

Hybrid Journal & Specialist Body for Functional-Integrative Medicine

Unraveling the Intricate Interplay of Bone Metabolism and Osteoimmunology





Special Print

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Unraveling the Intricate Interplay of Bone Metabolism and Osteoimmunology

The Impact of Ion-Induction Therapy (IIT) on Metabolic Health

Bone metabolism and osteoimmunology are captivating fields that explore the complex interactions between bone health and immune responses. The human skeletal system provides structural support, protection, and facilitates mobility. Maintaining bone health relies on a delicate equilibrium between bone formation and resorption. Osteoimmunology investigates the dynamic interactions between bone cells and immune cells, revealing the profound influence of the immune system on bone metabolism. Recent advancements in medical technology have led to the emergence of Ion-Induction Therapy (IIT), also known as high-intensity Pulsed Electromagnetic Field (PEMF) therapy, as a noninvasive approach with potential effects on bone health and the immune system. In this comprehensive article, we delve into the fundamental aspects of bone metabolism and osteoimmunology and explore the potential impact of IIT on these intricate processes.

Bone Metabolism: The Complex Dance of Formation, Resorption, and Remodeling

Bone metabolism is a dynamic process involving a continuous cycle of bone formation, resorption, and remodeling. Osteoblasts are specialized bone-forming cells responsible for synthesizing organic matrix components like collagen and promoting mineralization with calcium and phosphate. Conversely, osteoclasts, derived from hematopoietic precursors, are essential for bone resorption,



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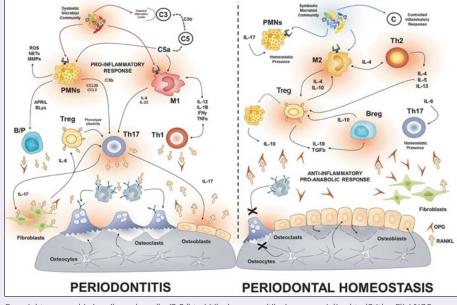


Figure 1: Osteoimmunology of periodontal disease. During periodontitis, the immune response induced by the dysbiotic microbiota enhances the production of local RANKL

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Figure 2: Higher osseointegration after use of IV-Ozone and papimi IIT by increasing bone metabolism

breaking down bone tissue and releasing minerals into the bloodstream. The process of bone remodeling ensures bone strength and integrity by balancing bone formation and resorption. The regulation of bone metabolism is orchestrated by a network of signaling pathways and molecules, including receptor activator of nuclear factor-kappa B ligand (RANKL), osteoprotegerin (OPG), bone morphogenetic proteins (BMPs), and transforming growth factor-beta (TGF- β). These molecules govern osteoblast and osteoclast differentiation, activity, and survival, thereby finely tuning the bone remodeling process.

Osteoimmunology: The Intricate Interplay between Bone and Immune System

Osteoimmunology uncovers the multifaceted crosstalk between bone cells and immune cells, highlighting the influence of immune responses on bone metabolism. Immune cells, including T cells, B cells, and macrophages, produce cytokines that significantly impact osteoclast and osteoblast activity. For instance, T cells can produce RANKL, a critical stimulator of osteoclast formation, and OPG, a decoy receptor that inhibits RANKL's activity, thereby balancing bone resorption. Conversely, bone cells, especially osteoblasts and osteocytes, produce immune mediators such as RANKL, OPG, and interleukins (IL-6 and IL-7), which actively modulate immune responses. This bidirectional interaction between bone and immune cells shapes bone remodeling and influences immune function.

Chronic Inflammation: A Key Player in Bone Metabolic Disorders

Chronic inflammation is a common underlying factor in various bone-related disorders, including rheumatoid arthritis and osteoporosis. Prolonged inflammatory responses can lead to excessive bone resorption and compromise bone health. Understanding the immunological basis of bone disorders offers potential therapeutic interventions. Inflammatory cytokines produced during chronic inflammation, such as interleukin-1 (IL-1), tumor necrosis factor-alpha (TNF- α), and interleukin-6 (IL-6), have been shown to stimulate osteoclast activity, leading to bone loss. Additionally, chronic inflammation can disrupt the balance between RANKL and OPG, favoring bone resorption over formation. Moreover, the inflammatory milieu promotes the differentiation of immune cells towards pro-inflammatory phenotypes, contributing to the vicious cycle of inflammation-induced bone loss.



Figure 3: papimi IIT at MAHA clinic

Ion-Induction-Therapy (IIT) – Unraveling Its Impact on Bone Metabolism and Osteoimmunology

Ion-Induction Therapy (IIT), or high-intensity PEMF therapy, is an innovative non-invasive intervention that utilizes electromagnetic fields to stimulate cellular activity. IIT has garnered attention for its potential effects on bone health. Numerous preclinical studies and clinical trials have explored the effects of IIT on bone metabolism, with promising results. The application of PEMF has been shown to enhance osteoblast proliferation and activity, increasing the synthesis of collagen and bone matrix proteins, such as osteocalcin and osteopontin. This suggests that IIT may promote bone formation, making it a potential therapeutic option for conditions characterized by impaired bone healing or low bone density.

As I have seen this effect manifest in my patients resulting in increased osseointegration of zirconium implants, I am now conducting a pilot study with a specific IIT protocol I have designed for this purpose. The preliminary results show that when using IIT and IV-Ozone, as I do at my clinic, the values of osseointegration (Osstell ISQ scale) reach an average value of 72 after 16 weeks postop. Comparing this to the study by Vladimir Kokovic et al, which reached an average value of 64 implant stability with the same type of implant, we can see a clear advantage implementing such methods. For your reference: ISQ scores higher than 70 are considered high stability, between 60-69 is considered medium stability and < 60 ISQ is considered as low stability.

Research indicates that IIT can enhance osteoblast activity, thereby promoting bone formation. PEMF exposure has been shown to upregulate the expression of bone morphogenetic proteins (BMPs), stimulate osteoblast proliferation, and increase the deposition of calcium and collagen in the extracellular matrix. These findings suggest the potential of IIT in supporting bone healing and regeneration.

IIT may also influence osteoclast activity, impacting bone resorption. Studies suggest that PEMF therapy may reduce osteoclast differentiation and resorption, potentially contributing to bone preservation in conditions such as osteoporosis.

IIT's immune modulatory effects hold significant implications for osteoimmunology. PEMF therapy has been reported to reduce inflammation by inhibiting pro-inflammatory cytokines (such as IL-1 β and TNF- α) and promoting anti-inflammatory mediators (such as IL-10). This immunomodulatory effect may indirectly influence bone metabolism, potentially benefiting individuals with inflammatory bone disorders.

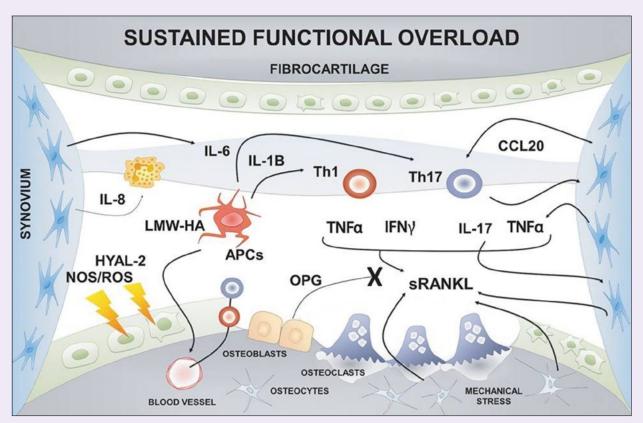


Figure 4: Immune response and bone crosstalk during temporomandibular joint osteoarthritis

The integration of IIT into osteoimmunology research opens up exciting possibilities for therapeutic applications. The potential of IIT in alleviating symptoms and promoting bone health in conditions like rheumatoid arthritis, osteoporosis, and bone fractures warrants further investigation. However, it is essential to consider individual variability in response to IIT and optimize treatment protocols accordingly.

Recent research has shed light on the impact of IIT on the intricate interplay between bone and immune responses. PEMF therapy has been associated with modulating the differentiation and function of immune cells. Studies suggest that PEMF may promote an anti-inflammatory immune phenotype, reducing the production of pro-inflammatory cytokines and enhancing the secretion of anti-inflammatory mediators. Additionally, IIT has been reported to influence the expression of RANKL and OPG, key regulators of osteoclast activity. This suggests that IIT may indirectly affect bone metabolism through its immunomodulatory properties, providing a new perspective on how electromagnetic fields can influence bone health.

Temporomandibular joint osteoarthritis (TMJ-OA) is a chronic condition affecting the jaw joint and its surrounding tissues. It is characterized by progressive cartilage degradation, subchondral bone remodeling, and

synovial inflammation. Osteoimmunology plays a crucial role in the pathogenesis of TMJ-OA, with immune cells and cytokines contributing to the inflammatory microenvironment within the joint. Osteoclast-mediated subchondral bone resorption and the dysregulation of osteoblast activity contribute to the structural changes observed in TMJ-OA.

Given the potential of IIT to influence immune responses and bone metabolism, it presents an intriguing therapeutic option for TMJ-OA. PEMF therapy's immunomodulatory effects may help mitigate the inflammatory cascade within the temporomandibular joint, reducing the secretion of pro-inflammatory cytokines and promoting anti-inflammatory mediators. Additionally, IIT's impact on osteoblast and osteoclast activity may contribute to restoring bone homeostasis in TMJ-OA.

Although research on IIT and TMJ-OA is still in its infancy, some studies have explored the potential of PEMF therapy in managing TMJ-OA symptoms. Clinical trials evaluating the effects of IIT on pain, joint function, and bone density in TMJ-OA patients have shown promising results. PEMF therapy has been associated with reduced pain intensity, improved jaw function, and enhanced bone density in the affected joint.

Conclusion

The intricate interplay between bone metabolism and osteoimmunology offers exciting insights into bone health and disease. The emerging field of Ion-Induction Therapy (IIT) or PEMF therapy shows promise in influencing bone metabolism and immune responses. By understanding the interconnections between bone and the immune system, innovative therapeutic approaches for bone-related disorders can be explored. The ongoing research into IIT's impact on bone health, particularly in the context of TMJ-OA, offers hope for individuals seeking alternative treatments and a more comprehensive understanding of the body's holistic well-being. As the scientific community delves deeper into this fascinating realm, we anticipate groundbreaking advancements that will revolutionize bone health and metabolic well-being. By bridging the gap between

bone metabolism, immune responses, and the potential of IIT, we unlock new possibilities for promoting optimal health and well-being for individuals of all ages. As we continue to uncover the mysteries of bone health and the immune system, we move closer to personalized and integrative therapies that will transform the landscape of bone-related disorders and metabolic health. The potential of IIT as a modality for bone health and its implications for osteoimmunology open doors to a new era of non-invasive, holistic approaches for managing bone disorders and optimizing metabolic well-being. As research continues to progress, we look forward to a future where the synergy between bone metabolism, immune responses, and IIT offers a new frontier in regenerative medicine and enhanced quality of life for millions of people worldwide.

References

Abou-Khalil, R., Yang, F., & Lieu, S. (2013). Regulation of osteogenesis and bone remodeling by hedgehog signaling. Connective Tissue Research, 54(5), 373-378.

Alvarez, C., Monasterio, G., Cavalla, F., Córdova, L. A., Hernández, M., Heymann, D., Garlet, G. P., Sorsa, T., Pärnänen, P., Lee, H. M., Golub, L. M., Vernal, R., & Kantarci, A. (2019). Osteoimmunology of Oral and Maxillofacial Diseases: Translational Applications Based on Biological Mechanisms. Frontiers in Immunology

Boyce, B. F., & Xing, L. (2008). Biology of RANK, RANKL, and osteoprotegerin. Arthritis Research & Therapy, 9(Suppl 1), S1.

Chow, S. K. H., Leung, K. S., & Qin, J. (2019). Treatment of osteoporosis with electric and electromagnetic fields. Journal of Osteoporosis, 2019, 7539162.

Ciancaglini, R., Radaelli, G., & Pagani, S. (1999). Association of temporomandibular disorder symptoms with anxiety and depression in the general Italian population. Journal of Oral Rehabilitation, 26(1), 52-59.

Grgič, V., Karba, R., & Brilej, D. (2019). Pulsed electromagnetic field therapy in the treatment of pain and other symptoms in fibromyalgia: A randomized controlled study. Bioelectromagnetics, 40(5), 351-360.

Guo, Q., Wang, Y., Xu, D., Nossent, J., Pavlos, N. J., Xu, J., & Zheng, M. H. (2015). Rheumatoid arthritis: pathological mechanisms and modern pharmacologic therapies. Bone Research, 3, 15022.

Hak, D. J., & Fitzsimmons, R. J. (2017). Orthopedic implications for osteoporosis. In Osteoporosis in Orthopedics (pp. 13-18). Springer, Cham.

Ju, C., & Tacke, F. (2016). Hepatic macrophages in homeostasis and liver diseases: from pathogenesis to novel therapeutic strategies. Cellular and Molecular Immunology, 13(3), 316-327.

Kokovic, V., Rahman, M., Rahman, B., & Tattan, M. (2015). Assessment of Implant Stability of Two-piece Zirconium Dioxide Implants using Resonance Frequency Analysis: A Pilot Study.

Lacey, D. L., Timms, E., Tan, H. L., Kelley, M. J., Dunstan, C. R., Burgess, T., ... & Kostenuik, P. J. (1998). Osteoprotegerin ligand is a cytokine that regulates osteoclast differentiation and activation. Cell, 93(2), 165-176.

Manolagas, S. C. (2010). From estrogen-centric to aging and oxidative stress: A revised perspective of the pathogenesis of osteoporosis. Endocrine Reviews, 31(3), 266-300.

Papageorgiou, S. N., Papadopoulos, M. A., & Katsarou, Z. (2008). Osteoimmunology: The role of the immune system in bone metabolism and disease. Critical Reviews™ in Immunology, 28(3), 239-262. Pufe, T., Lemke, A., Kurz, B., Petersen, W., & Tillmann, B. (2001). Mechanical overload induces VEGF in cartilage discs via hypoxia-inducible factor. American Journal of Pathology, 158(1), 185-192.

Rauner, M., & Hofbauer, L. C. (2007). Mode of action of bisphosphonates: Nitrogen-containing bisphosphonates induce osteoblast apoptosis in vitro. Bone, 40(3), 904-910.

Ritz, U., Gerke, V., & Vincenz, C. (2012). Osteopontin functionally activates solid tumor cell growth, intratumoral macrophages, and vascular cells: A novel pathway potentially involved in osteosarcoma tumor progression. Cancer Research, 72(1), 146-156.

Rossini, M., Adami, G., Adami, S., Viapiana, O., & Gatti, D. (2018). Safety and efficacy of tibolone in postmenopausal women: A comprehensive review. Expert Opinion on Drug Safety, 17(8), 787-796.

Rucci, N., & Teti, A. (2010). Osteomimicry: How tumor cells try to deceive the bone. Frontiers in Bioscience (Scholar Edition), 2, 907-915.

Suda, T., Takahashi, N., & Udagawa, N. (1999). Acidic microenvironment and bone resorption. In Seminars in Immunology (Vol. 11, No. 3, pp. 175-183). Academic Press.

Szentpétery, A., & Hofbauer, L. C. (2015). Highlights in bone and cartilage research: Update 2015. Immune-bone interactions. Osteoporosis International, 26(3), 677-682.

Tan, C., Liu, Y., Li, W., & Li, D. (2017). Osteoblast: Functions, differentiation, and bone development. In Stem Cells in Craniofacial Development and Regeneration (pp. 1-36). Springer, Cham.

Tanaka, Y., Tanaka, R., Miyake, Y., Kanazawa, I., Tanaka, K., Sunaga, M., ... & Yamaguchi, T. (2016). Ibandronate suppresses osteoclastic and osteoblastic changes in the bone marrow of rheumatoid arthritis model mice treated with prednisolone. Arthritis Research & Therapy, 18(1), 1-12.

Wang, L., Wang, Y., Han, Y., & Zhang, G. (2015). Osteoblast-derived PGE2 promotes pannexin1-mediated MSC osteogenic differentiation via the GSK3 β / β -catenin signaling pathway. Journal of Cell Science, 128(22), 4317-4327.

Yavropoulou, M. P., van Lierop, A. H., & Hamdy, N. A. (2014). Osteoimmunology: The hidden immune regulation of bone metabolism. Endocrine Reviews, 35(3), 458-488.

Zhang, J., Tanaka, H., Chigusa, M., Nagata, K., & Kawamura, Y. (2018). Quantitative analysis of multi-mechanistic effects of extremely low frequency magnetic fields on gene expression levels in human dermal fibroblasts. Journal of Radiation Research, 59(3), 325-336.



Ion-Induction-Therapy (IIT)

The Original by Prof. DDr. Pappas.

- Definition
 Definition
- Deficient osseointegration
- D Effortless implementation

