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Unlocking the Potential of Radial Shockwave Therapy: Can It Treat Uterine Leiomyoma? A Literature Review Article

Abstract

Background: Uterine leiomyoma is one of the most prevalent benign tumors affecting women of reproductive age. It is one of the common gynecological underlying causes of chronic pelvic pain.

Objective: Recently, there has been increasing interest in minimally invasive and non-invasive treatments for uterine leiomyoma. This article reviews the prevalence, clinical picture, diagnosis, and the available treatment strategies used to manage uterine leiomyomas. Also, it explores the proposed underlying mechanisms and role of the radial extracorporeal shockwave therapy [rESWT] in different soft tissue conditions, and outlines its potential as a promising physical therapy modality for treating uterine leiomyoma.

Methods: A comprehensive search strategy was conducted using the keywords “uterine leiomyoma,” “noninvasive treatment,” “uterine fibroids or leiomyoma,” and “extracorporeal shockwave therapy” on Google Scholar, Cochrane Library, PEDro, Scopus, and PubMed. Data from the identified sources were gathered to compile this review. The sources included clinical trials, as well as systematic and narrative reviews.

Conclusion: Extracorporeal shockwave therapy has demonstrated effectiveness as a non-invasive treatment for various soft tissue disorders. Therefore, it is suggested that rESWT may serve as a viable method for treating the debilitating benign tumor, uterine leiomyoma. Further clinical trials are necessary to confirm the safety and efficacy of this new treatment approach.

Keywords

Benign tumor • Chronic pelvic pain • Physical therapy • Shockwave therapy • Uterine leiomyoma • Uterine fibroids.

Research Article

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Introduction

Uterine leiomyomas, commonly known as fibroids, are the most frequent female pelvic tumor that occurs in up to 70 to 80% of women. [1]. Leiomyomas are non-cancerous tumors of monoclonal origin that develop from the smooth muscle tissue of the uterus [2]. These tumors mainly consist of extracellular matrix [ECM] and cells with a low rate of cell division [3]. They are surrounded by a pseudo capsule made up of areolar tissue [4]. Leiomyomas are estrogen-dependent neoformations that are considered a

significant health problem for women [5].

Although 50% of leiomyomas are asymptomatic [6], they represent the most common indication for hysterectomy in many countries [7]. Also, 40% of all annual hysterectomies performed annually in the USA are due to leiomyomas [8]. The annual cost of uterine leiomyomas in the USA was estimated to range between $5.9 billion and $34.4 billion, which places a significant financial burden on the USA healthcare system [9]. Miserable consequent complications following hysterectomies include uterine adhesions, pelvic prolapse, estrogen deficiency problems and high rate of morbidity and mortality. Alternative non-surgical approaches need to be investigated for uterine leiomyomas treatment. This article reviewed uterine leiomyoma's clinical picture, diagnostic tools, and current treatment strategies include a range of options such as pharmacological therapies, minimally invasive procedures, and surgical interventions. Also, it focused on the application of rESWT on soft tissue diseases as well as benign tumors and search the availability to represent it as an alternative method for uterine fibroid treatment.

Symptoms and Clinical Picture

Uterine leiomyomas can occur as single or multiple growths and can differ in size, location, and blood supply. They are typically classified into three subgroups based on their location: subserosal [extending outside the uterus], intramural [embedded within the uterine muscle], and submucosal [protruding into the uterine cavity] [10].

Recognized risk factors for the development of uterine fibroids include nulliparity, early onset of menarche, frequent menstruation, dysmenorrhea, a family history of fibroids, African ancestry, obesity, and age [with the highest incidence occurring between 40 and 50 years]. Additionally, conditions such as hypertension and diabetes appear to elevate the risk of fibroid formation [11].

These lesions interfere with normal uterine functions, leading to excessive uterine bleeding, anemia, impaired embryo implantation, recurrent pregnancy loss, preterm labor, labor obstruction, pelvic pain, and urinary incontinence. Additionally, they can mimic or obscure malignant tumors [12]. Leiomyomas are also associated with infertility and recurrent miscarriages [13].

Currently, uterine leiomyomas are the most common reason for hysterectomy worldwide, making it the second most frequent surgery for women after cesarean sections [14]. This procedure is associated with significant morbidity and mortality [15,16], contributing to substantial healthcare costs and economic burden on the healthcare system. As a result, women with symptomatic fibroids are increasingly seeking minimally invasive, uterus-preserving treatment options [7].

Histological Appearance

Histologically, uterine leiomyomas are benign tumors in smooth muscle and connective tissue of the myometrium. They mainly contain myocytes and are characterized by excessive deposition of ECM substances, primarily collagen [17].

The fact that uterine leiomyomas are firm, stiff nodular tumors, is recognized by all clinicians and supported by biomechanical studies [18, 19, 20]. ECM proteins, particularly interstitial collagen, are responsible for this firmness property and the mechanical strength of the tissue. The role of the ECM and mechanotransduction in the human uterus is just beginning to be recognized as a crucial signaling factor. The ECM not only surrounds the cells but also influences them through its stiffness, which can either compress or stretch the cells. These mechanical forces are then converted into intracellular chemical signals, depending on factors such as collagen content, cross-linking, hydration, and other ECM components. [21].

Uterine leiomyoma's tissue stiffness has a direct effect on tumor growth by the induction of fibrosis. There are two characteristics of fibrosis: (1) resistance to apoptosis leading to cell persistence and (2) secretion by these cells of collagen and other ECM components, such as proteoglycans, resulting in the abundant disposal of highly cross-linked, disoriented,

and often widely distributed collagen fibrils. By mechanotransduction, the dynamic signaling mechanism by which mechanical forces activate chemical signaling in cells, fibrosis impacts cell growth. Data suggest that uterine fibroids' structurally disordered and abnormally shaped ECM contributes to the development and growth of fibroids. An understanding of the essential role of ECM stiffness in the growth of fibroids may lead to new treatment approaches for this common disease [21].

Diagnosis

To study the natural progression of uterine leiomyomas and evaluate responses to experimental treatments, detailed mapping of these tumors, including their location, size, and characteristics is crucial [22]. Accurate assessment of the size, number, and position of leiomyomas is essential for selecting the most appropriate patients for medical therapy, noninvasive treatments, or surgery. Imaging techniques such as ultrasound, saline-infusion sonography [SIS], and MRI are commonly used to confirm the presence of uterine leiomyomas [23, 24].

Therapeutic Interventions

The treatment of a patient with uterine leiomyomas varies depending on the interpretation and the wishes of the patient. It is usually important to rule out other causes of excessive uterine bleeding, pelvic pressure/pain, and subfertility beforehand. In some instances, treating leiomyomas can lead to surgical complications, making it advisable to leave the fibroids untreated in certain women. Conservative management with analgesics and hematinics is recommended for women with mild leiomyoma symptoms, particularly those nearing menopauses or trying to conceive [25].

Pharmacotherapy

It is mainly aimed at reducing the abnormal uterine bleeding [AUB] caused by leiomyomas. Available medical treatments include anti-fibrinolytic agents, non-steroidal anti-inflammatory drugs [NSAIDs], combination hormonal contraceptives, progesterone-only treatments, selective progesterone-only receptor modulators [SPRMs], and gonadotropin-releasing [GnRH] agonists [26]. The new medical objectives currently under investigation include green tea extract, vitamin D, cabergoline, gestrinone, and somatostatin analogues [27].

GnRH agonists are the most effective drugs for reducing the size of uterine leiomyomas. However, their use is limited due to the risk of bone loss and other anti-estrogenic side effects [28]. Other medications provide only temporary symptom relief, and none offer a definitive cure [29].

Surgical Management

Hysterectomy: Hysterectomy is a definitive treatment for women with symptomatic leiomyomas who do not wish to preserve fertility, offering complete symptom relief and an improved quality of life. Although it is the most effective option for treating symptomatic uterine leiomyomas [30], it carries significant risks of post-operative complications and has an elevated rate of morbidity and mortality.

Myomectomy: Hysteroscopic myomectomy is the preferred surgical technique for women with submucosal leiomyomas who wish to preserve their uterus or fertility. It is considered the best option for submucosal fibroids smaller than 3 cm, especially when more than 50% of the tumor is located within the uterine cavity [31]. After myomectomy, 90% of women experience postoperative adhesions, which are more common than other complications such as fever, pain, or anemia. Leiomyoma's recurrence occurs in approximately 5-67% of cases, with 3-23% of women requiring further surgery [28].

Laparoscopic radiofrequency volumetric thermal ablation: Radiofrequency volumetric thermal ablation [RFVTA] is a minimally invasive laparoscopic procedure performed on an outpatient basis under ultrasound guidance. It involves the use of an electro-surgical probe, which is inserted into the leiomyoma to induce coagulative myolysis, effectively shrinking its tissue. [32]. In addition to the morbidity and mortality associated with these procedures, many treatment options can potentially impair or reduce

future fertility [33]. Consequently, novel nonsurgical alternatives for treating uterine leiomyomas are being actively investigated. [34].

Minimal Invasive Treatment Options for Uterine Leiomyomas

Although leiomyomas negatively affect women's health, few conservative treatment options are available to women with symptomatic uterine leiomyomas [35]. Surgery, in the form of myomectomy or hysterectomy, is currently the primary treatment for uterine fibroids [36], with uterine artery embolization and focused ultrasound ablation as emerging, less-invasive options [37].

Uterine artery embolization: Uterine artery embolization [UAE] is a viable alternative for patients who wish to preserve their uterus or avoid surgery due to medical comorbidities or personal preference [6]. This interventional radiology procedure involves the insertion of occluding agents into one or both uterine arteries, cutting off blood supply to the uterus and fibroids [38]. Although UAE typically results in shorter hospital stays compared to surgical options, it is associated with common complications, such as post-embolization syndrome, fever, pain, and higher re-intervention rates [39]. In some cases, an extended hospital stay may be necessary to manage vaginal expulsion of submucosal fibroids. The risk of adhesions is around 14%, the recurrence rate ranges from 10-25%, and 10-32% of patients ultimately require a hysterectomy [40].

Myolysis: Myolysis is a minimally invasive technique designed to remove fibroids using a concentrated energy delivery device, such as heat, LASER, or more recently, magnetic resonance-guided focused ultrasound surgery [MRgFUS] [38].

Magnetic resonance-guided focused radiofrequency ablation: MRgFUS, also known as High-Intensity Focused Ultrasound [HIFU] is an accessible but not widely recognized fibroid-specific therapy that uses high-intensity trans-abdominal convergent ultrasound waves to cause leiomyoma coagulated necrosis and regression [41]. HIFU has been associated with reduced morbidity and shorter hospital stays compared to traditional treatments, including surgery, with the added benefit of potentially preserving fertility [42]. However, pregnancy complications such as miscarriage, preterm birth, the need for cesarean section, and placenta previa have been reported following both UAE and MRgFUS procedures [28]. Therefore, it is crucial to explore novel noninvasive treatment options for this common type of benign female tumors.

Extracorporeal Shockwave Therapy

Extracorporeal shock waves [ESW] are single acoustic high-pressure pulses generated by electrohydraulic, electromagnetic, piezoelectric, or ballistic/radial methods [43, 44]. They are extensively used for treating kidney stones [extracorporeal shock wave lithotripsy; ESWL] [45], various conditions of the musculoskeletal system, and soft tissue injuries [46, 47].

Shockwaves are energy-carrying sound waves that can be targeted and directed non-invasively while propagating through a medium to impact a distant specified anatomical region. Shockwaves interact with the targeted deep tissues when applied to an organ and cause mechanical stress and micro-trauma. This stress and micro-trauma [also known as shear stress] cause a cascade of biological reactions [48].

Mechanism of action of ESW

However, the exact mechanism of how radial extracorporeal shockwave therapy [rESWT] affects human tissue is not clear, hypothetically there are four phases of reaction: During the physical phase, shock waves directly cause extracellular cavitation, ionization of molecules, and an increase in cell membrane permeability. In the physicochemical phase, interactions take place between dispersed radicals and biomolecules. This is followed by the chemical phase, where intracellular reactions and molecular changes occur, and ultimately, the biological phase is reached [49].

ESW, in addition to its use in urolithotripsy [extracorporeal shock wave lithotripsy, ESWL], has been shown to yield successful results in treating conditions such as pseudarthrosis, joint disorders, and epicondylitis [50, 51]. It has also proven effective for connective tissue diseases like Dupuytren's contracture, Ledderhose's syndrome, leg ulcers, and other conditions. Both experimental and clinical studies have demonstrated the efficacy of ESWT in treating connective tissue diseases, including fibromatosis [52].

Over the past decade, focused extracorporeal shockwave therapy [fESWT] has been recognized as a viable treatment via the perineal approach, with minimal side effects, leading to significant improvement in symptoms related to chronic pelvic pain syndrome, particularly in voiding conditions [53]. Additionally, the penile approach has been shown to effectively enhance erectile dysfunction [ED] outcomes [54].

[55], treated normal suspended fibroblasts with low- to medium-energy shock waves and evaluated fibroblast viability, growth rate, growth pattern, and gene expression for TGF-β1 and collagen type I, key factors involved in the repair process. The low- to medium-energy shockwave treatment resulted in fewer immediate cytodestructive effects and enhanced subsequent cell proliferation, consistent with findings from [56, 57, 58].

[59] were pioneers in exploring the effects of energy density and the number of applied shockwaves on the viability of normal fibroblast cell suspensions. Their research demonstrated a dose-dependent destructive effect of shockwaves on suspended cells. Specifically, they found that increasing the number of shockwave applications significantly reduced the growth potential of fibroblasts compared to control cells, with a greater number of shockwaves correlating with a more pronounced decline in cell viability. In a subsequent study, [49] further elucidated this relationship, revealing that fibroblast viability was more strongly affected by the number of shockwave applications than by the energy level itself. They also identified an optimal ratio of energy to shockwave applications that minimized cytotoxic effects, highlighting that shockwaves can exert both destructive and stimulatory effects on cell proliferation in a dose-dependent manner. Building on these findings, [60] discussed experimental observations indicating that shockwaves can effectively destroy cells in vitro while also delaying tumor growth in vivo. This prompted further investigation into the underlying mechanisms at play. Beyond cellular experiments, current biological research suggests another promising application of shockwaves related to the mechanical properties of tissues. It is well-established that tumors are generally stiffer than healthy tissues, a characteristic leveraged in breast cancer diagnosis through techniques like palpation and elastography, which detect rigid tissue structures. The mechanical properties of tissues are primarily influenced by the ECM, predominantly composed of collagen. The stiffness of the ECM plays a critical role in promoting cancer initiation and progression by regulating the malignant behaviors of cancer cells [61]. Research indicates that increased deposition of type I collagen significantly alters ECM stiffness, a hallmark feature of tumors. This change not only impacts the mechanical properties of the ECM but also has profound implications for disease progression, as stiffer matrices can facilitate malignant transformations [62]. Interestingly, recent studies emphasize that cells possess mechanoreceptors capable of detecting physical forces and converting them into biochemical signals, thereby enhancing their interaction with the ECM. This mechanotransduction process is essential for understanding how tumors manipulate their microenvironment [63]. These contemporary findings may pave the way for innovative cancer treatment strategies based on mechanical approaches alongside or in place of traditional pharmaceutical therapies.

ESWT is used for various purposes, including antifibrosis, loosening adhesions, and dissipating calcifications. Both experimental and clinical studies have demonstrated its effectiveness in managing pathological scars and capsular

fibrosis by degrading fibrotic tissue. This process is associated with changes in pro-fibrotic and anti-fibrotic proteins, such as transforming growth factor β1 and matrix metalloproteinase 2, respectively [64, 65, 66]. ESWT has been shown to improve myocardial fibrosis following acute myocardial infarction in pigs, which is associated with a reduction in fibrocyte levels [67]. Additionally, [68] found that ESWT is a safe and effective treatment for supportive care and rehabilitation in cancer patients. [69] highlighted rESWT as an effective, safe, and non-invasive treatment for symptomatic benign prostatic hyperplasia in selected patients who have not responded well to medical treatments and are poor candidates for surgery. A novel study by [70], examined the effect of low-intensity rESWT on induced uterine leiomyoma in rats and concluded that low-intensity rESWT with 500 impulses/ session (250 impulses for each uterine horn), energy flux (1bar), and a frequency of 15 HZ can be used to control the growth of uterine leiomyomas in rats. Typically, four sessions were effective for reducing the size of developed leiomyomas and controlling symptoms by softening the firm stiff leiomyomas through mechanical stimulation and degradation of fibrotic tissue.

Methods

A comprehensive search was conducted using the keywords “uterine leiomyoma,” “uterine fibroids or fibromyoma” and “extracorporeal shockwave therapy” on Google Scholar, Cochrane Library, PEDro, Scopus, and PubMed. Data from the identified sources were gathered to compile this review. The sources included clinical trials, as well as systematic and narrative reviews. Additionally, relevant conference proceedings, thesis, and academic-relevant textbooks were consulted during the search strategy.

Research needs

This literature review article discusses the prevalence of uterine leiomyoma, the clinical picture, the diagnosis, and the available treatment strategies. Also, it reported the underlying mechanisms and application of rESWT in an animal model and outlined its potential as a promising physical therapy modality for treating uterine leiomyoma. Based on the lack of human studies investigating the therapeutic effects of ESWT on uterine leiomyoma, we recommend advancing through several stages of development. Initially, the preclinical development stage should focus on clarifying the mode of action of ESWT, investigating potential toxicity, validating its efficacy on various in vitro and in vivo models, and starting to evaluate its formulation. Following successful preclinical results, the clinical stage would involve testing the therapy in human subjects to assess its safety and effectiveness. Finally, the reviewing, approval, and post-market monitoring stage would determine whether ESWT receives approval for clinical use and involve ongoing monitoring of its performance and safety in the clinical settings.

Conclusion

Uterine leiomyomas have negative impacts on women’s fertility and quality of life. This article provides valuable insights into their mechanisms, treatment options, and therapeutic advancements. While existing treatments: medical, surgical, and promising therapies like ESWT show potential, further comprehensive studies are essential to establish the efficacy and safety of the novel non-invasive ESWT before it can be applied to human patients.

Conflict of Interest

The authors declare that they do not have any conflict of interest.

References

1. Rezk, Andrew, Jenna Kahn, and Manvinder Singh. “Fertility sparing management in uterine fibroids.” (2021).

2. Stewart, Elizabeth A., Shannon K. Laughlin-Tommaso, William H. Catherino and Sujata Lalitkumar, Devashana Gupta, et al. “Uterine

fibroids." Nature reviews Disease primers 2, (2016): 1-18.

3. Ghosh, Srirupa, Joel Naftalin, Rachel Imrie, and Wee-Liak Hoo. "Natural history of uterine fibroids: a radiological perspective." Current obstetrics and gynecology reports 7 (2018): 117-121.

4. Holdsworth-Carson, Sarah J., Marina Zaitseva, Beverley J. Vollenhoven, and Peter AW Rogers. "Clonality of smooth muscle and fibroblast cell populations isolated from human fibroid and myometrial tissues." Molecular human reproduction 20, (2014): 250-259.

5. Laughlin, Shannon K., Jane C. Schroeder, and Donna Day Baird. "New directions in the epidemiology of uterine fibroids." In Seminars in reproductive medicine, 28 (2010). 204-217.

6. Vilos, George A., Catherine Allaire, Philippe-Yves Laberge and Nicholas Leyland, et al. "The management of uterine leiomyomas." Journal of Obstetrics and Gynaecology Canada 37 (2015): 157-178.

7. Taheri, Melody, Laura Galo, Callum Potts, Khaled Sakhel, et al. "Nonresective Treatments for Uterine Fibroids: A Systematic Review of Uterine and Fibroid Volume Reductions." Int. J. Hyperthermia 36 (2019): 294–300.

8. Farquhar, CM, and CA Steiner. "Hysterectomy Rates in the United States 1990-1997." Obstet. Gynecol. 99 (2002): 229–234.

9. Cardozo, ER, AD Clark, NK Banks, et al. "The Estimated Annual Cost of Uterine Leiomyomata in the United States." Am. J. Obstet. Gynecol. 206 (2012): 211.e1.

10. Munro, MG, HO Critchley, MS Broder, et al. "The FIGO Classification System ('PALM-COEIN') for Causes of Abnormal Uterine Bleeding in Non-Gravid Women in the Reproductive Years, Including Guidelines for Clinical Investigation." Int. J. Gynaecol. Obstet. 113 (2011): 3–13.

11. Flake, GP, J Andersen, and D Dixon. "Etiology and Pathophysiology of Uterine Leiomyomas: A Review." Environ. Health Perspect. 111 (2003): 1037–1054.

12. Catherino, WH, E Parrott, and J Segars. "Proceedings from the National Institute of Child Health and Human Development Conference on the Uterine Fibroid Research Update Workshop." Fertil. Steril. 95 (2011): 9–12.

13. Whynott, RM, KCC Vaught, and JH Segars. "The Effect of Uterine Fibroids on Infertility: A Systematic Review." Semin. Reprod. Med. 35 (2017): 523–532.

14. Canadian Institute for Health Information, Statistics Canada. Health Indicators. Ottawa: CIHI, 2010.

15. Boyd, LR, AP Novesky, and JP Curtin. "Effect of Surgical Volume on the Route of Hysterectomy and Short-Term Morbidity." Obstet. Gynecol. 116 (2010): 909–915.

16. Clark-Pearson, DL, and EL Geller. "Complications of Hysterectomy." Obstet. Gynecol. 121 (2013): 654–673.

17. Dolmans, MM, F Petraglia, WH Catherino, et al. “Pathogenesis of Uterine Fibroids: Current Understanding and Future Directions.” Fert. Steril. (2024).

18. Rogers, R, J Norian, M Malik, et al. “Mechanical Homeostasis Is Altered in Uterine Leiomyoma.” Am. J. Obstet. Gynecol. 198 (2008): 474.e1–474.e11.

19. Norian, JM, CM Owen, J Taboas, et al. “Characterization of Tissue Biomechanics and Mechanical Signaling in Uterine Leiomyoma.” Matrix Biol. 31 (2012): 57–65.

20. Jayes, FL, X Ma, EM Flannery, et al. “Biomechanical Evaluation of Human Uterine Fibroids after Exposure to Purified Clostridial Collagenase.” Soc. Study Reprod. (2013).

21. Leppert, PC, FL Jayes, and JH Segars. “The Extracellular Matrix Contributes to Mechanotransduction in Uterine Fibroids.” Obstet. Gynecol. Int. (2014): 783289.

22. Somigliana, E, P Vercellini, R Daguati, et al. “Fibroids and Female Reproduction: A Critical Analysis of the Evidence.” Hum. Reprod. Update 13 (2007): 465–476.

23. Parker, WH. “Etiology, Symptomatology, and Diagnosis of Uterine Myomas.” Fertil. Steril. 87 (2007): 725–736.

24. Kumar, K, S Pajai, GR Baidya, et al. “Utility of Saline Infusion Sonohysterography in Gynecology: A Review Article.” Cureus 15 (2023).

25. Simms-Stewart, D, and H Fletcher. “Counseling Patients with Uterine Fibroids: A Review of the Management and Complications.” Obstet. Gynecol. Int. (2012): 539365.

26. Donnez, J, and MM Dolmans. “Uterine Fibroids Management: From the Present to the Future.” Hum. Reprod. Update 22 (2016): 665–686.

27. Sohn, GS, S Cho, YM Kim, et al. “Current Medical Treatment of Uterine Fibroids.” Obstet. Gynecol. Sci. 61 (2018): 192–201.

28. Nezhat, C, BE Paka, C Nezhat, et al. Video-Assisted Laparoscopic Treatment of Endometriosis. In Nezhat’s Video-Assisted and Robotic-Assisted Laparoscopy and Hysteroscopy. New York: Cambridge University Press, 2013.

29. Nezhat, C, N Vang, M Vu, et al. “A Novel Approach for Treatment of Uterine Fibroids: Stereotactic Radiosurgery as a Proposed Treatment Modality.” Curr. Obstet. Gynecol. Rep. 9 (2020): 1–6.

30. Aarts, JW, TE Nieboer, N Johnson, et al. “Surgical Approach to Hysterectomy for Benign Gynecological Disease.” Cochrane Database Syst. Rev. (2015): CD003677.

31. Camanni, M, L Bonino, EM Delpiano, et al. “Hysteroscopic Management of Large Symptomatic Submucous Uterine Myomas.” J. Minim. Invasive Gynecol. 17 (2010): 59–65.

32. Havryliuk, Y, R Setton, JJ Carlow, et al. “Symptomatic Fibroid Management: Systematic Review of the Literature.” JSLS 21 (2017):

e2017.00041.

33. Al-Hendy, A, and S Salama. “Gene Therapy and Uterine Leiomyoma: A Review.” Hum. Reprod. Update 12 (2006): 385–400.

34. Al-Hendy, A, and M Badr. “Can Vitamin D Reduce the Risk of Uterine Fibroids?” Women’s Health 10 (2014): 353–358.

35. Walker, CL, and EA Stewart. “Uterine Fibroids: The Elephant in the Room.” Science 308 (2005): 1589–1592.

36. Bachmann, G. “Expanding Treatment Options for Women with Symptomatic Uterine Leiomyomas: Timely Medical Breakthroughs.” Fertil. Steril. 85 (2006): 46–47.

37. Stein, K, and C Ascher-Walsh. “A Comprehensive Approach to the Treatment of Uterine Leiomyomata.” Mt. Sinai J. Med. 76 (2009): 546–556.

38. De La Cruz, MS, and EM Buchanan. “Uterine Fibroids: Diagnosis and Treatment.” Am. Fam. Physician 95 (2017): 100–107.

39. Fatima, K, HW Ansari, A Ejaz, et al. “Uterine Artery Embolization versus Myomectomy: A Systematic Review and Meta-Analysis.” SAGE Open Med. 12 (2024): 20503121241236141.

40. Nodler, J, and JH Segars. “Evidence-Based Indications for Treatment of Uterine Fibroids in Gynecology.” In Fibroids, edited by J Segars, 24–35. West Sussex, UK: John Wiley & Sons Ltd., 2013.

41. Lee, BB, and SP Yu. “Radiofrequency Ablation of Uterine Fibroids: A Review.” Curr. Obstet. Gynecol. Rep. 5 (2016): 318–324.

42. Patel, N, K Chaudhari, D Patel, et al. “High-Intensity Focused Ultrasound Ablation of Uterine Fibroids: A Review.” Cureus 15 (2023).

43. Wang, CJ. “Extracorporeal Shockwave Therapy in Musculoskeletal Disorders.” J. Orthop. Surg. Res. 7 (2012): 11.

44. Császár, NB, and C Schmitz. “Extracorporeal Shock Wave Therapy in Musculoskeletal Disorders.” J. Orthop. Surg. Res. 7 (2012): 11.

45. Rassweiler, JJ, et al. “Shock Wave Technology and Application: An Update.” Eur. Urol. 59 (2011): 784–796.

46. Schmitz, C, NB Császár, JD Rompe, et al. “Treatment of Chronic Plantar Fasciopathy with Extracorporeal Shock Waves (Review).” J. Orthop. Surg. Res. 8 (2013): 31.

47. Speed, C. “A Systematic Review of Shockwave Therapies in Soft Tissue Conditions: Focusing on the Evidence.” Br. J. Sports Med. 48 (2014): 1538–1542.

48. Gruenwald, I, B Appel, ND Kitrey, et al. “Shockwave Treatment of Erectile Dysfunction.” Therapeutic Adv. Urol. 5 (2013): 95–99.

49. Frairia, R, and L Berta. “Biological Effects of Extracorporeal Shock Waves on Fibroblasts: A Review.” Muscles Ligaments Tendons J. 1 (2012): 138–147.

50. Metzner, G, C Dohnalek, and E Aigner. “High-Energy Extracorporeal Shock-Wave Therapy (ESWT) for the Treatment of Chronic Plantar Fasciitis.” Foot Ankle Int. 31 (2010): 790–796.

51. Storheim, K, L Gjersing, K Bstad, et al. “Extracorporeal Shock Wave Therapy (ESWT) and Radial Extracorporeal Shock Wave Therapy (rESWT) in Chronic Musculoskeletal Pain.” Tidsskr. Nor. Laegeforen. 130 (2010): 2360–2364.

52. Hausdorf, J, B Sievers, M Schmitt-Sody, et al. “Stimulation of Bone Growth Factor Synthesis in Human Osteoblasts and Fibroblasts after Extracorporeal Shock Wave Application.” Arch. Orthop. Trauma Surg. 131 (2010): 303–309.

53. Vahdatpour, B, F Alizadeh, A Moayednia, et al. “Efficacy of Extracorporeal Shock Wave Therapy for the Treatment of Chronic Pelvic Pain Syndrome: A Randomized, Controlled Trial.” ISRN Urology (2013): 972601.

54. Abu-Ghanem, Y, ND Kitrey, I Gruenwald, et al. “Penile Low-Intensity Shock Wave Therapy: A Promising Novel Modality for Erectile Dysfunction.” Korean J. Urol. 55 (2014): 295–299.

55. Berta, L, A Fazzari, AM Ficco, et al. “Extracorporeal Shock Waves Enhance Normal Fibroblast Proliferation in Vitro and Activate mRNA Expression for TGF-β1 and for Collagen Types I and III.” Acta Orthop. 80 (2009): 612–617.

56. Wang, FS, CJ Wang, HJ Huang, et al. “Physical Shock Wave Mediates Membrane Hyperpolarization and Ras Activation for Osteogenesis in Human Bone Marrow Stromal Cells.” Biochem. Biophys. Res. Commun. 287 (2001): 648–655.

57. Wang, FS, KD Yang, RF Chen, et al. “Extracorporeal Shock Wave Promotes Growth and Differentiation of Bone-Marrow Stromal Cells Towards Osteoprogenitors Associated with Induction of TGF-β1.” J. Bone Joint Surg. Br. 84 (2002): 457–461.

58. Martini, L, M Fini, G Giavaresi, et al. “Primary Osteoblasts Response to Shock Wave Therapy Using Different Parameters.” Artif. Cells Blood Substit. Immobil. Biotechnol. 31 (2003): 449–466.

59. Johannes, EJ, DM Kaulesar Sukul, and E Matura. “High-Energy Shock Waves for the Treatment of Nonunions: An Experiment on Dogs.” J. Surg. Res. 57 (1994): 246–252.

60. Steinhauser, MO. “On the Destruction of Cancer Cells Using Laser-Induced Shock Waves: A Review on Experiments and Multiscale Computer Simulations.” Radiol. Open J. 1(2016): 60–75.

61. Mai, Z, Y Lin, P Lin, et al. “Modulating Extracellular Matrix Stiffness: A Strategic Approach to Boost Cancer Immunotherapy.” Cell Death Dis. 15(2024): 307.

62. Wullkopf, L, AKV West, N Leijnse, et al. “Cancer Cells’ Ability to Mechanically Adjust to Extracellular Matrix Stiffness Correlates with

Their Invasive Potential." Mol. Biol. Cell 29 (2018): 2378–2385.

63. Sun, B. "The Mechanics of Fibrillar Collagen Extracellular Matrix." Cell Rep. Phys. Sci. 2 (2021): 183.

64. 64. Fioramonti, P, E Cigna, MG Onesti, et al. "Extracorporeal Shock Wave Therapy for the Management of Burn Scars." Dermatol. Surg. 38(2012): 778–782.

65. Heine, N, L Prantl, and M Eisenmann-Klein. "Extracorporeal Shock Wave Treatment of Capsular Fibrosis After Mammary Augmentation – Preliminary Results." J. Cosmet. Laser Ther. 15(2013): 330–333.

66. Fischer, S, W Mueller, M Schulte, et al. "Multiple Extracorporeal Shock Wave Therapy Degrades Capsular Fibrosis After Insertion of Silicone Implants." Ultrasound Med. Biol. 41(2015): 781–789.

67. 67. Lei, PP, SM Tao, Q Shuai, et al. "Extracorporeal Cardiac Shock Wave Therapy Ameliorates Myocardial Fibrosis by Decreasing the Amount of Fibrocytes After Acute Myocardial Infarction in Pigs." Coron. Artery Dis. 24 (2013): 509–515.

68. Crevenna, R, M Mickel, and M Keilani. "Extracorporeal Shock Wave Therapy in the Supportive Care and Rehabilitation of Cancer Patients." Support Care Cancer 27 (2019): 4039–4041.

69. Zhang, D, YL Wang, DX Gong, et al. "Radial Extracorporeal Shock Wave Therapy as a Novel Agent for Benign Prostatic Hyperplasia Refractory to Current Medical Therapy." Am. J. Mens Health 13 (2019): 1557988319831899.

70. Mamoon, RS, AS Mawas, AM Youssef, et al. "Therapeutic Modality of Induced Uterine Leiomyoma with Shock Waves in Rats: The Uterine Blood Flow, Circulating Ovarian Hormones and Histopathological Findings." Reprod. Biol. 21 (2021):100501.

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