IV CONGRESSO NAZIONALE

SOCIETÀ ITALIANA
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PER LA GESTIONE UNIFICATA E INTERDISCIPLINARE
DEL DOLORE MUSCOLO-SCHELETRICO E DELL'ALGODISTROFIA

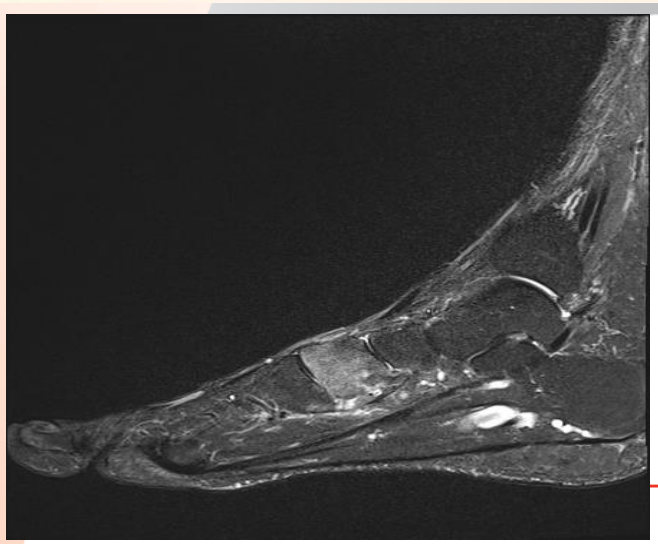
Centro Congressi Unione Industriali

TORINO 11-13 MAGGIO 2023

STEFANO FARINA

U.O. RIABILITAZIONE NEUROMOTORIA

ASST CREMA



Review Article

Bone Marrow Edema, Clinical Significance, and Treatment Options: A Review

Sam Akhavan, MD
Stephen C. Martinkovich, MD
Connor Kasik, DO
Patrick J. DeMeo, MD

Abstract

Bone marrow edema (BME) is a descriptive term used to describe high-signal intensity changes detected on magnetic resonance fluid-sensitive sequences that could be attributed to a number of underlying pathologies. Regardless of the cause, physiologic remodeling of the subchondral bone can be limited because of ongoing joint forces, increased focalization of stress, and reduced healing capacity of the subchondral bone. BME is a known prognostic factor associated with pain, dysfunction, and progressive cartilage damage. This review summarizes the current known causes of BMEs, theories related to histopathological changes, and current treatment options including novel biologic surgical options.

Table 2

Classification of Diseases Associated With Bone Marrow Edema Grouped According to Etiology

Etiology	Etiologies of Bone Marrow Edema
Trauma	Fracture (acute, osteoporotic, and stress) Local transient osteoporosis Bone bruise Osteochondral injuries (osteochondritis dissecans) Altered stress/biomechanics (plantar fasciitis, tendinitis/enthesitis)
Degenerative lesions	Osteoarthritis
Inflammatory lesions	Inflammatory arthropathies and enthesitis (RA, ankylosing spondylitis, psoriasis) Systemic chronic inflammation
Vascular lesions	Osteonecrosis, CRPS-1 CRPS-1 Sickle cell anemia
Infectious lesions	Osteomyelitis, diabetic foot Charcot foot Sepsis (bone infarcts)
Metabolic/endocrine lesions	Hydroxyapatite deposition disease Gout
Iatrogenic lesions	Local surgery Radiation therapy
Neoplastic lesions	Neoplastic bone or soft-tissue lesions or neoplastic-like lesions

CRPS = chronic regional pain syndrome, RA = rheumatoid arthritis. See Starr et al[8] and Eriksen et al.[1]

CURRENT CONCEPTS REVIEW

Bone Marrow Edema

Overview of Etiology and Treatment Strategies

Umberto Tarantino, MD, Chiara Greggi, PhD, Ida Cariati, PhD, Patrizio Caldora, MD, Rodolfo Capanna, MD, Antonio Capone, MD, Roberto Civinini, MD, Stefano Colagrande, MD, Pietro De Biase, MD, Francesco Falez, MD, Giovanni Iolascon, MD, Davide Maraghelli, MD, Laura Masi, MD, Marco Matucci Cerinic, MD, Giuseppe Sessa, MD, and Maria L. Brandi, MD

increased intraosseous pressure with irritation or disruption of sensory nerves within the bone marrow, venous hypertension, raised focal bone turnover with or without microfractures, and irritation of the periosteum and periarticular structures could all be possible mechanisms[4,9].

TABLE II Schematic Representation of the Etiological Classification of Proximal Femoral BME*

Classification	Characteristics	Studies
Reversible		
TBMES	• Caused by a local ischemic episode • Hip pain • Decreased range of motion • Limping gait	Berger et al.[12] (2003), Trevisan et al.[13] (2002), James et al.[30] (2008), Bilgici et al.[38] (2010), and Geith et al.[39] (2017)
RMES	• Spontaneous development or caused by a minor trauma • Clinical presentation like TBMES	James et al.[30] (2008), Balakrishnan et al.[41] (2003), Korompilias et al.[42] (2008), and Ergun and Lakadamyali[43] (2008)
Progressive		
ONFH	• Idiopathic or secondary ischemic lesion • Clinical presentation like TBMES and RMES • Hip pain and joint degeneration	Fernandez-Canton[45] (2009), Moya-Angeler et al.[46] (2015), and Zeng et al.[47] (2020)
SIF	• Secondary to osteoporosis or osteopenia • Usually, unilateral	Davies et al.[36] (2004), Bangil et al.[56] (1996), and Yamamoto et al.[57] (2001)
OA	• Hip pain • Joint destruction	Boutry et al.[61] (2002) and Watanabe et al.[63] (2002)

*BMES = bone marrow edema syndrome, TBMES = transient BMES, RMES = regional migratory BMES, ONFH = osteonecrosis of the femoral head, SIF = subchondral insufficiency fracture, and OA = osteoarthritis.

frontiers in Physiology

REVIEW
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The Physiology of Bone Pain. How Much Do We Really Know?

Sara Nencini and Jason J. Ivanusic **

Department of Anatomy and Neuroscience, University of Melbourne, Melbourne, VIC, Australia

There are many studies that have reported the existence of sensory neurons that innervate the periosteum and marrow cavity, and it has become clear that most of these have a morphology and molecular phenotype consistent with a role in nociception. However, very little is known of the physiology of these neurons. The periosteum has received greater attention relative to the bone marrow, reflecting the easier access of the periosteum for experimental assessment than the marrow cavity of bone. Electrophysiological recordings of sensory neurons in both the periosteum and the bone marrow have confirmed that they both contain nociceptors likely to provide the CNS with

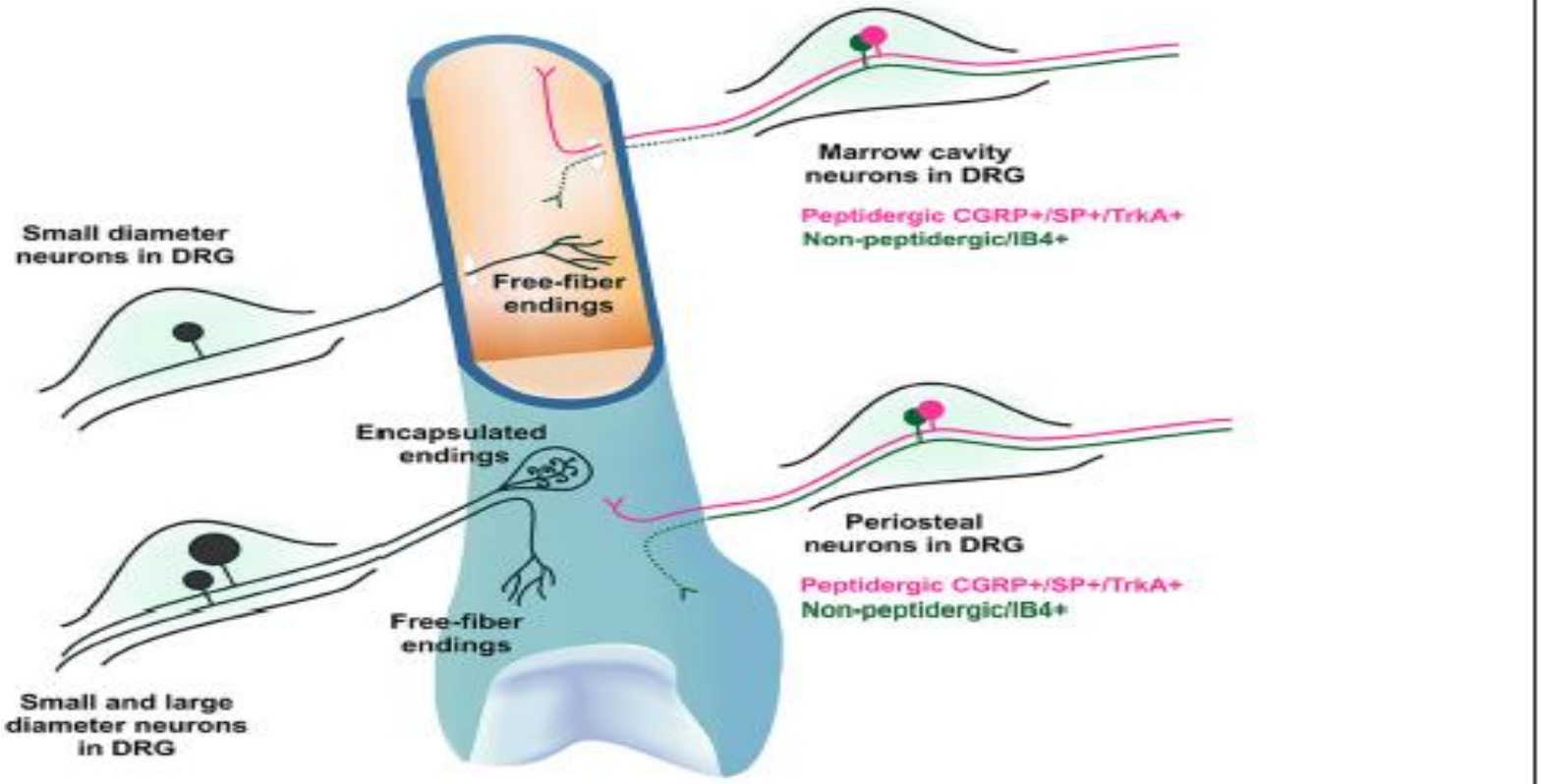

FIGURE 1 | Morphology and molecular phenotype of sensory neurons that innervate bone. The DRG soma of primary afferent neurons that innervate the bone marrow and periosteum are mostly small diameter myelinated and unmyelinated neurons with free fiber endings, although some larger neurons with encapsulated endings do exist in the periosteum. They express varying combinations of markers characteristic of nociceptive neurons, including calcitonin gene-related peptide (CGRP), substance P (SP) and the tyrosine receptor kinase A (TrkA), and/or bind isolectin B4 (IB4). IB4 binding has not been observed in peripheral nerve terminals (represented by dotted line).

Pergamon

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0306-4522/02 $22.00+0.00

ORIGINS OF SKELETAL PAIN: SENSORY AND SYMPATHETIC INNERVATION OF THE MOUSE FEMUR

D. B. MACH,[a,b] S. D. ROGERS,[a,b] M. C. SABINO,[a,b] N. M. LUGER,[a,b] M. J. SCHWEI,[a,b] J. D POMONIS,[a,b] C. P. KEYSER,[a,b] D. R. CLOHISY,[c] D. J. ADAMS,[d] P. O'LEARY[c] and P. W. MANTYH[a,b]*

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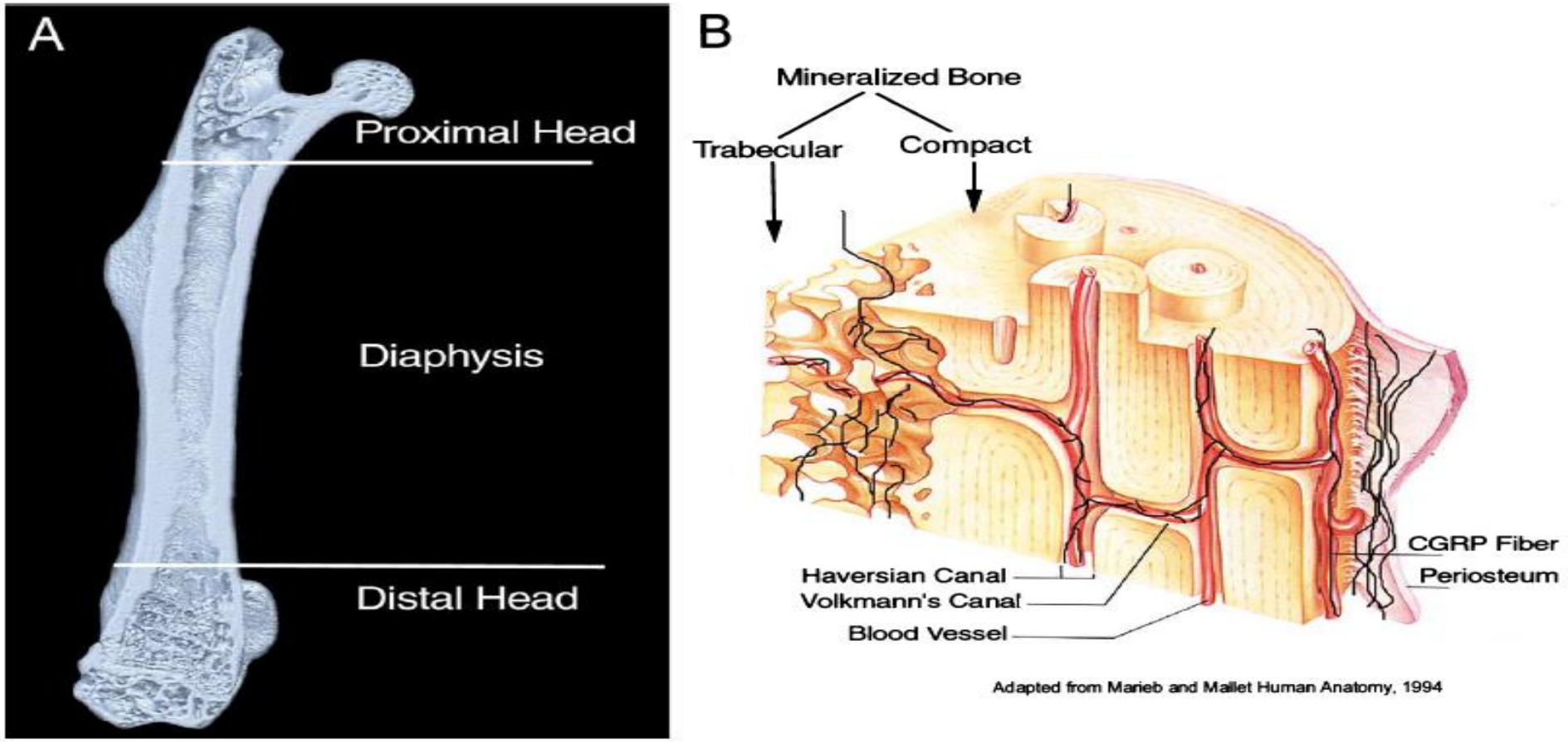

Fig. 1. Micro-computerized tomography scan (A) of the mouse femur with the proximal head, diaphysis and distal head divisions of the bone labeled. The horizontal white lines indicate the three divisions of bone based on the presence of trabeculae in the intramedullary space. A schematic diagram (B) illustrating the general pattern and course of the sensory fibers in periosteum and mineralized bone. Note that of all the tissue types shown, the periosteum receives the densest sensory innervation. However, because the total volume of mineralized bone and bone marrow are greater than periosteum, the total number of sensory and sympathetic fibers is greatest in bone marrow followed by mineralized bone and then the periosteum. The schematic is adapted from Marieb and Mallat, 1997.

ELSEVIER

Bone Vol. 25, No. 6
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ORIGINAL ARTICLES

Evidence for a Dense and Intimate Innervation of the Bone Tissue, Including Glutamate-Containing Fibers

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Neuroscience. 2011 March 31; 178: 196–207. doi:10.1016/j.neuroscience.2011.01.039.

THE MAJORITY OF MYELINATED AND UNMYELINATED SENSORY NERVE FIBERS THAT INNERVATE BONE EXPRESS THE TROPOMYOSIN RECEPTOR KINASE A

Gabriela Castañeda-Corral[1,2], Juan M. Jimenez-Andrade[1], Aaron P. Bloom[1], Reid N. Taylor[1], William G. Mantyh[1], Magdalena J. Kaczmarska[1], Joseph R. Ghilardi[3], and Patrick W. Mantyh[1,3,4]

Research Article

Open Access

Wang Jianchuan, Yang Lei, Wang Benjie, Zhao Dewei*

Study on correlation between bone marrow edema, stage of necrosis and area ratio of necrosis with the hip pain grading in nontraumatic osteonecrosis of the femoral head

In conclusion, we believe that the hip pain grading is positively correlated with the degree of bone marrow edema, necrosis staging and ratio of necrotic area in NONFH patients. Such correlation may be associated with intraosseous pressure and pain factors. Increase in bone

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Journal of Orthopaedic Translation

journal homepage: www.journals.elsevier.com/journal-of-orthopaedic-translation

Perspectives

Guidelines for clinical diagnosis and treatment of osteonecrosis of the femoral head in adults (2019 version)

Dewei Zhao [a,*], Feng Zhang [b], Benjie Wang [a], Baoyi Liu [a], Lu Li [a], Shin-Yoon Kim [c], Stuart B. Goodman [d], Philippe Hernigou [e], Quanjun Cui [f], William C. Lineaweaver [b], Jiake Xu [g], Wolf R. Drescher [h], Ling Qin [i]

Osteonecrosis of the femoral head (ONFH) is a common and refractory disease in orthopaedic clinics. The number of patients with ONFH is increasing worldwide every year. There are an estimated 8.12 million patients with nontraumatic osteonecrosis in China alone. Treatment of nontraumatic osteonecrosis has always been a clinical

Definition: ONFH is a disease in which local death of osteocytes and the component of the bone marrow occurs owing to venous stasis or arterial blood supply damage or interruption in the femoral head; the subsequent repair process attempts to heal the necrotic area, but structural deterioration and collapse of the femoral head causes pain and dysfunction of the hip joint [2,

Table 2
The Steinberg - University of Pennsylvania classification of osteonecrosis [61].

Stage 0	Normal or non-diagnostic radiograph, bone scan, and MRI
Stage I	Normal radiograph; abnormal bone scan and/or MRI
	A Mild <15% of head affected
	B Moderate 15–30%
	C Severe: >30%
Stage II	Lucent and sclerotic changes in femoral head
	A Mild: <15%
	B Moderate: 15–30%
	C Severe: >30%
Stage III	Subchondral collapse (crescent sign) without flattening
	A Mild: < 15% of articular surface
	B Moderate: 15–30%
	C Severe: > 30%
Stage IV	Flattening of femoral head
	A Mild: <15% of surface and <2 mm depression
	B Moderate: 15–30% of surface or 2–4 mm depression
	C Severe: >30% of surface or >4 mm depression
Stage V	Joint narrowing and/or acetabular changes
	A Mild
	B Moderate
	C Severe
	Average of femoral head involvement, as determined in stage IV, and estimated acetabular involvement
Stage VI	Advanced degenerative changes

MRI = magnetic resonance imaging.

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journal homepage: www.elsevier.com/locate/jautimm

The pathogenesis, diagnosis and clinical manifestations of steroid-induced osteonecrosis

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Table 1
Risk factors for osteonecrosis.

Anatomical	Hematologic/oncologic	Iatrogenic	Infectious	Metabolic	Rheumatologic
Congenital hip dislocation	Acute lymphoblastic leukemia	Alcoholism	HIV	Chronic liver disease	Antiphospholipid syndrome
Legg-Calve-Perthes disease	Disseminated intravascular coagulation	Bisphosphonates	Meningococcemia	Diabetes	Mixed connective tissue disease
Slipped capital femoral epiphyses	Hemoglobinopathies	Cigarette smoking	Osteomyelitis	Fabry's disease	Mucocutaneous lymph node syndrome
Trauma	Hemophilia	Corticosteroids		Fat embolism	Necrotizing arteritis
	Hypofibrinolysis	Dysbaric osteonecrosis		Gaucher's disease	Rheumatoid arthritis
	Marrow infiltrative disorders	Radiation therapy		Gout	Systemic lupus erythematosus
	Renal transplant	Regional deep hyperthermia		Hypercholesterolemia	
	Sickle cell anemia			Pancreatitis	
	Thalassemia			Pregnancy	

Patogenesi della ANFH da Steroide

Studio in vitro (culture cellulari) ed in vivo (pulcini) dell'effetto del Cortisone sulle cellule multipotenti del midollo osseo.

Il trattamento delle cellule multipotenti del midollo osseo (linea cellulare D1) con Desametasone ha determinato una differenziazione cellulare verso la linea adipocitica. Il Cortisone stimola e regola il processo di adipogenesi midollare a scapito della differenziazione verso la linea osteoblastica.
La Lovastatina ha dimostrato di prevenire l'Osteoporosi e l'Osteonecrosi nel modello animale di osteonecrosi indotta da Steroide.

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Häußer *et al. Journal of Orthopaedic Surgery and Research* (2021) 16:369
https://doi.org/10.1186/s13018-021-02484-5

Journal of Orthopaedic Surgery and Research

SYSTEMATIC REVIEW Open Access

The use of extracorporeal shock wave therapy for the treatment of bone marrow oedema — a systematic review and meta-analysis

Jonathan Häußer[1*], Juliane Wieber[1,2*] and Philip Catalá-Lehnen[1]

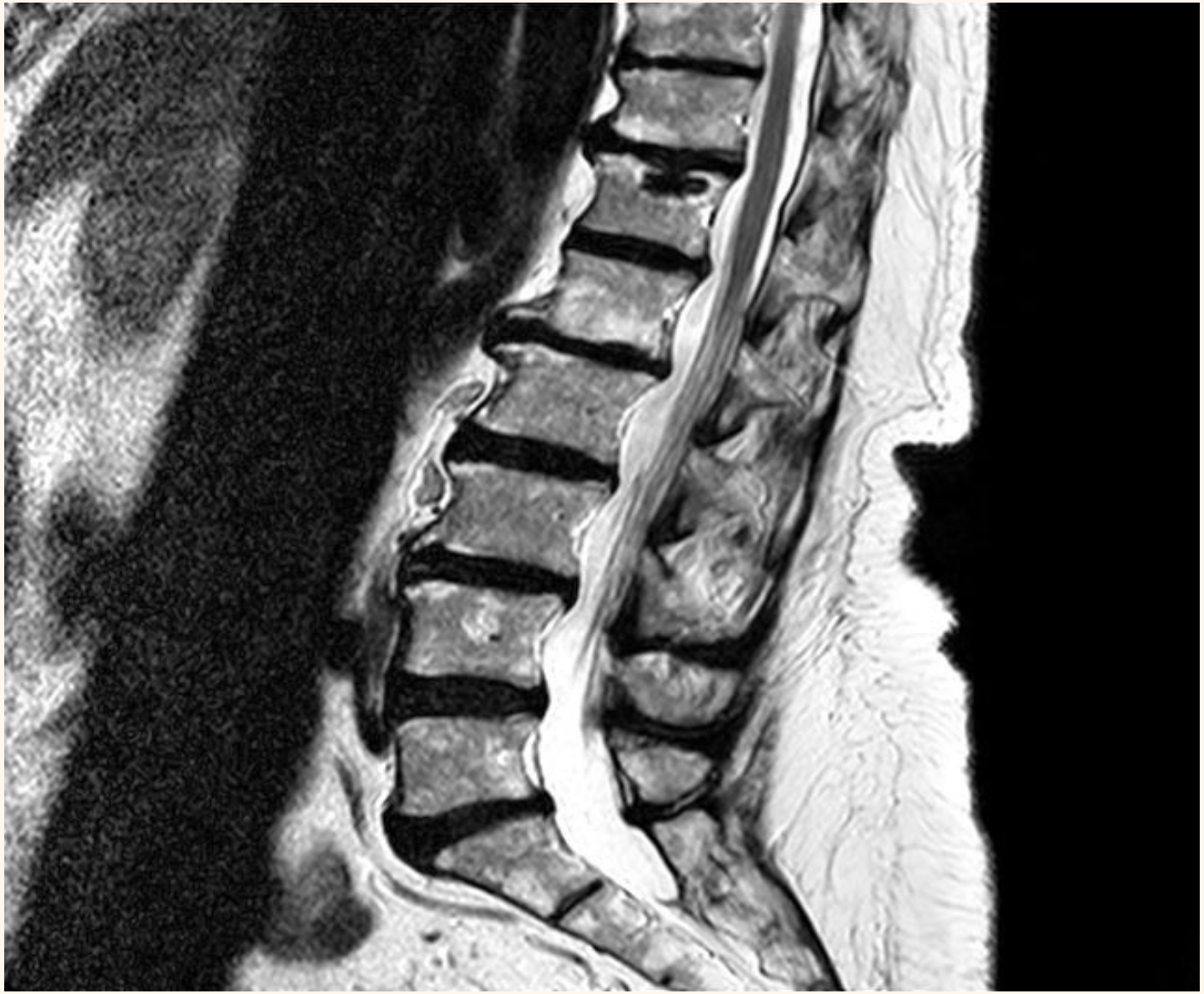
Conclusions: Based on the available evidence, ESWT may be an adequate option for conservative therapy in pathologies involving BME.

Donna di 78 anni alt 170 cm peso 80 kg ottobre 2016-

a.p.p

da 4 mesi :
Dolore lombare irradiato alla regione inguinale e glutea sin – esacerbato dal cammino- migliora a riposo ma e' presente anche nelle ore notturne
Eseguita rmn rachide ls ed esami ematici (funzionalità renale, epatica, indici di flogosi nella norma)

Vas a riposo 3 – durante cammino 8
a.p.r. Intolleranza al lattosio, rettocolite ulcerosa trattata con terapia cortisonica
ad alte dosi per 6 mesi, ora ridotto a Deltacortene 5 mg 1 cp die



Dopo esecuzione rmn inviato all'ambulatorio di terapia antalgica dove ha eseguito 2 infiltrazioni epidurali senza alcun risultato

Terapia farmacologica.
Pregabalin 75 mg 1x2 al giorno
Tachipirina-paracetamolo 1x2

Pantoprazolo 40 mg die
Asacol 1 cp die
Deltacortene 5 mg die

In considerazione della persistenza della sintomatologia viene inviata in visita fisiatrica

Cosa da fare?

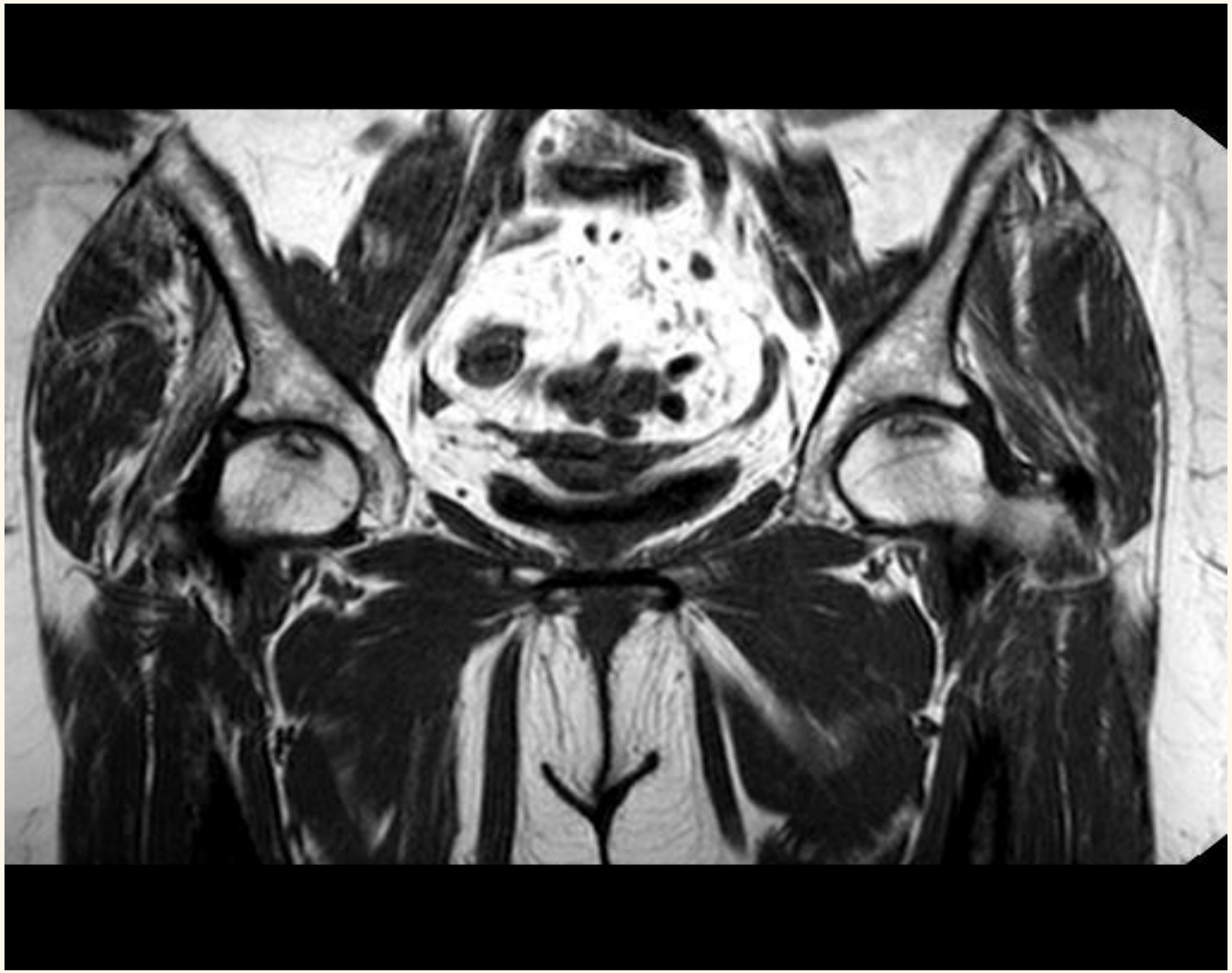
Visitare la paziente!

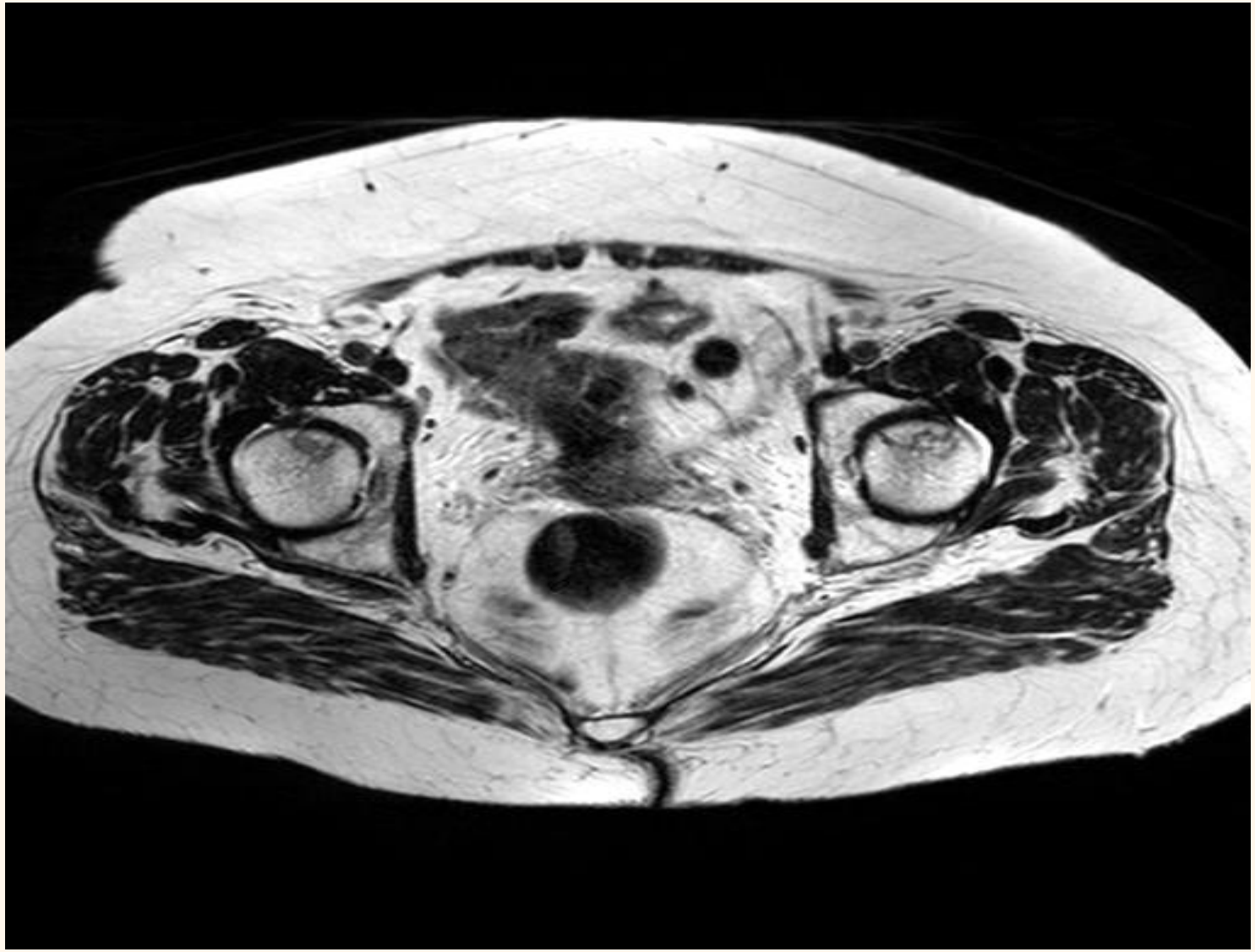
E.O. Dolenzia alla palpazione dei processi spinosi e delle faccette articolari a livello ls e intenso dolore a livello della regione trocanterica di sinistra (VAS 9)

Mobilita' della colonna ridotta in flesso-estensione negli ultimi 30 °
Mobilita' coxofemorale: bilateralmente dolore nel movimento sia attivo che passivo
Bilateralmente limitazione ultimi 20° di abduzione,
Dolore in intra-extrarotazione. Di maggiore gravita' a sinistra (VAS 7-8)
Lasegue debolmente + a 90 °a dx
Sensibilità aaii conservata
Rot evocabili , ipoeccitabili simmetricamente
Forza segmentaria conservata

E ORA? ACCERTAMENTI DIAGNOSTICI?

Scintigrafia ossea
Rx bacino
Tc bacino
Rmn bacino
Altri esami ematici?





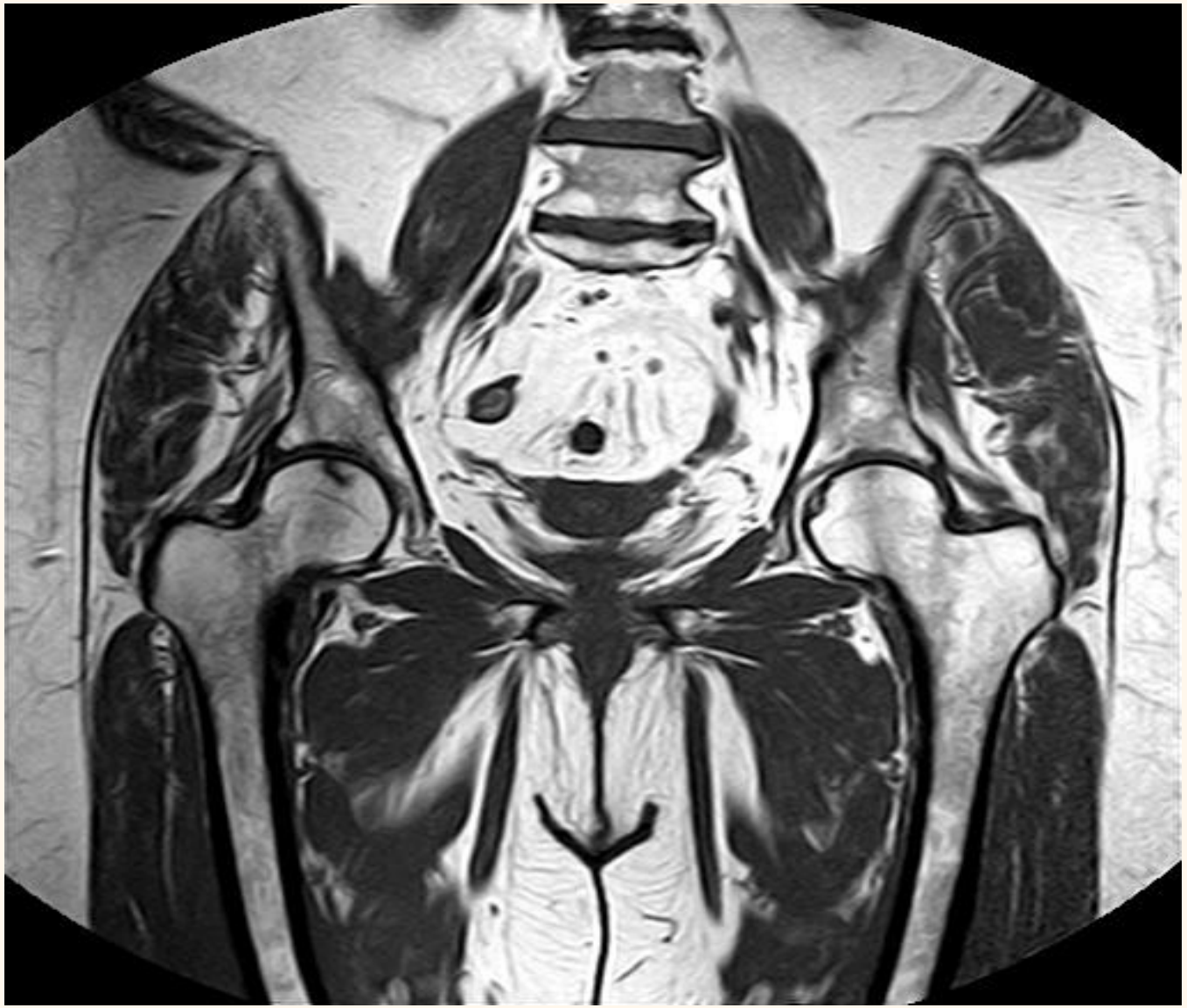
Terapia

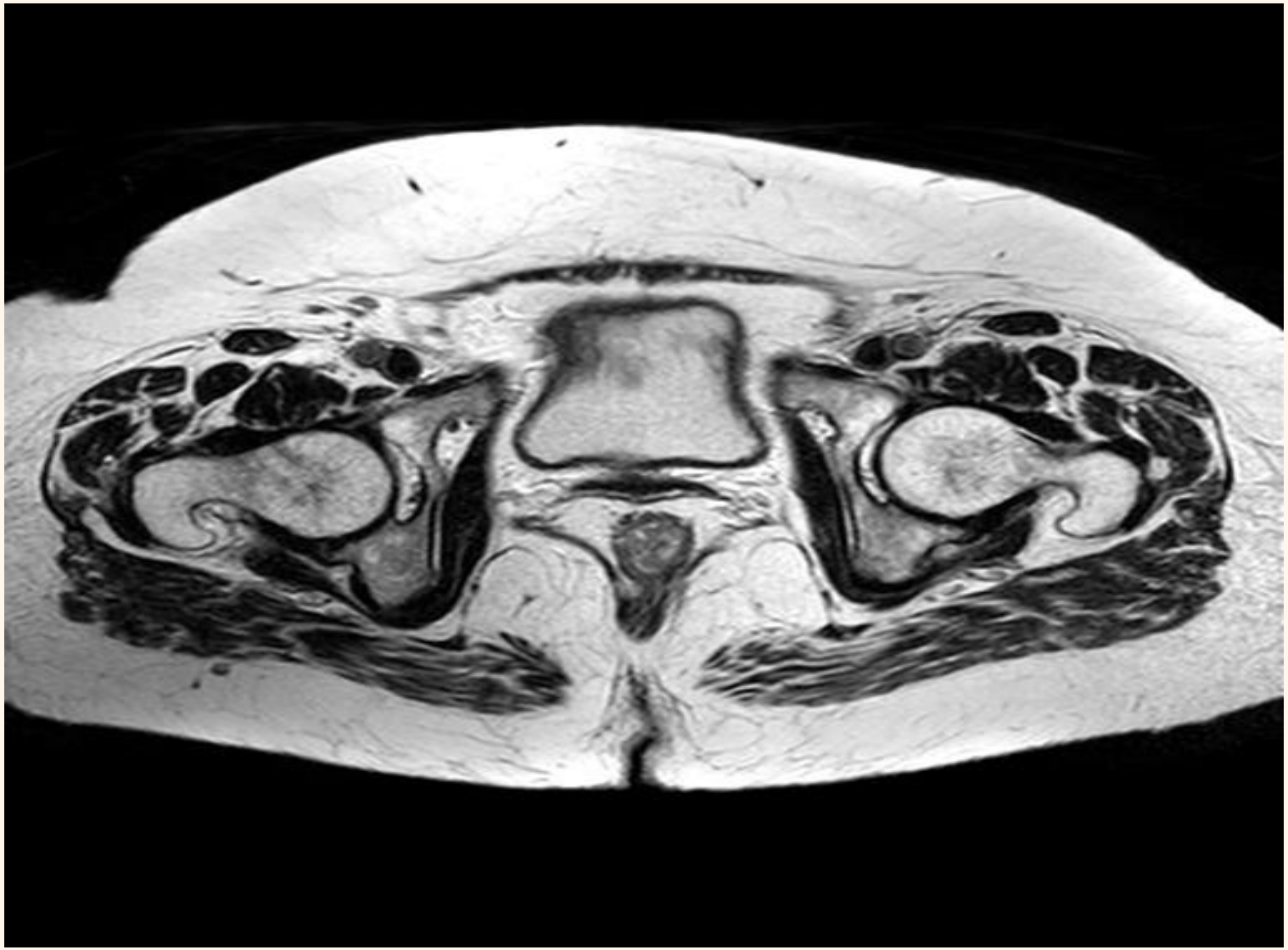
previa esecuzione esami ematourinari per indici di flogosi (nella norma)
metabolismo calcico (vit d3 25 ng /ml)

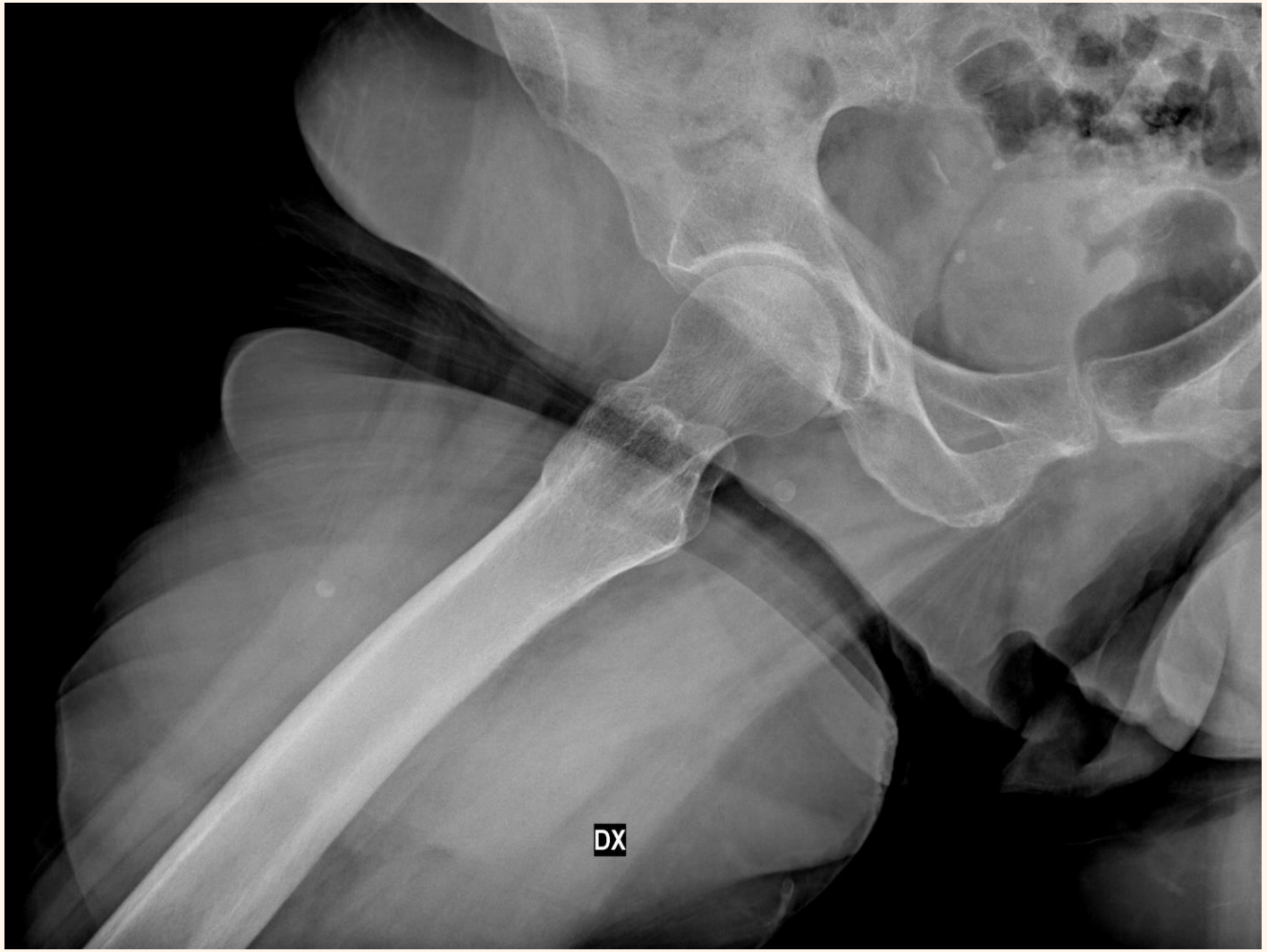
Neridronato 100 mg 1 f in infusione e.v. x 4 sedute in 2 settimane
Calcio carbonato 500 mg 1 cp al giorno dopo pranzo

Colecalciferolo 25000 ui 1 f alla settimana dopo pranzo per 1 mese
quindi 1 f al mese

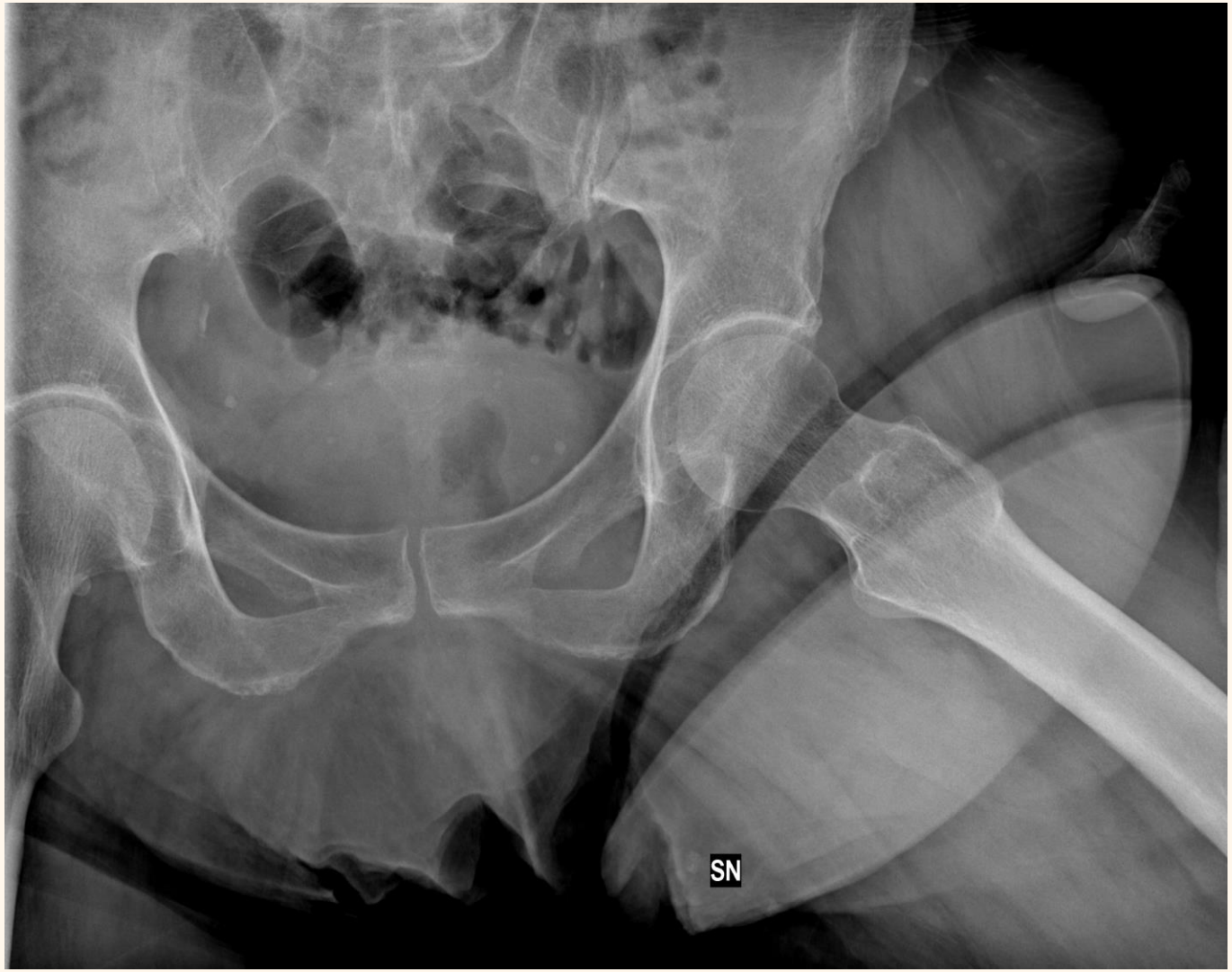
Arto in scarico con bastoni antibrachiali
Magnetoterapia
Chinesiterapia







26 aprile
2023

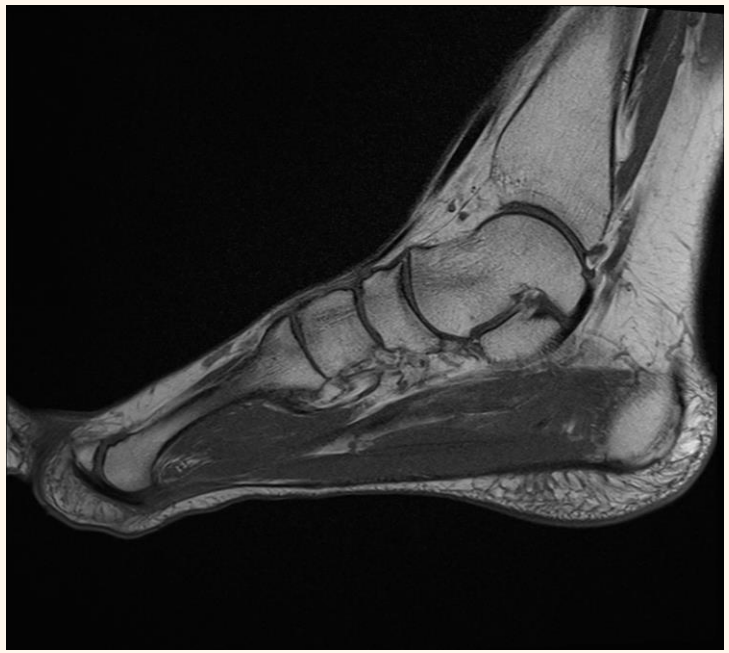


26 aprile 2023

CONCLUSIONI

edema osseo e algodistrofia
dolore , edema osseo e osteoporosi.
edema osseo – necrosi avascolare .

edema vertebrale – bifosfonati ?



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Mini-review

Extra-skeletal effects of bisphosphonates

Argyro Panagiotakou [a], Maria Yavropoulou [b,1], Narjes Nasiri-Ansari [a,1], Polyzois Makras [c], Efthimia K. Basdra [a], Athanasios G. Papavassiliou [a], Eva N. Kassi [a,b,*]

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ABSTRACT

Background: Bisphosphonates (BPs) are pyrophosphate analogues widely used in diseases related to bone loss and increased bone turnover. Their high affinity for bone hydroxyapatite makes them ideal agents for bone diseases, while preventing them from reaching other cells and tissues. Data of the last decade, however, have demonstrated extra-skeletal tissue deposition and a variety of non-skeletal effects have been recently recognized. As such, BPs have been shown to exert anti-tumor, immunomodulatory, anti-inflammatory and anti-diabetic effects.

In addition, new delivery systems (liposomes, nanoparticles, hydrogels) are being developed in an effort to expand BPs clinical application to extra-skeletal tissues and enhance their overall therapeutic spectrum and effectiveness.

In the present review, we outline current data on extra-skeletal actions of bisphosphonates and attempt to unravel the underlying pathophysiological mechanisms.

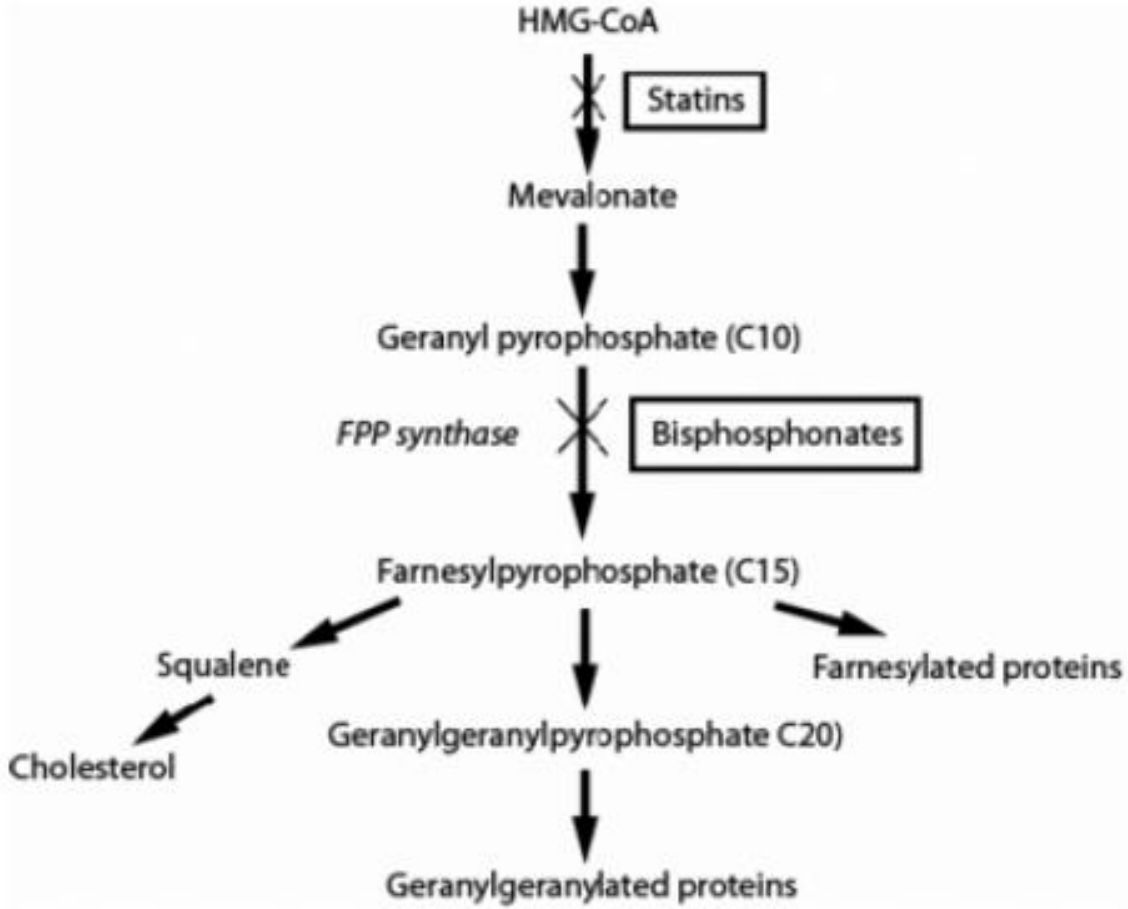

Fig. 7 meccanismo d'azione dei farmaci bifosfonati

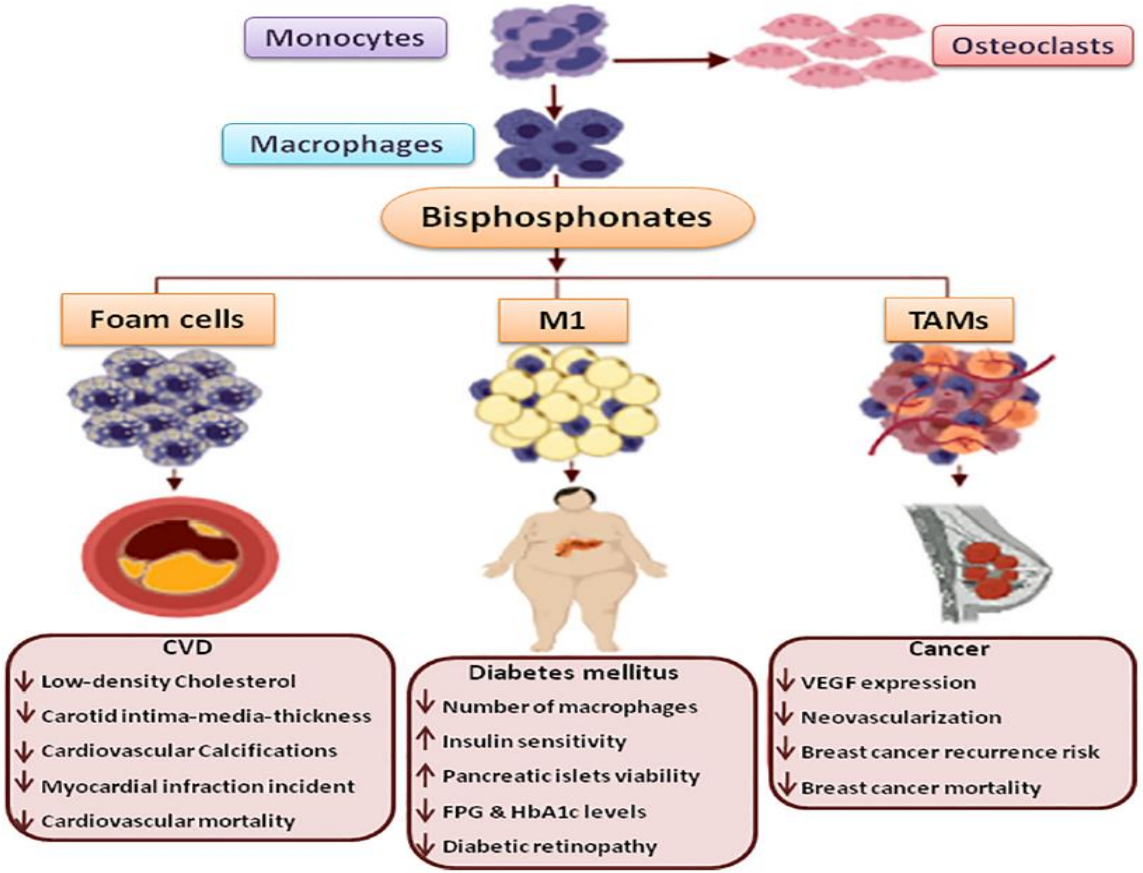

Fig. 2. Upon administration bisphosphonates are taken up by cells with endocytic ability (osteoclasts, monocytes and macrophages). Depleting visceral macrophages bisphosphonates can downregulate inflammation and ameliorate insulin resistance. In atherosclerosis, bisphosphonate can act both in an early stage in the formation of the plaque (depleting macrophages before their transformation to foam cells) and plaque calcification process. In breast cancer, they abate tumor associated macrophages and affect the tumor's micro-environment and neovascularization. However, since bisphosphonates can be integrated and remain for a long period only in calcified tissues, in order to affect non-skeletal macrophages their administration needs to be regularly repeated. The figure was made by using BIORENDER program.