Information: Effective in the treatment of complex regional pain syndrome and posttraumatic stress disorder

Target: It is situated at the level of C7

Required equipment: Mobile C-arm fluoroscopic X-ray systems, RF lesion generator, the cannula (a 22-gauge, 5-10 cm length, 2 mm active-curved tip (with matching electrode) of the RF, the grounding line

Patient position: Supine, prevent patient swallowing during procedure!

View: Antero-posterior X-ray view of the cervical spine

Treatment modality: Pulsed RF (42°C for 120 s), continuous RF (70–75°C for 60 s)

Attention: Ask the patient to phonate (recurrent laryngeal nerve!), Horner's syndrome!

• Thoracic sympathetic ganglion pulsed RF/continuous RF [12, 52–54]

Information: Effective in the treatment of complex regional pain syndrome, palmar hyperhidrosis and compensatory hyperhidrosis of the trunk

Target: It is situated at the levels of T4, T2, T3 and T6

Required equipment: Mobile C-arm fluoroscopic X-ray systems, RF lesion generator, the cannula (a 22-gauge, 5-10 cm length, 2 mm active-curved tip (with matching electrode) of the RF, the grounding line

Patient position: Prone

View: Postero-anterior X-ray view of the thoracic spine

Treatment modality: Pulsed RF (42°C for 120 s), continuous RF (75–80°C for 60–90 s)

Attention: Pneumothorax!

• Splanchnic nerve pulsed RF/continuous RF [12, 55–58]

Information: Effective in the treatment of chronic abdominal pain, chronic pancreatitis and cancer pain

Target: It is situated at the level of T11 at the costovertebral angle (about 4 cm from the midline)

Required equipment: Mobile C-arm fluoroscopic X-ray systems, RF lesion generator, the cannula (a 22-gauge, 15 cm length, 2-5 mm active-curved tip (with matching electrode) of the RF, the grounding line

Patient position: Prone

View: Postero-anterior X-ray view of the thoracic spine

Treatment modality: Pulsed RF (42°C for 120 s), continuous RF (75–80°C for 60–90 s)

Attention: Pneumothorax!

• Lumbar sympathetic ganglion continuous RF/pulsed RF [12, 59-61]

Information: Effective in the treatment of complex regional pain syndrome, plantar hyperhidrosis, chronic pelvic and perineal pain and cancer pain

Target: It is situated at the level of L4, L2 and L3

Required equipment: Mobile C-arm fluoroscopic X-ray systems, RF lesion generator, the cannula (a 22-gauge, 15 cm length, 2-5 mm active-pinned tip (with matching electrode) of the RF, the grounding line

Patient position: Prone

View: Postero-anterior-oblique and lateral X-ray view of the lumbar spine (no double end plate)

Treatment modality: Continuous RF (80°C for 90 s), pulsed RF (42°C for 120–300 s)

Miscellaneous procedures

• Trigeminal ganglion continuous RF/pulsed RF [12, 62–64]

Information: Effective in the trigeminal neuralgia treatment of combined pulsed and continuous radiofrequency

Target: Foramen ovale

Required equipment: Mobile C-arm fluoroscopic X-ray systems, RF lesion generator, the cannula (a 22-gauge, 10 cm length, 2-5 mm active-pinned tip (with matching electrode) of the RF, the grounding line

Patient position: Supine

View: X-ray beam in an antero-posterior axis over the head, move the axis of the intensifier caudo-cranially so that the X-ray beam makes an angle of 45°, next, 45–50° between the sagittal and the vertical planes. Lateral control (Clivus must be seen!)

Treatment modality: Continuous RF (60°C for 60 s, followed by; 65°C for 60 s, followed by; 70°C for 60 s, followed by; 75°C for 60 s, and next, 80°C for 60 s), pulsed RF (42°C for 120–240 s)

Attention: The procedure is very painful (Sedoanalgesia may be required!), CSF may be seen (If so, position is correct). Exhibit eye movements or facial contractions may be seen (If so, position is incorrect), blood may be seen (If so, position is incorrect), contractions of the masseter muscles can be seen (If so, position is incorrect), corneal reflex should be protected!

• Intradiscal RF/pulsed RF [12, 65, 66]

Target: Posterior anulus tear

Required equipment: Mobile C-arm fluoroscopic X-ray systems, RF lesion generator, the cannula (a 22-gauge, 15 cm length, 2–5 mm active-pinned tip (with matching electrode) of the RF, the grounding line

Patient position: Prone

View: Postero-anterior-oblique view of the lumbar spine (no double end plate)

Treatment modality: Continuous RF (50°C for 120 s, followed by; 55°C for 120 s, followed by; 60°C for 120 s, and next; 65°C for 240 s), pulsed RF (42°C for 120–900 s)

Attention: Monitor external temperature of disc, never exceeds 44°C

• Occipital nerve pulsed RF [12, 67, 68]

Information: Effective in the treatment of occipital neuralgia, migraine and cervicogenic headaches

Target: Greater occipital nerve (C2), lesser occipital nerve (C3)

Required equipment: RF lesion generator, the cannula (a 22-gauge, 5 cm length, 4 mm active-pinned tip (with matching electrode) of the RF, the grounding line, ultrasonography

Patient position: The sitting position

View: Occipital artery can be viewed with ultrasonography

Treatment modality: Pulsed RF (42°C for 180–600 s)

Attention: Temperature not to exceed 42°C

• Suprascapular nerve pulsed RF [12, 69–71]

Information: Effective in the treatment of adhesive capsulitis, chronic shoulder pain

Target: Suprascapular notch

Required equipment: RF lesion generator, the cannula (a 22-gauge, 10 cm length, 5 mm active-pinned tip (with matching electrode) of the RF, the grounding line, ultrasonography

Patient position: The sitting position

View: Suprascapular artery can be viewed with ultrasonography

Treatment modality: Pulsed RF (42°C for 180–600 s)

Attention: Temperature not to exceed 42°C, Be careful about pneumothorax!

• *Percutaneous cervical cordotomy* [12, 72–74]

Information: Indicated for unilateral pain due to malignant disease, when the pain is not responsive to drug therapy or other less invasive methods of treatment. The patient cannot be sedated

Target: C1/C2 intervertebral space, lateral spinothalamic tract

Required equipment: RF lesion generator, the cannula (a 22-gauge, 5-10 cm length, 2 mm active-pinned tip (with matching electrode) of the RF (Cordotomy kit!), the grounding line, computerized tomography

Patient position: Supine

View: Lateral view of cervical spine

Treatment modality: Continuous RF (75°C for 60 s, followed by; 75°C for 60 s, followed by; 75°C for 60 s, and next; 75°C for 60 s)

Attention: Working on the side opposite to the pain! Protect motor fibers!

Also, pulsed RF are reported in the literature that it can be used in treatment of Morton's neuroma [13], coccygodynia [14], pudendal neuralgia [75], vaginismus [76], carpal tunnel syndrome [77], chronic hip pain [78], post herniorrhaphy pain [79], chronic inquinal neuralgia [80], plantar heel pain [81], osteoarthritis [82], intra-articular pain [83], plantar fascitis pain [84], tarsal tunnel syndrome [85], myofascial pain syndrome [86], postamputation phantom pain [87], meralgia paresthetica [88], lingual neuralgia [89] and chronic testicular pain [90].

This chapter suggests the use of continuous and pulsed RF with a minimally invasive procedure for patients with chronic pain as an alternative to surgical treatment and it might be an additional option among non-surgical treatment methods. On the other hand, further randomized prospective controlled studies in patients with chronic pain are needed to fully evaluate the effectiveness of continuous and pulsed RF.

Author details

Suleyman Deniz*, Omer Bakal and Gokhan Inangil

*Address all correspondence to: sdeniz.md@gmail.com

Gulhane Military Medical Academy, Haydarpasa Training Hospital, Department of Anesthesiology, Pain Management Unit, Istanbul, Turkey

References

- [1] Cosman ER Jr, Cosman ER Sr. Electric and thermal field effects in tissue around radiofrequency electrodes. Pain Med. 2005;6:405–24.
- [2] Hunter RJ, Baker V, Finlay MC, Duncan ER, Lovell MJ, Tayebjee MH, Ullah W, Siddiqui MS, McLEAN A, Richmond L, Kirkby C, Ginks MR, Dhinoja M, Sporton S, Earley MJ, Schilling RJ. Point-by-point radiofrequency ablation versus the cryoballoon or a novel combined approach: a randomized trial comparing 3 methods of pulmonary vein isolation for paroxysmal atrial fibrillation (the cryo versus RF trial). J Cardiovasc Electrophysiol. 2015;26:1307–14. doi: 10.1111/jce.12846.
- [3] Lencioni R, de Baere T, Martin RC, Nutting CW, Narayanan G. Image-guided ablation of malignant liver tumors: recommendations for clinical validation of novel thermal and non-thermal technologies a western perspective. Liver Cancer. 2015;4:208–14. doi: 10.1159/000367747.
- [4] Nakatsuka A, Yamakado K, Uraki J, Takaki H, Yamanaka T, Fujimori M, Hasegawa T, Sakuma H. Safety and clinical outcomes of percutaneous radiofrequency ablation for intermediate and large bone tumors using a multiple-electrode switching system: a phase ii clinical study. J Vasc Interv Radiol. 2015 Dec 23. pii: S1051-0443(15)01068-4. doi: 10.1016/j.jvir.2015.10.025.
- [5] Kim J, Cho S, Joh JH, Ahn HJ, Park HC. Effect of diameter of saphenous vein on stump length after radiofrequency ablation for varicose vein. Vasc Specialist Int. 2015;31:125– 9. doi: 10.5758/vsi.2015.31.4.125.
- [6] Cosman BJ, Cosman ER. Guide to Radio Frequency Lesion Generation in Neurosurgery. Burlington, MA: Radionics; 1974.
- [7] Cosman ER, Cosman BJ. Methods of making nervous system lesions. In: Wilkens RH, Rengachary SS, eds. Neurosurgery. New York: McGraw-Hill; 1984:2490–9.
- [8] Cosman ER, Nashold BS, Ovelman-Levitt J. Theoretical aspects of radiofrequency lesions in the dorsal root entry zone. Neurosurgery. 1984;15:945–50.

- [9] Sluijter ME, Cosman ER, Rittman WJ, Van Kleef M. The effects of pulsed radiofrequency fields applied to the dorsal root ganglion: a preliminary report. The Pain Clinic. 1998;II(2):109-17.
- [10] Chua NH, Vissers KC, Sluijter ME. Pulsed radiofrequency treatment in interventional pain management: mechanisms and potential indications-a review. Acta Neurochir (Wien). 2011;153:763–71. doi: 10.1007/s00701-010-0881-5.
- [11] Sluijter ME. Pulsed radiofrequency. In Radiofrequency, Part 1. Fliovopress SA, Meggen (LU), Switzerland; 2001. 55-68.
- [12] Gauci CA. The Manual of RF-Techniques. Flivo Press SA, Meggen (LU), Switzerland; 2004. 8-140.
- [13] Deniz S, Purtuloglu T, Tekindur S, Cansız KH, Yetim M, Kılıckaya O, Senkal S, Bilgic S, Atim A, Kurt E. Ultrasound-guided pulsed radio frequency treatment in Morton's neuroma. J Am Podiatr Med Assoc. 2015;105:302-6. doi: 10.7547/13-128.1.
- [14] Atim A, Ergin A, Bilgiç S, Deniz S, Kurt E. Pulsed radiofrequency in the treatment of coccygodynia. Agri. 2011;23:1-6.
- [15] Cosman ER. A comment on the history of the pulsed radiofrequency technique for pain therapy. Anesthesiology. 2005;103:1312.
- [16] Sluijter ME, van Kleef M. Pulsed radiofrequency. Pain Med. 2007;8:388–9; author reply 390-1.
- [17] van Boxem K, van Eerd M, Brinkhuizen T, Patijn J, van Kleef M, van Zundert J. Radiofrequency and pulsed radiofrequency treatment of chronic pain syndromes: the available evidence. Pain Pract. 2008;8:385–93.
- [18] Higuchi Y, Nashold BS Jr, Sluijter M, Cosman E, Pearlstein RD. Exposure of the dorsal root ganglion in rats to pulsed radiofrequency currents activates dorsal horn lamina I and II neurons. Neurosurgery 2002;50:850–5; discussion 856.
- [19] Basal S, Goktas S, Ergin A, Yildirim I, Atim A, Tahmaz L, Dayanc M. A novel treatment modality in patients with premature ejaculation resistant to conventional methods: the neuromodulation of dorsal penile nerves by pulsed radiofrequency. J Androl. 2010;31:126–30.
- [20] Munglani R. The longer term effect of pulsed radiofrequency for neuropathic pain. Pain. 1999;80:437-9.
- [21] Richebé P, Rathmell JP, Brennan TJ. Immediate early genes after pulsed radiofrequency treatment: neurobiology in need of clinical trials. Anesthesiology. 2005;102:1–3.
- [22] Hagiwara S, Iwasaka H, Takeshima N, Noguchi T. Mechanisms of analgesic action of pulsed radiofrequency on adjuvant induced pain in the rat: roles of descending adrenergic and serotonergic systems. Eur J Pain. 2009;13:249-52.

- [23] Cahana A, Van Zundert J, Macrea L, van Kleef M, Sluijter M. Pulsed radiofrequency: current clinical and biological literature available. Pain Med. 2006;7:411–23.
- [24] Hamann W, Abou-Sherif S, Thompson S, Hall S. Pulsed radiofrequency applied to dorsal root ganglia causes a selective increase in ATF3 in small neurons. Eur J Pain. 2006;10:171–6.
- [25] Igarashi A, Kikuchi S, Konno S. Correlation between inflammatory cytokines released from the lumbar facet joint tissue and symptoms in degenerative lumbar spinal disorders. J Orthop Sci. 2007;12:154–60.
- [26] Varani K, Gessi S, Merighi S, Iannotta V, Cattabriga E, Spisani S, Cadossi R, Borea PA. Effect of low frequency electromagnetic fields on A2A adenosine receptors in human neutrophils. Br J Pharmacol. 2002;136:57–66.
- [27] Erdine S, Yucel A, Cimen A, Aydin S, Sav A, Bilir A. Effects of pulsed versus conventional radiofrequency current on rabbit dorsal root ganglion morphology. Eur J Pain. 2005;9:251–6.
- [28] Podhajsky RJ, Sekiguchi Y, Kikuchi S, Myers RR. The histologic effects of pulsed and continuous radiofrequency lesions at 42 degrees C to rat dorsal root ganglion and sciatic nerve. Spine (Phila Pa 1976). 2005;30:1008–13.
- [29] Tanaka N, Yamaga M, Tateyama S, Uno T, Tsuneyoshi I, Takasaki M. The effect of pulsed radiofrequency current on mechanical allodynia induced with resiniferatoxin in rats. Anesth Analg. 2010;111:784–90. doi: 10.1213/ANE.0b013e3181e9f62f.
- [30] Rozen D, Parvez U. Pulsed radiofrequency of lumbar nerve roots for treatment of chronic inguinal herniorraphy pain. Pain Physician. 2006;9:153–6.
- [31] Bogduk N. Pulsed radiofrequency. Pain Med. 2006;7:396–407.
- [32] Manchikanti L, Kaye AD, Boswell MV, Bakshi S, Gharibo CG, Grami V, Grider JS, Gupta S, Jha SS, Mann DP, Nampiaparampil DE, Sharma ML, Shroyer LN, Singh V, Soin A, Vallejo R, Wargo BW, Hirsch JA. A systematic review and best evidence synthesis of the effectiveness of therapeutic facet joint interventions in managing chronic spinal pain. Pain Physician. 2015;18:E535–82.
- [33] Liliang PC, Lu K, Hsieh CH, Kao CY, Wang KW, Chen HJ. Pulsed radiofrequency of cervical medial branches for treatment of whiplash-related cervical zygapophysial joint pain. Surg Neurol. 2008;70(Suppl 1):S1:50–5; discussion S1:55. doi: 10.1016/j.surneu. 2008.07.006.
- [34] van Kleef M, Stolker RJ, Lataster A, Geurts J, Benzon HT, Mekhail N. Thoracic pain. Pain Pract. 2010;10:327–38. doi: 10.1111/j.1533-2500.2010.00376.x.
- [35] Manchikanti L, Abdi S, Atluri S, Benyamin RM, Boswell MV, Buenaventura RM, Bryce DA, Burks PA, Caraway DL, Calodney AK, Cash KA, Christo PJ, Cohen SP, Colson J, Conn A, Cordner H, Coubarous S, Datta S, Deer TR, Diwan S, Falco FJ, Fellows B, Geffert S, Grider JS, Gupta S, Hameed H, Hameed M, Hansen H, Helm S 2nd, Janata

- JW, Justiz R, Kaye AD, Lee M, Manchikanti KN, McManus CD, Onyewu O, Parr AT, Patel VB, Racz GB, Sehgal N, Sharma ML, Simopoulos TT, Singh V, Smith HS, Snook LT, Swicegood JR, Vallejo R, Ward SP, Wargo BW, Zhu J, Hirsch JA. An update of comprehensive evidence-based guidelines for interventional techniques in chronic spinal pain. Part II: guidance and recommendations. Pain Physician. 2013;16(2 Suppl):S49-283.
- [36] Koh W, Choi SS, Karm MH, Suh JH, Leem JG, Lee JD, Kim YK, Shin J. Treatment of chronic lumbosacral radicular pain using adjuvant pulsed radiofrequency: a randomized controlled study. Pain Med. 2015;16:432-41. doi: 10.1111/pme.12624.
- [37] Yoon YM, Han SR, Lee SJ, Choi CY, Sohn MJ, Lee CH. The efficacy of pulsed radiofrequency treatment of cervical radicular pain patients. Korean J Spine. 2014;11:109-12. doi: 10.14245/kjs.2014.11.3.109.
- [38] Ke M, Yinghui F, Yi J, Xeuhua H, Xiaoming L, Zhijun C, Chao H, Yingwei W. Efficacy of pulsed radiofrequency in the treatment of thoracic postherpetic neuralgia from the angulus costae: a randomized, double-blinded, controlled trial. Pain Physician. 2013;16:15-25.
- [39] van Kleef M, Barendse GA, Dingemans WA, Wingen C, Lousberg R, de Lange S, Sluijter ME. Effects of producing a radiofrequency lesion adjacent to the dorsal root ganglion in patients with thoracic segmental pain. Clin J Pain. 1995;11:325-32.
- [40] Cohen SP, Sireci A, Wu CL, Larkin TM, Williams KA, Hurley RW. Pulsed radiofrequency of the dorsal root ganglia is superior to pharmacotherapy or pulsed radiofrequency of the intercostal nerves in the treatment of chronic postsurgical thoracic pain. Pain Physician. 2006;9:227–35.
- [41] Nagda JV, Davis CW, Bajwa ZH, Simopoulos TT. Retrospective review of the efficacy and safety of repeated pulsed and continuous radiofrequency lesioning of the dorsal root ganglion/segmental nerve for lumbar radicular pain. Pain Physician. 2011;14:371-6.
- [42] Ramanavarapu V, Simopoulos TT. Pulsed radiofrequency of lumbar dorsal root ganglia for chronic post-amputation stump pain. Pain Physician. 2008;11:561–6.
- [43] Apiliogullari S, Aydin BK, Onal O, Kirac Y, Celik JB. Pulsed radiofrequency of dorsal root ganglia for the treatment of complex regional pain syndrome in an adolescent with poliomyelitis sequel: a case report. Pain Med. 2015;16:1369–72. doi: 10.1111/pme.12710.
- [44] Shah RV, Racz GB. Long-term relief of posttraumatic headache by sphenopalatine ganglion pulsed radiofrequency lesioning: a case report. Arch Phys Med Rehabil. 2004;85:1013-6.
- [45] Day M. Neurolysis of the trigeminal and sphenopalatine ganglions. Pain Pract. 2001;1:171-82.

- [46] Bayer E, Racz GB, Miles D, Heavner J. Sphenopalatine ganglion pulsed radiofrequency treatment in 30 patients suffering from chronic face and head pain. Pain Pract. 2005;5:223-7.
- [47] Fang L, Jingjing L, Ying S, Lan M, Tao W, Nan J. Computerized tomography-guided sphenopalatine ganglion pulsed radiofrequency treatment in 16 patients with refractory cluster headaches: twelve- to 30-month follow-up evaluations. Cephalalgia. 2015 Apr 20. pii: 0333102415580113.
- [48] Koning HM, Dyrbye BA, van Hemert FJ. Percutaneous radiofrequency lesion of the superior cervical sympathetic ganglion in patients with tinnitus. Pain Pract. 2015 Aug 27. doi: 10.1111/papr.12348.
- [49] Martin DC, Willis ML, Mullinax LA, Clarke NL, Homburger JA, Berger IH. Pulsed radiofrequency application in the treatment of chronic pain. Pain Pract. 2007;7:31–5.
- [50] Lipov E. Successful use of stellate ganglion block and pulsed radiofrequency in the treatment of posttraumatic stress disorder: a case report. Pain Res Treat. 2010;2010:963948. doi: 10.1155/2010/963948.
- [51] van Eijs F, Stanton-Hicks M, Van Zundert J, Faber CG, Lubenow TR, Mekhail N, van Kleef M, Huygen F. Evidence-based interventional pain medicine according to clinical diagnoses. 16. Complex regional pain syndrome. Pain Pract. 2011;11:70-87. doi: 10.1111/j.1533-2500.2010.00388.x.
- [52] Purtuloğlu T, Deniz S, Atım A, Tekindur Ş, Gürkök S, Kurt E. A new target of percutaneous sympathetic radiofrequency thermocoagulation for treatment of palmar hyperhidrosis: T4. Agri. 2013;25:36-40. doi: 10.5505/agri.2013.09226.
- [53] Purtuloglu T, Atim A, Deniz S, Kavakli K, Sapmaz E, Gurkok S, Kurt E, Turan A. Effect of radiofrequency ablation and comparison with surgical sympathectomy in palmar hyperhidrosis. Eur J Cardiothorac Surg. 2013;43:e151–4. doi: 10.1093/ejcts/ezt024.
- [54] Deniz S, Kavaklı K, Çaylak H, Purtuloğlu T, Sapmaz E, İnangil G, Atım A, Gürkök S, Kurt E. Treatment of compensatory hyperhidrosis of the trunk with radiofrequency ablation. Agri. 2015;27:42-6. doi: 10.5505/agri.2015.37167.
- [55] Raj PP, Thomas J, Heavner J, Racz G, Lou L, Day M, Shaw BC. The development of a technique for radiofrequency lesioning of splanchnic nerves. Curr Rev Pain. 1999;3:377-387.
- [56] Garcea G, Thomasset S, Berry DP, Tordoff S. Percutaneous splanchnic nerve radiofrequency ablation for chronic abdominal pain. ANZ J Surg. 2005;75:640-4.
- [57] Gangi A, Buy X, Garnon J, Tsoumakidou G, Moser T, Bierry G, Muller A. Pain management in oncology. J Radiol. 2011;92:801-13. doi: 10.1016/j.jradio.2011.07.014.
- [58] Verhaegh BP, van Kleef M, Geurts JW, Puylaert M, van Zundert J, Kessels AG, Masclee AA, Keulemans YC. Percutaneous radiofrequency ablation of the splanchnic nerves in

- patients with chronic pancreatitis: results of single and repeated procedures in 11 patients. Pain Pract. 2013;13:621–6. doi: 10.1111/papr.12030.
- [59] Aşik ZS, Orbey BC, Aşik I. Sympathetic radiofrequency neurolysis for unilateral lumbar hyperhidrosis: a case report. Agri. 2008;20:37–9.
- [60] Straube S, Derry S, Moore RA, McQuay HJ. Cervico-thoracic or lumbar sympathectomy for neuropathic pain and complex regional pain syndrome. Cochrane Database Syst Rev. 2010 Jul 7;(7):CD002918. doi: 10.1002/14651858.CD002918.pub2.
- [61] Rigaud J, Delavierre D, Sibert L, Labat JJ. Sympathetic nerve block in the management of chronic pelvic and perineal pain. Prog Urol. 2010;20:1124–31. doi: 10.1016/j.purol. 2010.08.047.
- [62] Zhao WX, Wang Q, He MW, Yang LQ, Wu BS, Ni JX. Radiofrequency thermocoagulation combined with pulsed radiofrequency helps relieve postoperative complications of trigeminal neuralgia. Genet Mol Res. 201513;14:7616–23. doi: 10.4238/2015.July.13.5.
- [63] Ali Eissa AA, Reyad RM, Saleh EG, El-Saman A. The efficacy and safety of combined pulsed and conventional radiofrequency treatment of refractory cases of idiopathic trigeminal neuralgia: a retrospective study. J Anesth. 2015;29:728-33. doi: 10.1007/ s00540-015-2029-5.
- [64] Thapa D, Ahuja V, Dass C, Verma P. Management of refractory trigeminal neuralgia using extended duration pulsed radiofrequency application. Pain Physician. 2015;18:E433-5.
- [65] Fukui S, Nitta K, Iwashita N, Tomie H, Nosaka S, Rohof O. Intradiscal pulsed radiofrequency for chronic lumbar discogenic low back pain: a one year prospective outcome study using discoblock for diagnosis. Pain Physician. 2013;16:E435–42.
- [66] Kapural L, Vrooman B, Sarwar S, Krizanac-Bengez L, Rauck R, Gilmore C, North J, Girgis G, Mekhail N. A randomized, placebo-controlled trial of transdiscal radiofrequency, biacuplasty for treatment of discogenic lower back pain. Pain Med. 2013;14:362–73. doi: 10.1111/pme.12023.
- [67] Hamer JF, Purath TA. Response of cervicogenic headaches and occipital neuralgia to radiofrequency ablation of the C2 dorsal root ganglion and/or third occipital nerve. Headache. 2014;54:500-10. doi: 10.1111/head.12295.
- [68] Cohen SP, Peterlin BL, Fulton L, Neely ET, Kurihara C, Gupta A, Mali J, Fu DC, Jacobs MB, Plunkett AR, Verdun AJ, Stojanovic MP, Hanling S, Constantinescu O, White RL, McLean BC, Pasquina PF, Zhao Z. Randomized, double-blind, comparative-effectiveness study comparing pulsed radiofrequency to steroid injections for occipital neuralgia or migraine with occipital nerve tenderness. Pain. 2015;156:2585-94. doi: 10.1097/ j.pain.0000000000000373.
- [69] Keskinbora K, Aydinli I. Long-term results of suprascapular pulsed radiofrequency in chronic shoulder pain. Agri. 2009;21:16–21.

- [70] Gofeld M, Restrepo-Garces CE, Theodore BR, Faclier G. Pulsed radiofrequency of suprascapular nerve for chronic shoulder pain: a randomized double-blind active placebo-controlled study. Pain Pract. 2013;13:96–103. doi: 10.1111/j. 1533-2500.2012.00560.x.
- [71] Wu YT, Ho CW, Chen YL, Li TY, Lee KC, Chen LC. Ultrasound-guided pulsed radiofrequency stimulation of the suprascapular nerve for adhesive capsulitis: a prospective, randomized, controlled trial. Anesth Analg. 2014;119:686-92. doi: 10.1213/ ANE.0000000000000354.
- [72] Lippe PM. Neurosurgery-epitomes of progress: percutaneous radiofrequency cervical cordotomy: treatment of chronic intractable pain. West J Med. 1977;127:233–4.
- [73] Raslan AM. Percutaneous computed tomography-guided radiofrequency ablation of upper spinal cord pain pathways for cancer-related pain. Neurosurgery. 2008;62(3 Suppl 1):226–33; discussion 233–4. doi: 10.1227/01.neu.0000317397.16089.f5.
- [74] Fonoff ET, Lopez WO, de Oliveira YS, Teixeira MJ. Microendoscopy-guided percutaneous cordotomy for intractable pain: case series of 24 patients. J Neurosurg. 2015 Jul 31:1-8.
- [75] Hong MJ, Kim YD, Park JK, Hong HJ. Management of pudendal neuralgia using ultrasound-guided pulsed radiofrequency: a report of two cases and discussion of pudendal nerve block techniques. J Anesth. 2015 Dec 23.
- [76] Carvalho JC, Agualusa LM, Moreira LM, Costa JC. Multimodal therapeutic approach of vaginismus: an innovative approach through trigger point infiltration and pulsed radiofrequency of the pudendal nerve. Rev Bras Anestesiol. 2015 Nov 30. pii: S0034– 7094(15)00047-1. doi: 10.1016/j.bjan.2014.10.005.
- [77] Chen LC, Ho CW, Sun CH, Lee JT, Li TY, Shih FM, Wu YT. Ultrasound-guided pulsed radiofrequency for carpal tunnel syndrome: a single-blinded randomized controlled study. PLoS One. 2015;10:e0129918. doi: 10.1371/journal.pone.0129918. eCollection 2015.
- [78] Chye CL, Liang CL, Lu K, Chen YW, Liliang PC. Pulsed radiofrequency treatment of articular branches of femoral and obturator nerves for chronic hip pain. Clin Interv Aging. 2015;10:569–74. doi: 10.2147/CIA.S79961. eCollection 2015.
- [79] Gupta M, Gupta P. Ultrasound out of plane approach for pulsed radiofrequency treatment of post herniorrhaphy pain: synchronizing treatment and imaging modality. Saudi J Anaesth. 2015;9:224-5. doi: 10.4103/1658-354X.152897.
- [80] Makharita MY, Amr YM. Pulsed radiofrequency for chronic inguinal neuralgia. Pain Physician. 2015;18:E147-55.
- [81] Ye L, Mei Q, Li M, Gu M, Ai Z, Tang K, Shi D, Wu X, Wang X, Zheng Y. A comparative efficacy evaluation of ultrasound-guided pulsed radiofrequency treatment in the

- gastrocnemius in managing plantar heel pain: a randomized and controlled trial. Pain Med. 2015;16:782–90. doi: 10.1111/pme.12664.
- [82] Rahimzadeh P, Imani F, Faiz SH, Entezary SR, Nasiri AA, Ziaeefard M. Investigation the efficacy of intra-articular prolotherapy with erythropoietin and dextrose and intraarticular pulsed radiofrequency on pain level reduction and range of motion improvement in primary osteoarthritis of knee. J Res Med Sci. 2014;19:696–702.
- [83] Eyigor C, Eyigor S, Akdeniz S, Uyar M. Effects of intra-articular application of pulsed radiofrequency on pain, functioning and quality of life in patients with advanced knee osteoarthritis. J Back Musculoskelet Rehabil. 2015;28:129-34.
- [84] Thapa D, Ahuja V. Combination of diagnostic medial calcaneal nerve block followed by pulsed radiofrequency for plantar fascitis pain: a new modality. Indian J Anaesth. 2014;58:183-5. doi: 10.4103/0019-5049.130824.
- [85] Chon JY, Hahn YJ, Sung CH, Jung SH, Moon HS. Pulsed radiofrequency under ultrasound guidance for the tarsal tunnel syndrome: two case reports. J Anesth. 2014;28:924–7. doi: 10.1007/s00540-014-1831-9.
- [86] Niraj G. Ultrasound-guided pulsed radiofrequency treatment of myofascial pain syndrome: a case series. Br J Anaesth. 2012;109:645-6. doi: 10.1093/bja/aes331.
- [87] Imani F, Gharaei H, Rezvani M. Pulsed radiofrequency of lumbar dorsal root ganglion for chronic postamputation phantom pain. Anesth Pain Med. 2012;1:194-7. doi: 10.5812/kowsar.22287523.3768.
- [88] Choi HJ, Choi SK, Kim TS, Lim YJ. Pulsed radiofrequency neuromodulation treatment on the lateral femoral cutaneous nerve for the treatment of meralgia paresthetica. J Korean Neurosurg Soc. 2011;50:151–3. doi: 10.3340/jkns.2011.50.2.151.
- [89] Rehman SU, Khan MZ, Hussain R, Jamshed A. Pulsed radiofrequency modulation for lingual neuralgia. Br J Oral Maxillofac Surg. 2012;50:e4-5. doi: 10.1016/j.bjoms. 2011.06.001.
- [90] Misra S, Ward S, Coker C. Pulsed radiofrequency for chronic testicular pain-a preliminary report. Pain Med. 2009;10:673–8. doi: 10.1111/j.1526-4637.2009.00581.x.

IntechOpen

IntechOpen